Bursts and Isolated Spikes Code for Opposite Movement Directions in Midbrain Electrosensory Neurons

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Abstract

Directional selectivity, in which neurons respond strongly to an object moving in a given direction but weakly or not at all to the same object moving in the opposite direction, is a crucial computation that is thought to provide a neural correlate of motion perception. However, directional selectivity has been traditionally quantified by using the full spike train, which does not take into account particular action potential patterns. We investigated how different action potential patterns, namely bursts (i.e., packets of action potentials followed by quiescence) and isolated spikes, contribute to movement direction coding in a mathematical model of midbrain electrosensory neurons. We found that bursts and isolated spikes could be selectively elicited when the same object moved in opposite directions. In particular, it was possible to find parameter values for which our model neuron did not display directional selectivity when the full spike train was considered but displayed strong directional selectivity when bursts or isolated spikes were instead considered. Further analysis of our model revealed that an intrinsic burst mechanism based on subthreshold T-type calcium channels was not required to observe parameter regimes for which bursts and isolated spikes code for opposite movement directions. However, this burst mechanism enhanced the range of parameter values for which such regimes were observed. Experimental recordings from midbrain neurons confirmed our modeling prediction that bursts and isolated spikes can indeed code for opposite movement directions. Finally, we quantified the performance of a plausible neural circuit and found that it could respond more or less selectively to isolated spikes for a wide range of parameter values when compared with an interspike interval threshold. Our results thus show for the first time that different action potential patterns can differentially encode movement and that traditional measures of directional selectivity need to be revised in such cases.

Introduction

Motion perception is often required to control animal behavior such as tracking [1–5], postural balance [6–9] and prey capture [10,11]. Directional selectivity, in which neurons respond strongly to an object moving in a given direction (‘preferred’) but respond weakly or not at all when the same object moves in the opposite direction (‘null’), is thought to provide a neural correlate of motion perception [12]. Directionally selective neurons have been found in several species including cats [12], rabbits [13], flies [14], and weakly electric fish [15–18]. Since the discovery of direction selective neurons [12], several models have been proposed to explain how this selectivity emerges in the brain [19–22]. Among these models, so called “Reichardt detectors” have received considerable attention and have been used to describe directional selectivity across several animal species [3,12–14,18,23–29]. These rely on two fundamental operations to generate directional selectivity [30,31]: first, asymmetric filtering of information from at least two separate zones within the receptive field generates a directional bias [13,14,18,27,32,33] and, second, subsequent nonlinear integration of these inputs [13,14,28,29,31,34,35]. Directional selectivity has been traditionally characterized by comparing the maximum firing rate obtained when a given object moves in a given direction to that obtained when the same object moves in the opposite direction. However, this does not take into account particular action potential patterns. Previous studies have shown that, for stationary stimuli, particular action potential patterns such as bursts (i.e., packets of action potential followed by quiescence) as well as isolated spikes could carry information that is qualitatively different than that carried by the full spike train [36–54]. However, whether these action potential patterns carry information about motion direction is poorly understood in general [26,43].

Weakly electric fish sense distortions of their self-generated electric organ discharge (EOD) via an array of electroreceptor neurons on their skin [55,56]. These electroreceptors synapse onto pyramidal cells within the hindbrain electrosensory lateral line lobe (ELL), which in turn project to the midbrain torus semicircularis (TS). It was previously shown that TS but not ELL neurons display directionally selective responses to moving objects [18,35]. The mechanism by which TS neurons generate directionally selective responses has been previously elucidated and is consistent with the Reichardt model. It consists of asymmetric filtering of afferent ELL input across the fish’s body surface that is achieved by different time constants of synaptic depression across the receptive field [18] followed by nonlinear...
introduction of these inputs via subthreshold T-type calcium currents [26,35] (see [53] for review). We have recently found that bursts were more reliable indicators of motion direction than either the full spike or the isolated spike train in TS neurons [26]. These results suggest that isolated spikes actually code for other stimulus features than motion direction. However, a systematic analysis of movement direction coding by bursts and isolated spikes has not been carried out to date.

To address whether isolated spikes can actually code for motion direction, we systematically varied parameters in a previously established model of directional selectivity. Confirming our previous results, we found parameter regimes for which bursts were better indicators of motion direction than either the full spike or the isolated spike trains. However, we also found parameter regimes in which bursts and isolated spikes could both code for movement direction. Specifically, bursts were then preferentially elicited when the object moves in a given direction while isolated spikes were preferentially elicited when the object moves in the opposite direction. Further, our results show that, while the subthreshold T-type calcium conductance was not necessary to observe such regimes, it greatly enhanced the set of parameter values for which they were observed. Experimental recordings from TS neurons confirmed our model’s prediction that bursts and isolated spikes can actually code for opposite movement directions. Finally, we considered a plausible neural circuit that can extract isolated spikes from a spike train and quantified this circuit’s ability to extract the isolated spikes from a spike train consisting of a mixture of bursts and isolated spikes. Our results show for the first time that different action potential patterns in a given neuron can carry information about different movement directions and suggest that differential coding of stimulus attributes by bursts and isolated spikes is a general feature of sensory processing that is applicable to a wide range of stimuli including motion.

Results

Bursts and isolated spikes can code for opposite movement directions

Our biophysical model is based on the Hodgkin-Huxley formalism [57] (see Materials and Methods). The receptive field is modeled in one dimension as two adjacent zones (ON and OFF) that have time constants of depression $\tau_{ON}$ and $\tau_{OFF}$, respectively (Fig. 1A). In this model, the OFF zone represents the output of T-type (i.e. inhibited by increases in the stimulus) ELL pyramidal cells and the ON zone represents the output of E-type (i.e. excited by increases in the stimulus) ELL pyramidal cells as both cell types made excitatory connections onto TS neurons [58]. The summed input from each zone is convolved with an alpha function to mimic the synaptic PSP shape and fed into a Hodgkin-Huxley model with leak, spiking sodium, delayed rectifier potassium, and T-type calcium conductances (Fig. 1A, see Materials and Methods). T-type calcium channels are inactivated at resting membrane potential values (i.e. $\sim -60 \text{ mV}$) and require $\sim 100 \text{ ms}$ hyperpolarisation to $\sim -70 \text{ mV}$ in order to remove their inactivation after which a subsequent depolarisation will lead to a subthreshold calcium spike, leading to nonlinear integration of synaptic input. Moreover, bursts of sodium action potentials can occur on top of these calcium spikes [59,60]. However, a simple depolarization from the resting potential will not lead to burst firing as the calcium channel is still inactivated and will instead lead to isolated spike firing [60]. We mimicked the effect of the massive synaptic bombardment that neurons receive under in vivo conditions [61], by including a noise term that causes membrane potential fluctuations. This noise term can give rise to a mixture of burst and isolated action potential firing as observed for TS neurons under in vivo conditions [26].

The stimulus consists of an object that moves across the receptive field in both directions (see Materials and Methods). Fig. 1B shows the outputs from the ON and OFF zones to this stimulus. When the object moves from left to right (i.e. from the OFF zone to the ON zone), the hyperpolarisation from the OFF zone precedes the depolarisation from the ON zone. However, when the object moves in the opposite direction (i.e. from the ON zone to the OFF zone), the depolarisation from the ON zone is truncated by the hyperpolarisation from the OFF zone (Fig. 1C). The membrane potential responses of the model neuron to these moving stimuli are shown in Fig. 1D. When the object moves from left to right, the hyperpolarisation from the OFF zone removes the inactivation of the calcium conductance and the depolarisation from the ON zone activates this conductance, which tends to result in a burst of action potentials (Fig. 1D, top). In contrast, when the object moves in the opposite direction, the depolarisation from ON zone is not preceded by a hyperpolarisation, and thus tends to elicit isolated action potentials (Fig. 1D, top).

We used an ISI threshold criterion to separate the model’s output spiketrain into bursts and isolated spikes (Fig. 1D, bottom, see Materials and Methods). Specifically, when a given interspike interval was less than the threshold, the two spikes associated with this interspike interval were considered to belong to a burst [41,42,44]. The spikes that were not deemed part of a burst were labelled isolated spikes (Fig. 1D, bottom). We used this criterion to separate the spike train into the burst train (i.e. the train of action potentials that belong to bursts) and the isolated spike train (i.e. the train of action potentials that do not belong to bursts) (see Materials and Methods).

The response of our model to this stimulus is presented in Fig. 2. When we used the full spike train to compute the peri-stimulus time histogram (PSTH), the model displayed a strong response when the object moved in the left to right direction and a weaker response when the object moved in the left to right direction (Figs. 2A and 2B, middle). We quantified this difference using a directional bias (DB) index that ranges between $-1$ and $1$ with 0 implying no directional selectivity (see Materials and Methods). Specifically, DB values of 1 and $-1$ indicate complete direction preference for movement from left to right and from right to left, respectively, while a value of 0 indicates no direction selectivity. We found that this neuron displayed selectivity to the object moving from left to right when using the full spike train (DB = 0.51) (Fig. 2C, purple column).

However, qualitatively different results were obtained when we instead used the burst and isolated spike trains to compute the PSTH from this same neuron. We found that bursts mostly occurred when the object moved from left to right (Fig. 2A arrows; Fig. 2C green column), thereby giving rise to a larger directional bias (DB = 0.72) than that of the full spike train. In contrast, isolated spikes mostly occurred when the object moved from right to left (Fig. 2A arrows; Fig. 2C orange column), giving rise to a negative directional bias (DB = $-0.34$). These results show that bursts and isolated spikes can encode opposite directions of movement.

Effects of T-type calcium channels on movement direction coding by bursts and isolated spikes

We next investigated movement direction coding by bursts and isolated spikes in our model without the calcium conductance. To do this, we performed numerical simulations of our model with $g_T = 0$. We note that our model then does not generate calcium-mediated burst firing, but can generate short interspike intervals
that would be considered as “bursts” according to the ISI threshold criterion when the bias current is sufficiently high. We found that our model displayed a stronger response when the object moved from right to left and a weaker response when the object moved from left to right when the full spike train was used (Fig. 3A, Fig. 3B middle). Our model thus still displayed directional selectivity (DB = 0.46). When we used the burst train, we observed a stronger directional bias (DB = 0.97) as bursts were almost exclusively elicited when the object moves from right to left. In contrast, the isolated spikes tended to be elicited when the object moves from left to right as reflected by a weaker directional bias (DB = 0.21). As such, our results show that both bursts and isolated spikes encoded the same movement direction (i.e. right to left) when we set $g_T = 0$ in our model as they displayed negative directional biases (Fig. 3C).

In order to better understand these results, we then plotted the inputs to the model when the object moves from left to right (Fig. 4A, left) and right to left (Fig. 4A, right). In the left to right direction, the hyperpolarisation from the OFF zone attenuates the subsequent depolarisation from the ON zone (Fig. 4A, left). In contrast, in the right to left direction, the initial depolarisation from the ON zone is truncated by the subsequent hyperpolarisation from the OFF zone (Fig. 4A, right). The response of our model to these different inputs strongly depends on the value of the T-type conductance $g_T$. When $g_T$ is present, the initial hyperpolarisation from the OFF zone removes the inactivation of this conductance and the subsequent depolarization activates it, thereby causing a burst of action potentials as explained above when the object moves from left to right (Fig. 4B, left). In contrast, the initial depolarisation gives rise to isolated spikes when the object moves from right to left as the T-type conductance is then inactivated (Fig. 4B, right). The following hyperpolarisation only partially removes this inactivation and the subsequent repolarisation gives rise to a burst of action potentials albeit with a larger intraburst interval (Fig. 4B, right). Therefore, our model tends to
respond with a mixture of bursts and isolated spikes when the object moves from right to left.

Qualitatively different results were seen when we removed the T-type conductance (i.e. \(g_T = 0\)). When the object moves from left to right, the depolarization from the ON zone is partially occluded by the preceding hyperpolarisation from the OFF zone and thus gives rise to isolated spiking (Fig. 4C, left). When the object moves from right to left, the initial depolarisation from the ON zone gives rise to a burst of action potentials. The subsequent hyperpolarization from the OFF zone silences spiking and the repolarisation then gives rise to isolated spikes (Fig. 4C, right). As such, our model gives rise to isolated spikes when the object moves in both directions and to bursts preferentially when the object moves from right to left.

Exploring the effect of the synaptic depression time constants on movement direction coding by bursts and isolated spikes

We then systematically varied model parameters and characterized the directional biases of bursts and isolated spikes with the T-type conductance present. We first varied the synaptic depression time constants from the ON (\(\tau_{\text{ON}}\)) and OFF (\(\tau_{\text{OFF}}\)) zones in our model. Our results show that varying these can lead to dramatic qualitative differences between the directional biases of bursts and isolated spikes. Indeed, for small \(\tau_{\text{OFF}}\) and large \(\tau_{\text{ON}}\) values (i.e. \(\tau_{\text{OFF}} < 0.1\) sec and \(\tau_{\text{ON}} > 0.1\) sec), the full (Fig. 5A), burst (Fig. 5B), and isolated (Fig. 5C) spike trains all displayed positive directional biases and thus encoded the same movement direction. However, the
directional bias of isolated spikes was smaller in magnitude than that of the full and burst trains, which corresponds to the regime described in our previous study [26]. We will henceforth refer to this regime as “same direction selectivity”. In contrast, for large $t_{\text{OFF}}$ and small $t_{\text{ON}}$ values (i.e., $t_{\text{OFF}} > 0.1$ sec and $t_{\text{ON}} < 0.1$ sec), both the full (Fig. 5A) and burst (Fig. 5B) trains displayed a positive directional bias while the isolated spike train (Fig. 5C) displayed a negative directional bias. We will henceforth refer to this regime as “opposite direction selectivity”.

In order to better characterize both regimes, we computed an opposite directionality index (ODI, see Materials and Methods). This index is positive when the directional biases of both bursts and isolated spikes have the same sign, negative when they are opposite in sign, and 0 when one does not display significant directional selectivity. We found that the ODI was positive for small $t_{\text{OFF}}$ and large $t_{\text{ON}}$ values (i.e., $t_{\text{OFF}} < 0.1$ sec and $t_{\text{ON}} > 0.1$ sec) and negative for large $t_{\text{OFF}}$ and small $t_{\text{ON}}$ values (i.e., $t_{\text{OFF}} > 0.1$ sec and $t_{\text{ON}} < 0.1$ sec) (Fig. 5D).

In order to better understand why varying the depression time constants $t_{\text{ON}}$ and $t_{\text{OFF}}$ can give rise to qualitatively different regimes, we plotted the PSTH curves for the full, burst, and isolated spike trains for two sets of parameter values that gave rise to the same and opposite direction selectivity regimes in Figs. 5E and 5F, respectively. The parameter values used for the same and opposite direction selectivity regimes are shown in Fig. 5D as points “E” and “F”, respectively. For the same direction selectivity regime, the maximum firing rate from the full, burst, and isolated spike trains was strongest when the object moves from left to right (Fig. 5E). In contrast, for the opposite direction selectivity regime, the maximum firing rate for the full spike and burst trains were higher when the object moves from left to right while that of isolated spike train is highest when the object moves from right to left (Fig. 5F).

We thus conclude that the ratio $t_{\text{OFF}}/t_{\text{ON}}$ has a strong influence on whether bursts and isolated spikes code for the same or opposite movement directions. Indeed, the former regime tended to occur for low values of $t_{\text{OFF}}/t_{\text{ON}}$ while the latter regime tended to occur for high values of $t_{\text{OFF}}/t_{\text{ON}}$. We also varied the gains from the ON and OFF zones, $G_{\text{ON}}$ and $G_{\text{OFF}}$, and found that varying these gave rise
to qualitatively similar results in that opposite movement direction regimes were mostly seen for high values of $G_{OFF}/G_{ON}$ (Fig. S1).

Exploring the effect of bias current on movement direction coding by bursts and isolated spikes

We next explored whether the bias current $I_{bias}$ influenced coding of movement direction by bursts and isolated spikes. To do so, we plotted the directional biases of the full (Fig. 6A), burst (Fig. 6B), and isolated (Fig. 6C) spike trains as a function of both the bias current $I_{bias}$ and the ratio of the synaptic depression time constants $t_{OFF}/t_{ON}$ which was varied so as to observe both same and opposite direction selectivity regimes (see Materials and Methods). Our results show that when $I_{bias}$ was low (i.e. $< -1.8$ nA) or high (i.e. $> 0.5$ nA), neither bursts (Fig. 6B) nor isolated spikes (Fig. 6C) displayed significant directional selectivity, resulting in an ODI of zero (Fig. 6D). Regimes in which the

Figure 5. The synaptic depression time constants $t_{ON}$ and $t_{OFF}$ strongly influence movement direction coding by bursts and isolated spikes. A) Directional bias computed from the full spike train as a function of $t_{ON}$ and $t_{OFF}$. B) Directional bias computed from the burst spike train as a function of $t_{ON}$ and $t_{OFF}$. C) Directional bias computed from the isolated spike train as a function of $t_{ON}$ and $t_{OFF}$. D) Opposite direction selectivity index (ODI) as a function of $t_{ON}$ and $t_{OFF}$. E) PSTH values near the maximum values in the left to right (blue arrow) and right to left (red arrow) directions for the full spike (purple), burst (green), and isolated (orange) spike trains for an example data point marked with a star in panel D. F) PSTH values near the maximum values in the left to right (blue arrow) and right to left (red arrow) directions for the full spike (purple), burst (green), and isolated (orange) spike trains for another example data point marked with a star in panel D.

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ODI was non-zero tended to occur for intermediate values of $I_{bias}$ (i.e., $2.1.8\, \text{nA} < I_{bias} < 0.5\, \text{nA}$). For low values of $\tau_{OFF}/\tau_{ON}$ (i.e., $\tau_{OFF}/\tau_{ON} < 0.2$), we observed same directional selectivity regimes characterized by positive ODI (Fig. 6D). In contrast, for high values of $\tau_{OFF}/\tau_{ON}$ (i.e., $\tau_{OFF}/\tau_{ON} > 0.2$), we observed regimes of opposite direction selectivity characterized by negative ODI (Fig. 6D). In particular, we found that, for some parameter values (i.e., $I_{bias} = -1\, \text{nA}$ and $\tau_{OFF}/\tau_{ON} = 1$), the full spike train displayed weak directional selectivity (Fig. 6A) while both the burst (Fig. 6B) and isolated (Fig. 6C) spike trains displayed strong selectivity for opposite movement directions. We return to this point below in the discussion.

The PSTH curves for the full, burst, and isolated spike trains are shown for two sets of parameter values that gave rise to same and opposite direction selectivity regimes in Figs. 6E and 6F, respectively. The parameter values used for the same and opposite direction selectivity regimes are shown in Fig. 6D as points “E” and “F”, respectively. For the same direction selectivity regime,
the maximum firing rate from the full spike, burst, and isolated spike trains was strongest when the object moves from left to right (Fig. 6E). On the other hand, for the opposite directional selectivity regime, the maximum firing rates for the full spike and the burst trains were both greatest when the object moves from left to right while that of isolated spikes was greatest when the object moves from right to left (Fig. 6F).

**T-type calcium currents promote coding of opposite movement directions by bursts and isolated spikes**

We next explored how different parameters influenced movement coding by bursts and isolated spikes in our model without the T-type calcium conductance (i.e. \( g_T = 0 \)). When using the full spike train, we obtained directional bias values that were negative for low values of \( t_{ON} \) (i.e. \( t_{ON}<0.1 \) sec) and zero otherwise (Fig. 7A). In contrast, when using the burst train, we obtained directional bias values that were near zero when \( t_{ON} \) was large (i.e. \( t_{ON}>0.2 \) sec) and \( t_{OFF} \) was small (i.e. \( t_{OFF}<0.2 \) sec) and negative otherwise (Fig. 7B). The isolated spike train (Fig. 7C) tended to display directional bias values near zero except for low values of \( t_{ON} \) (i.e. \( t_{ON}<0.02 \) sec) and \( t_{OFF} \) (i.e. \( t_{OFF}<0.2 \) sec) where it was positive. As such, the ODI was zero for almost all values of \( t_{ON} \) and \( t_{OFF} \) except for low values of \( t_{ON} \) (i.e. \( t_{ON}<0.02 \) sec) and \( t_{OFF} \) (i.e. \( t_{OFF}<0.2 \) sec) for which it was negative (Fig. 7D). We also varied the gains \( G_{ON} \) and \( G_{OFF} \) and found qualitatively similar results in that the parameter regions for which opposite directional selectivity was observed were greatly reduced (compare Figs. S2 and S1).

The PSTH curves for the full spike train, bursts, and isolated spikes are shown for parameter values for which the ODI was negative and null in Figs. 7E and 7F, respectively. These values correspond to those indicated by the points “E” and “F” in Fig. 7D. In the regime where the opposite directional selectivity regime was observed, the firing rates from the full spike and burst trains were both greatest when the object moves from right to left while the maximum firing rate from the isolated spike train was greatest when the object moves from left to right (Fig. 7E). In contrast, in the regime where no directional selectivity was observed, the maximum firing rates of the full, burst, and isolated spike trains were all approximately equal for both movement directions (Fig. 7F).

We next plotted the directional biases of the full (Fig. 8A), burst (Fig. 8B), and isolated (Fig. 8C) spike trains as a function of both the bias current \( I_{bias} \) and the ratio of the synaptic depression time constants \( t_{OFF}/t_{ON} \) when \( g_T = 0 \). Our results show that the bias current \( I_{bias} \) can significantly influence movement direction coding by the full, burst, and isolated spike trains (Figs. 8A, B, C). Indeed, both the full spike (Fig. 8A) and burst (Fig. 8B) trains displayed similar profiles: no directional selectivity was observed for low values of \( t_{OFF}/t_{ON} \) (i.e. \( t_{OFF}/t_{ON}<3 \)) and negative directional biases were observed for higher values. In contrast, the isolated spike train (Fig. 8C) displayed a qualitatively different profile in that negative directional biases were observed for higher values of \( t_{OFF}/t_{ON} \) (i.e. \( t_{OFF}/t_{ON}>10 \)) and low bias current values (i.e. \( I_{bias}>-5 \) nA) while positive values were observed for larger bias current values (i.e. \( I_{bias}>3.1 \) nA) (Fig. 8C). As a result, the opposite directional selectivity index ODI displayed both positive and negative values when plotted as a function of \( I_{bias} \) and \( t_{OFF}/t_{ON} \) (Fig. 8D). As such, we observed both same and opposite direction selectivity regimes in our model without the T-type conductance.

The PSTH curves for the full spike train, bursts, and isolated spikes are shown for example same and opposite direction selectivity regimes in Figs. 8E and 8F, respectively. The parameter values used for the same and opposite direction selectivity regimes are shown in Fig. 8D as points “E” and “F”, respectively. For the same direction selectivity regime, the maximum firing rate from the full spike, burst, and isolated spike trains is strongest when the object moves from right to left (Fig. 8E). On the other hand, for the opposite direction selectivity regime, the maximum firing rate for the full spike and the burst trains are higher when the object moves from right to left while that of isolated spikes is highest when the object moves from left to right (Fig. 8F).

These results show that bursting mediated by T-type calcium channels is not necessary to observe opposite direction selectivity. However, such bursting greatly extends the range of values of the synaptic time constants \( t_{ON} \) and \( t_{OFF} \) and the bias current \( I_{bias} \) for which such coding is observed. We also note that the magnitude of directional biases observed for either of the full, burst, and isolated spike trains was smaller overall without the T-type conductance (compare Figs. 5 and 7 as well as Figs. 6 and 8). We conclude that T-type calcium channels promote movement coding by bursts and isolated spikes.

**Electroscopic midbrain neurons display opposite coding of movement direction by bursts and isolated spikes**

Our analysis of the effects of different parameters on movement direction coding by bursts and isolated spikes has shown the existence of regimes for which bursts and isolated spikes code for the same movement direction and regimes for which bursts and isolated spikes code for opposite movement directions. In order to test this prediction, we performed extracellular recordings from \( N = 32 \) TS neurons *in vivo* while moving an object back and forth along the rostro-caudal axis of the animal as done previously [18,26,35,62] (see Materials and Methods). We found that bursts and isolated spikes could code for opposite movement directions in 5 neurons. The PSTH obtained for the full, burst, and isolated spike trains for these three neurons are shown in Figs. 9A, 9B, 9C. We found that opposite coding of movement direction by bursts and isolated spikes was most pronounced for the neuron from Fig. 9C. Indeed, this neuron responded mostly with bursts when the object moved from tail to head and responded mostly with isolated spikes when the same object moved from head to tail (Fig. 9C). This was reflected in the directional biases from the burst and isolated spike trains that were 0.6, and -0.63, respectively. As such, bursts and isolated spikes displayed directional biases that were almost equal in magnitude for this neuron. These data suggest that there exists neurons in TS for which bursts and isolated spikes can code for opposite movement directions.

**Decoding isolated spikes using a delay mechanism coupled with inhibition**

Any information carried by action potential patterns such as bursts and isolated spikes is only functionally relevant if it is decoded by downstream neurons. We have previously proposed a biologically plausible circuitry for extracting burst spikes [26]. However, plausible neural circuits that can selectively respond to isolated spikes but are insensitive to bursts have not been proposed to date. We note that the ISI threshold criterion that we have used to separate bursts and isolated spikes is acural in nature. This is because any given spike can only be classified as being part of a burst based on whether the next spike occurs after an interval of time that is less than the burst threshold. Similarly, any given spike can only be classified as isolated if the next spike occurs after an interval of time that is greater than the burst threshold.

A schematic of a biophysically plausible neural circuit that is sensitive to isolated spikes is shown in Figure 10A (see Materials and Methods).
and Methods). It consists of two synapses: the first is excitatory and displays no synaptic plasticity (i.e., the EPSP amplitude elicited by each presynaptic action potential is the same), and the second is inhibitory and displays strong short-term facilitation. The second synapse, therefore, responds preferentially to bursts as shown previously [26]. The output of the excitatory synapse is delayed with respect to the output of the inhibitory synapse, and both inputs are then summed and half-wave rectified (Fig. 10A). Intuitively, this circuit should be sensitive to isolated spikes for the following reason: bursts will give rise to greater facilitation of the inhibitory synapse, thereby causing a larger inhibition in the postsynaptic cell that will tend to prevent a response to the bursts from the excitatory synapse due to the delay. In contrast, isolated spikes will not induce such facilitation. As a result the inhibition is

Figure 7. The synaptic depression time constants $\tau_{\text{ON}}$ and $\tau_{\text{OFF}}$ influence movement direction coding by bursts and isolated spikes with $g_T = 0$. A) Directional bias computed from the full spike train as a function of $\tau_{\text{ON}}$ and $\tau_{\text{OFF}}$. B) Directional bias computed from the burst spike train as a function of $\tau_{\text{ON}}$ and $\tau_{\text{OFF}}$. C) Directional bias computed from the isolated spike train as a function of $\tau_{\text{ON}}$ and $\tau_{\text{OFF}}$. D) Opposite direction selectivity index as a function of $\tau_{\text{ON}}$ and $\tau_{\text{OFF}}$. E) PSTH values near the maximum values in the left to right (blue arrow) and right to left (red arrow) directions for the full spike (purple), burst (green), and isolated (orange) spike trains for an example data point marked with a star in panel D. F) PSTH values near the maximum values in the left to right (blue arrow) and right to left (red arrow) directions for the full spike (purple), burst (green), and isolated (orange) spike trains for another example data point marked with a star in panel D.

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sufficiently low such that the excitation from the first synapse can reach threshold for spiking. We note that such a scheme is not unreasonable since inhibition can sometimes precede excitation in midbrain neural circuits [63,64].

We next tested the performance of this simple model in segregating isolated spikes from bursts to that of an ISI threshold. Our results show that this model was accurate at detecting isolated spikes (Fig. 10B). The spikes that were incorrectly classified tended to be the first spikes of bursts as determined by the ISI threshold that occurred after a period of isolated spiking, as the inhibition is then too weak and too short to block these (Fig. 10B). We then quantified this performance by using signal detection theory [65].

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**Figure 8.** The bias current $I_{bias}$ and synaptic depression time constant ratio $\tau_{OFF}/\tau_{ON}$ influence movement direction coding by bursts and isolated spikes with $g_T = 0$. 

A) Directional bias computed from the full spike train as a function of $\tau_{OFF}/\tau_{ON}$ and $I_{bias}$.  
B) Directional bias computed from the burst train as a function of $\tau_{OFF}/\tau_{ON}$ and $I_{bias}$.  
C) Directional bias computed from the isolated spike train as a function of $\tau_{OFF}/\tau_{ON}$ and $I_{bias}$.  
D) Opposite direction selectivity index as a function of $\tau_{OFF}/\tau_{ON}$ and $I_{bias}$.  
E) PSTH values near the maximum values in the left to right (blue arrow) and right to left (red arrow) directions for the full spike (purple), burst (green), and isolated (orange) spike trains for an example data point marked with a star in panel D.  
F) PSTH values near the maximum values in the left to right (blue arrow) and right to left (red arrow) directions for the full spike (purple), burst (green), and isolated (orange) spike trains for another example data point marked with a star in panel D.

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Figure 9. Electrosensory midbrain neurons can display opposite movement direction coding by bursts and isolated spikes.

A) Peri-stimulus time histogram (PSTH) for an example neuron computed from all spikes (purple), bursts (green), and isolated spikes (orange). The curves have been normalized by their maximum values. Directional bias (DB) values were $-0.64$, $-0.39$, and $0.36$ for burst, all spikes, and isolated spikes, respectively. B) PSTH for another example neuron computed from all spikes (purple), bursts (green), and isolated spikes (orange). The curves have been normalized to 1. Directional bias (DB) values were $-0.59$, $-0.5$, and $0.56$ for burst, all spikes, and isolated spikes, respectively. C) PSTH for another example neuron computed from all spikes (purple), bursts (green), and isolated spikes (orange). The curves have been normalized to 1. Directional bias (DB) values were $0.6$, $0.5$, and $-0.63$ for burst, all spikes, and isolated spikes, respectively.

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(see Materials and Methods) and found that this model gave high probabilities of correct classification for a wide range of delay $\tau_d$ and synaptic facilitation time constant $\tau_f$ values (Fig. 11A). We also investigated whether the incorrectly classified spikes actually belonged to bursts and isolated spikes as determined by the ISI threshold. To do so, we plotted the probability of misclassification for spikes that, according to the ISI threshold, were considered isolated spikes (Fig. 11B), the first spike of a burst (Fig. 11C), or any other spike of a burst (Fig. 11D). Thus, our results show that, for the parameter values that gave rise to the maximum probability of correct classification, the majority ($\approx 90\%$) of spikes that were incorrectly classified were actually the first spikes of a burst for the reason mentioned above. We found that these percentages strongly depended on parameter values (Figs. 11B, C, D). For example, increasing the delay for a given value of the facilitation time constant reduces the percentage of misclassified first spikes of a burst (Fig. 11C), increases the percentage of misclassified isolated spikes (Fig. 11B), and does not affect the remaining percentage of misclassified spikes that are part of a burst (Fig. 11D), but decreases the probability of correct classification (Fig. 11A).

We next varied both the inhibition time constant $\tau_I$ and gain $G_I$ in our model. Our results show that the maximum probability of correct classification could be obtained for a wide range of values (Fig. 11E). Again, for the parameter values that gave rise to maximum probability of correct classification, the majority of misclassified spikes were actually the first spikes of bursts as seen by plotting the percentage of misclassified spikes that were considered isolated spikes (Fig. 11F), the first spike of a burst (Fig. 11G), or any other spike of a burst (Fig. 11H).

We next tested whether the extracted isolated spikes could indeed code for the opposite movement direction than that coded by both the burst and full spike trains, as observed using an ISI threshold. As such, we used the spiketrain from the example neuron shown in Fig. 9B as an input to the model. We found that the input and output PSTHs were maximal for opposite movement directions (Fig. 12A) and thus displayed opposite directional biases (Fig. 12B). Finally, we computed the directional bias of isolated spikes obtained with our model against that computed from isolated spikes obtained with the ISI threshold criterion across our experimental dataset (Fig. 12C) and observed a significant positive correlation between both quantities ($R = 0.52$, $p = 0.0023$, $N = 32$). These results show that a generic circuit with a temporal delay can be used to selectively extract directional information carried by isolated spikes.

Discussion

Summary of results

We have explored the coding of movement direction by specific action potential patterns, namely bursts and isolated spikes, in a biophysical model of directional selectivity in midbrain neurons of weakly electric fish. We found that, for a wide range of parameter values, bursts displayed strong directional selectivity and isolated spikes displayed little or no directional selectivity consistent with previous findings [26]. However, we also found a qualitatively different regime for which bursts and isolated spikes were preferentially elicited when the object moved in opposite directions. As such, our results show for the first time that bursts and isolated spikes can code for opposite movement directions. We have also shown that subthreshold T-type calcium channels can greatly enhance the range of parameter values for which this regime was observed. This is because such channels must be de-inactivated by inhibition in order to be activated by subsequent excitation and give rise to a burst of action potentials. We have also shown experimental recordings from TS neurons in weakly electric fish for which bursts and isolated spikes coded for opposite movement directions. Finally, we have shown that plausible simple neural circuits can reliably extract isolated spikes from spike trains that consist of both bursts and isolated spikes. To our knowledge,
these results constitute the first demonstration that bursts and isolated spikes can both code for movement direction in the same neuron. The relative simplicity and generality of our mathematical model suggests that our results will be applicable to other systems.

Role of active burst dynamics in generating directional selectivity

Previous studies have shown that, for most TS neurons, bursts and isolated spikes were the most and least reliable indicators of motion direction, respectively [26]. Therefore, it was suggested that isolated spikes coded for stimulus attributes other than motion direction. In this study we have shown that, for some TS neurons, bursts and isolated spikes can code for opposite movement directions. Our model predicts that an active burst mechanism mediated by a T-type calcium conductance is not necessary in order to observe opposite coding of movement direction by bursts and isolated spikes. Nevertheless, this active burst mechanism greatly extended the range of parameter values for which we observed opposite coding of movement direction by bursts and isolated spikes. These results constitute the first demonstration that bursts and isolated spikes can both code for movement direction in the same neuron. The relative simplicity and generality of our mathematical model suggests that our results will be applicable to other systems.

Functional relevance of opposite directional selectivity of bursts and isolated spikes

What is the functional relevance of having bursts and isolated spikes encode opposite movement direction in the same neuron? We propose that such parallel encoding may be used to discriminate different objects moving in opposite directions within the neuron’s receptive field. Such parallel coding is entirely consistent with an emerging general picture in which bursts and isolated spikes can code for different stimulus attributes simultaneously and in parallel in the same neuron [25,39,41,44,66,67]. In weakly electric fish, foreground and background motion in opposite directions could occur during prey capture [10] or during tracking behavior [5] and the simultaneous encoding of both fore and background movement may be necessary for proper motor control.

Extracting bursts and isolated spikes

Our results are consistent with a growing body of literature that shows that bursts and isolated spikes can encode different stimulus attributes and thus might serve different functions [25,41,42,44,66,68,69]. This assumes that downstream neural circuits can somehow extract bursts and isolated spikes from a spike train. While previous studies have considered neural circuits that can selectively extract bursts [26,41,51,70], we are not aware of any previous studies that have proposed biophysically plausible neural circuits that would be sensitive exclusively to isolated spikes prior to this one.

Specifically, we have proposed that the neural circuits that would respond exclusively to isolated spikes need to include a delay. This delay is necessary because any given spike cannot be
Figure 11. Extracting isolated spikes using a biologically plausible model. A) Probability of correct classification PCC as a function of the facilitation time constant $t_f$ and delay $t_d$. B, C, D) Probability of misclassification $P_{\text{misclassification}}$ for the spikes that, according to the ISI threshold, were considered to be isolated spikes (B), the first spikes of a burst (C), or any other spikes of a burst (D), as a function of the facilitation time constant $t_f$ and delay $t_d$. Other parameter values used were $t_D = 500$ msec, $t_E = 5$ msec, $t_I = 5$ msec, $G_I = 7$, $I_0 = 3.41$ msec. E) Probability of correct classification PCC as a function of the inhibition time constant $t_I$ and gain $G_I$. F, G, H) Probability of misclassification $P_{\text{misclassification}}$ for the spikes that, according to the ISI threshold, were considered to be isolated spikes (F), the first spikes of a burst (G), or any other spikes of a burst (H), as a function of the inhibition time constant $t_I$ and gain $G_I$. Other parameter values used were $t_F = 200$ msec, $t_D = 500$ msec, $t_E = 5$ msec, $I_0 = 3.41$ msec, $t_d = 4$ msec.

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unambiguously assigned as being part of a burst or being isolated without knowing at what time the next action potential will occur. Thus, it is necessary to compare the spike train at the present with the same spike train delayed by a time interval on the order of the burst threshold.

We note that neural circuits that use temporal combinations of delayed excitation and inhibition in order to achieve response selectivity have been described in other midbrain circuits and may be a general feature of sensory processing [63,64,71,72]. In Apteronotus leptorhynchus, many TS neurons project to the optic tectum (OT) where neurons respond selectively to moving objects in a directionally biased fashion [4,73]. It is possible that plasticity at the TS-OT synapses or a combination of excitation and inhibition from TS might enable OT neurons to decode bursts and/or isolated spikes from TS neurons. Future studies should investigate this interesting possibility.

Implications for other systems

Our results show that the traditional method for measuring directional selectivity, in which the maximum firing rates elicited in response to the moving object in each direction are compared, can in some cases fail to capture salient information transmitted by direction selective neurons. This is because such techniques take the full spike train into account. Indeed, we found parameter regimes for which the isolated and full spike trains displayed selectivity for opposite movement directions. Moreover, for subsets of these parameters, the full spike train displayed little directional selectivity but for which the burst and isolated spike trains displayed opposite directional selectivity (see e.g. Fig. 6).

This result may have important consequences for the generation of direction selectivity in the mammalian visual cortex. Indeed, the electro-sensory system has many parallels with thalamocortical pathways [74]. In particular, thalamic relay neurons within the lateral geniculate nucleus (LGN) have subthreshold T-type calcium channels that mediate burst firing [45,59,60,75–80]. The spike trains from thalamic relay neurons consist of a mixture of bursts and isolated spikes in the awake-behaving animals [42,81,82]. While previous studies have shown that these neurons are not directionally selective [12], these did not consider action potential patterns such as bursts and isolated spikes. We hypothesize that bursts of action potentials from thalamic relay neurons in LGN carry specific directional information that is then used by postsynaptic neurons within the primary visual cortex to generate directionally biased responses. This hypothesis is supported by the fact that thalamocortical synapses display strong depression and that sustained isolated action potential firing from thalamic relay neurons activates this depression [45,60,83]. Nevertheless, ~100 ms of inhibition can remove this depression as well as deinactivate T-type calcium channels. A subsequent depolarization caused by excitation can thus cause burst firing as well as an amplified post-synaptic response [45,60,83]. Studies performed within the LGN are necessary to validate this hypothesis and are beyond the scope of this paper.

Figure 12. Comparison of a biologically plausible model with the ISI threshold. A) Input PSTH (gray) and output PSTH (black) from the model when the input consists of the full spike train from an example TS neuron. B) Output directional bias (black) and input directional bias (gray) computed from the ISI threshold criterion. There was a significant positive correlation between both quantities (R = 0.52, p = 0.0023, N = 32). Parameter values used were $t_F = 70$ msec, $t_D = 500$ msec, $t_E = 5$ msec, $t_I = 8$ msec, $G_F = 7$, $I_0 = 3.41$ msec, $t_D = 4$ msec. doi:10.1371/journal.pone.0040339.g012
Conclusion
We investigated whether action potential patterns such as bursts and isolated spikes encoded movement direction in a model of directional selectivity in electrosensory midbrain neurons. We found parameter regimes in which bursts and isolated spikes could encode opposite movement directions in the same neuron even though the full spike train displays little or no directional selectivity. As such, neurons that are categorized as non-directionally selective using the full spike train may in fact be highly directional selective if one considers instead particular action potential patterns. Such coding of opposite movement directions by bursts and isolated spikes could be used in discriminating different objects moving in opposite directions within the neuron's receptive field and is likely to be found across sensory systems.

Materials and Methods

Ethics statement
McGill University's institutional Animal Care and Use Committee approved all experimental procedures and animal husbandry.

Animals
We used the weakly electric fish Apteronotus leptorhynchus in this study. Animals were obtained from tropical fish suppliers and were housed in laboratory tanks for several days in order to become acclimated to the new environment. This was performed according to published guidelines [84]. The surgical and experimental procedures have been described in detail elsewhere [18,35,62,85–88].

Stimulation and recording
Extracellular recordings from TS neurons were made using previously described techniques [18,35,62,89]. We used both patch [62,89] and metal-filled micropipettes [62,90–92] to obtain these recordings. The stimulus consisted of a 1.8 cm wide metal plate coated with a plastic coating on the side opposite to the animal that was actuated using a pen plotter (HP 7010B). This object moved back and forth along the animal's rostro-caudal axis over a distance of 20 cm [17,18,35,93,94] for at least 30 cycles. The sinusoid was centered at the animal's midpoint and had a frequency of 0.25 Hz, corresponding to an average velocity of ~10 cm/sec. These velocities correspond to those that the animal experiences during prey capture [10] and within the velocities of error signals observed during refuge tracking [5].

Data were acquired with a Cambridge Electronic Design Power1401 hardware and Spike2 software (Cambridge, UK) and analyzed using Spike2 (CED) and custom-made routines in MATLAB (The Mathworks, Natick, MA). The recorded membrane potentials were thresholded in order to obtain the action potential times. We excluded neurons whose total spike count was less than 100 were not analyzed.

Burst and isolated spike classification
We used an interspike interval threshold to separate the simulated spiking responses into burst and isolated spikes [25,36,41,44] (Fig. 1D). Specifically, two consecutive action potentials that were separated by a time interval less than the burst threshold were considered as part of a burst. Spikes that were not part of bursts were included in the isolated spike train. The burst threshold was computed as the time at which the falling phase of initial peak of the autocorrelogram crossed the 99.9% Poisson confidence limit as done previously [25,26,36,95].

Quantifying directional selectivity and opposite directionality
The full spike, burst (i.e. the train of spikes that belong to bursts) and the isolated (i.e. the train of spikes that are isolated) spike trains were each used to compute peri-stimulus time histograms (PSTHs) in response to the moving object. We then computed a measure of directional bias as [18,33]:

\[ DB = \frac{R_{LR} - R_{RL}}{\max(R_{LR}, R_{RL})} \]

where \( R_{LR} \) and \( R_{RL} \) are the maximum firing rates obtained when the object moves from “left to right” and “right to left”, respectively (note that “left to right” corresponds to the object moving from the animal’s snout to the tail and that “right to left” corresponds to the object moving from the tail to the snout) and \( \max(R_{LR}, R_{RL}) \) is the maximum of the two. This measure varies between −1 and 1. DB values of 1 and −1 indicate complete direction preference for movement from left to right and from right to left, respectively, while a value of 0 indicates no direction selectivity.

To quantify the opposite directionality we used the directional biases computed from burst spikes and isolated spikes and then computed the opposite directionality index as:

\[ ODI = i[DB_{burst} - DB_{isolatedspikes}] \]

where \( i \) is 1 if the maximum firing rate of burst spikes and isolated spikes happen preferentially for the same object movement direction and is −1 otherwise. \( i \) is 0 if directional biases of bursts or isolated spikes equal 0.

Modeling TS neurons
Our model TS neuron’s one-dimensional receptive field consists of two 10 mm long adjacent ‘ON’ and ‘OFF’ zones. The ‘ON’ zone represents the output of E-type ELL pyramidal cells that are excited by the stimulus while the ‘OFF’ zone represents the output of I-type ELL pyramidal cells that are inhibited by the stimulus as observed experimentally [83,96]. Then a point object moved at a speed of 10 cm/s back and forth across these zones. The output of each zone is then given by [18]:

\[ O_i(t) = F_I + v_i G_i \Theta(-t_{i} - \lambda_i) \exp \left( - \frac{t - \lambda_i}{\tau_i} \right) \]

where \( F_I \) is the bias current which represents the baseline activity from E and I-type pyramidal cells which are approximately equal on average [97,98] and \( v_i = 1, -1 \) for \( i = \text{ON}, \text{OFF} \), respectively. Here \( \tau_i \) is the depression time constant associated with zone \( i \) and \( \lambda_i \) is the time that object enters zone \( i \) and \( G_i \) is the gain of zone \( i \). The responses of each zone were then convolved with an alpha function with time constant 20 msec to mimic synaptic EPSPs. Consistent with anatomical data showing that both E and I-type ELL pyramidal neurons make excitatory connections onto TS neurons [99], the input \( I(t) \) to our neuron model is taken to be:

\[ I(t) = O_{ON} + O_{OFF} \]
We note that the outputs from the ON and OFF zone, \(O_{ON}\) and \(O_{OFF}\), were not delayed with respect to one another, which is consistent with recent experimental results showing no significant delay between the inputs from E and I-type sources onto TS neurons [88]. The TS neuron was modeled using the Hodgkin-Huxley formalism based on available experimental data [35], the model contains spiking sodium, delayed rectifier potassium, low threshold calcium (T-type), and lead conductances:

\[
\begin{align*}
    \frac{dV}{dt} &= -g_{Na}m^3h(V-E_{Na}) - g_{K}n^4(V-E_{K}) \\
    &- g_{Ca}T^3h(V-E_{Ca}) + A I(t) + I_{bias} + \sigma \xi(t)
\end{align*}
\]

\[
\begin{align*}
    \frac{dh}{dt} &= \Phi_h(V) - h \\
    \frac{dn}{dt} &= \frac{z_n(V) - n}{\tau_n(V)} \\
    \frac{dz}{dt} &= \frac{z_o(V) - z}{\tau_z(V)}
\end{align*}
\]

where \(C\) is the membrane capacitance, \(V\) is the transmembrane potential difference, \(g_{Na}\), \(g_{K}\), and \(g_{Ca}\) are the voltage-gated calcium, sodium, and potassium conductances with reversal potentials \(E_{Na}\), \(E_{K}\), and \(E_{Ca}\), respectively. \(A\) is the synaptic weight calcium, sodium, and potassium conductances with reversal potential \(E_{leak}\). Here \(g_{Na}, g_{K}, \text{ and } g_{Ca}\) were set at 10 \(\mu\)S, \(g_{leak}\) was the leak conductance with low-pass filtered Gaussian white noise with standard deviation \(\sigma\) that mimics sources of synaptic input [100].

We simulated this model numerically using an Euler-Maruyama Algorithm with integration time step \(dt = 0.0025\) msec. Other parameter values used, unless otherwise stated, were \(g_{Na} = 0.18\) \(\mu\)S, \(g_s = 0.32\) \(\mu\)S, \(g_{ON} = 30\) \(\mu\)S, \(g_{OFF} = 10\) \(\mu\)S, \(E_{leak} = -65\) mV, \(E_{Ca} = 120\) mV, \(E_{Na} = 60\) mV, \(E_{K} = -85\) mV, \(C = 1\) \(\mu\)F, \(A = 0.75\), \(B = 0.1\), \(\gamma = 2\), \(G_1 = G_2 = 1\), \(I_{bias} = -1.3\) nA, \(g_{ON} = g_{OFF} = 1\), \(t_{ON} = 500\) msec, \(t_{OFF} = 500\) msec. These values are comparable to those used in previous modeling studies [35, 59]. For some simulations, we set \(g_s = 0\) and \(I_{bias} = 3.1\) nA to adjust for firing rate. All simulations for computing PSTHs and directional biases were done over 1000 trials. We explored the parameter spaces by systematically varying synaptic depression time constants of ON and OFF zones in a range of 5 msec to 500 msec which is biologically relevant [18]. To explore the effect of synaptic depression time constants and bias current together we used synaptic depression time constants ratio \(t_{OFF}/t_{ON}\) in the range of 1/50 to 50 in which \(t_{OFF}\) and \(t_{ON}\) were in (sec) \([0.01 0.5], [0.01 0.4], [0.01 0.3], [0.01 0.3], [0.01 0.2], [0.01 0.1], [0.01 0.05], [0.01 0.04], [0.01 0.03], [0.01 0.02], [0.01 0.01], [0.02 0.01], [0.03 0.01], [0.04 0.01], [0.05 0.01], [0.1 0.01], [0.2 0.01], [0.3 0.01], [0.4 0.01], [0.5 0.01]\).

In all our analysis and figures in which the directional biases from our model were plotted as a function of parameters, directional biases whose magnitude was below 0.15 were set to zero. This is because previous analysis has shown that such directional biases were not significantly different from zero [18]. The burst threshold that was used for our model simulations was set at 10 msec as done previously [26].

**Modeling biophysically plausible mechanisms to extract isolated spikes**

While the interspike interval threshold procedure described above is a simple computational method for segregating bursts and isolated spikes, it is not clear how such a threshold mechanism could be implemented in CNS circuits. A neural circuit which responds to bursts and is insensitive to isolated spikes has been previously considered [26]. However, the complement problem of designing a neural circuit that would be unresponsive to bursts but sensitive to isolated spikes has, to our knowledge, not been considered before.

Here we introduce a plausible circuit that can extract isolated spikes. Specifically, we consider the presynaptic spike train as a sum of delta functions:

\[
X(t) = \sum_{i=1}^{N} \delta(t - t_i)
\]

where \(t_i\) is the \(i^{th}\) spike time. \(X(t)\) is first passed through two parallel synapses. The first is excitatory and does not have any synaptic dynamics (i.e. no plasticity and the amplitude of the output EPSP is the same for all presynaptic action potentials), the output of this synapse is thus given by convolving the input spike train \(X(t)\) with an alpha function with time constant \(\tau_E\):

\[
Y_E(t) = \sum_{i=1}^{N} \Theta(t - t_i) \frac{I_i}{\tau_E} \exp\left(-\frac{t - t_i}{\tau_E}\right).
\]

The second synapse is inhibitory and displays plasticity. This plasticity is described by facilitation and depression terms [101–104]:

\[
\frac{dD}{dt} = \frac{1 - D}{\tau_D}; \quad t = t_i \Rightarrow D(t_i) = D(t_i)(1 - F(t_i))
\]

\[
\frac{dF}{dt} = -\frac{F}{\tau_F}; \quad t = t_i \Rightarrow F(t_i) = F(t_i) + \Delta F(t_i - t_{i-1})
\]

\[
\Delta F(t) = \frac{I_0}{T}
\]
At the time of an input spike $t_i$, $D$ is first decreased by an amount $F(t_i)D(t_i)$; then $F$ is updated by an increment $\Delta F$. The increment $\Delta F$ is inversely proportional to the time interval between the current action potential and the last one. As such, short time intervals such as those that occur during burst firing will cause more potentiation than longer ones. We have also introduced an upper bound for $F$ (i.e. $F(t) \leq 1$) to prevent negative values for the update factor of the depression variable. The output of this synapse is thus given by:

$$Y_I(t) = -G_I \sum_{i \neq t} O(t - t_i)D(t_i)F(t_i) \frac{t - t_i}{\tau f} \exp \left( -\frac{t - t_i}{\tau f} \right),$$

where $D$, $F$ are the depression and facilitation terms, respectively. Here $\tau_f$ is the time constant of the alpha function that models the time course of the IPSP and $G_I$ is a gain term. As such, the inhibitory synapse displayed strong facilitation in response to a burst of presynaptic action potentials. We assume that the output $Y_I(t)$ is delayed by a time $\tau_d$. The postsynaptic output is then given by:

$$Z(t) = TF(Y_E(t - \tau_d) + Y_I(t)),$$

with $TF$ defined as:

$$TF(Y) = \begin{cases} Y & \text{if } Y \geq 0 \\ 0 & \text{if } Y < 0 \end{cases}$$

The post-synaptic spike train was obtained by thresholding $Z(t)$ (i.e. finding the times at which $Z(t)$ crosses a threshold value from below). We then took experimentally recorded spike sequences, and segregated them into bursts and isolated spikes using both our decoding model and ISI threshold methods. Then, we compared the sequences of burst and isolated spikes obtained from each model in the following way. We used signal detection theory [65] in order to quantify the decoding model's performance at detecting isolated spikes as defined by the ISI threshold. We computed the probability of correct detection ($PD$) as the fraction of spike times deemed to be part of isolated spike train according to the decoding model that were also deemed part of isolated spike train using the ISI threshold criterion (i.e. that were “correctly” classified). The probability of false alarm ($PFA$) was computed as the fraction of spike times deemed to be part of isolated spike train according to the decoding model that were deemed to be burst using the ISI threshold criterion (i.e. that were “incorrectly” classified). The overall performance can then be quantified by computing the probability of correct classification (PCC) as:

$$PCC = \frac{PD}{2} + \frac{1 - PFA}{2}.$$

A value of PCC = 0.5 implies that our model performs at chance level compared to the ISI threshold criterion (i.e. that any given spike is randomly assigned as being part of a burst or isolated). In contrast, PCC = 1 indicates that the model performs identically to the ISI threshold criterion. We note that this does not imply that the ISI threshold criterion is optimal in any way as segregating bursts and isolated spikes, merely that our biophysically plausible decoding model performs as well. As such, signal detection theory is used here to determine how well the decoding model performs relative to the ISI threshold criterion.

**Supporting Information**

**Figure S1** The gains $G_{ON}$ and $G_{OFF}$ strongly influence movement direction coding by bursts and isolated spikes. A) Directional bias computed from the full spike train as a function of $G_{ON}$ and $G_{OFF}$. B) Directional bias computed from the burst spike train as a function of $G_{ON}$ and $G_{OFF}$. C) Directional bias computed from the isolated spike train as a function of $G_{ON}$ and $G_{OFF}$. D) Opposite direction selectivity index (ODI) as a function of $\tau_{ON}$ and $\tau_{OFF}$.

**Figure S2** The gains $G_{ON}$ and $G_{OFF}$ influence movement direction coding by bursts and isolated spikes with $\delta T = 0$. A) Directional bias computed from the full spike train as a function of $G_{ON}$ and $G_{OFF}$. B) Directional bias computed from the burst spike train as a function of $G_{ON}$ and $G_{OFF}$. C) Directional bias computed from the isolated spike train as a function of $G_{ON}$ and $G_{OFF}$. D) Opposite direction selectivity index as a function of $G_{ON}$ and $G_{OFF}$.

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**Author Contributions**

Conceived and designed the experiments: MJC. Performed the experiments: NKH MJC. Analyzed the data: NKH. Contributed reagents/materials/analysis tools: NKH MJC. Wrote the paper: NKH MJC.

**References**

1. Tannemuro LF, Frye MA, Dickinson MH (2004) Spatial organization of visuomotor reflexes in Drosophila. J Exp Biol 207: 113–122.
2. Frye MA (2001) Effects of stretch receptor ablation on the optomotor control of lift in the hawkmoth Manduca sexta. J Exp Biol 204: 3681–3691.
3. Srinivasan MV, Potener M, Kral K (1999) Motion detection in insect orientation and navigation. Vision Res 39: 2749–2766.
4. Rose GJ, Call SJ (1993) Temporal filtering properties of midbrain neurons in an electric fish: implications for the function of dendritic spines. Journal of Neuroscience 13: 1178–1189.
5. Cowan NJ, Fortune ES (2007) The critical role of locomotion mechanics in an electric fish displayed strong facilitation in response to a burst of presynaptic action potentials. We assume that the output $Y_I(t)$ is delayed by a time $\tau_d$. The postsynaptic output is then given by:

$$Z(t) = TF(Y_E(t - \tau_d) + Y_I(t)),$$

with $TF$ defined as:

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$$PCC = \frac{PD}{2} + \frac{1 - PFA}{2}.$$

A value of PCC = 0.5 implies that our model performs at chance level compared to the ISI threshold criterion (i.e. that any given spike is randomly assigned as being part of a burst or isolated). In contrast, PCC = 1 indicates that the model performs identically to the ISI threshold criterion. We note that this does not imply that the ISI threshold criterion is optimal in any way as segregating bursts and isolated spikes, merely that our biophysically plausible decoding model performs as well. As such, signal detection theory is used here to determine how well the decoding model performs relative to the ISI threshold criterion.

**Supporting Information**

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**Figure S2** The gains $G_{ON}$ and $G_{OFF}$ influence movement direction coding by bursts and isolated spikes with $\delta T = 0$. A) Directional bias computed from the full spike train as a function of $G_{ON}$ and $G_{OFF}$. B) Directional bias computed from the burst spike train as a function of $G_{ON}$ and $G_{OFF}$. C) Directional bias computed from the isolated spike train as a function of $G_{ON}$ and $G_{OFF}$. D) Opposite direction selectivity index as a function of $G_{ON}$ and $G_{OFF}$.

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**Author Contributions**

Conceived and designed the experiments: MJC. Performed the experiments: NKH MJC. Analyzed the data: NKH. Contributed reagents/materials/analysis tools: NKH MJC. Wrote the paper: NKH MJC.
78. McCormick DA, Huguenard JR (1992) A model of the electrophysiological properties of thalamocortical relay neurons. Journal of Neurophysiology 68: 1384–1400.

79. Mukherjee P, Kaplan E (1995) Dynamics of neurons in the cat lateral geniculate nucleus: in vivo electrophysiology and computational modeling. Journal of Neurophysiology 74: 1222–1243.

80. Smith GD, Cox CL, Sherman SM, Rinzel J (2000) Fourier analysis of sinusoidally driven thalamocortical relay neurons and a minimal integrate-and-fire-or-burst model. Journal of Neurophysiology 83: 588–610.

81. Reinaud P, Godwin D, Sherman SM, Koch C (1999) Encoding of visual information by LGN bursts. Journal of Neurophysiology 81: 2538–2569.

82. Wolfart J, Dehay D, Le Masson G, Destexhe A, Bal T (2005) Synaptic background activity controls spike transfer from thalamus to cortex. Nature Neuroscience 8: 1760–1767.

83. Sherman SM (1996) Dual response modes in lateral geniculate neurons: mechanisms and functions. Visual Neuroscience 13: 205–213.

84. Hirschfeld EM, Stamper SA, Vonderschen K, Fortune ES, Chacron MJ (2009) Effects of Restraint and Immobilization on Electroscopic Behaviors of Weakly Electric Fish. ILAR Journal 50: 361–372.

85. Bastian J, Chacron MJ, Maler L (2002) Receptive field organization determines pyramidal cell stimulus-encoding capability and spatial stimulus selectivity. Journal of Neuroscience 22: 4577–4590.

86. Chacron MJ (2006) Nonlinear information processing in a model sensory system. Journal of Neurophysiology 95: 2933–2946.

87. Toporikova N, Chacron MJ (2009) Dendritic SK channels gate information processing in vivo by regulating an intrinsic bursting mechanism seen in vitro. Journal of Neurophysiology 102: 2273–2287.

88. McGillivray P, Vonderschen K, Fortune ES, Chacron MJ (2012) Parallel coding of first and second order stimulus attributes by midbrain electrosensory neurons. Journal of Neuroscience 32: 5510–5524.

89. Rose GJ, Fortune ES (1996) New techniques for making whole-cell recordings from CNS neurons in vivo. Neuroscience Research 26: 89–94.

90. Frank K, Becker MC (1964) Microelectrodes for recording and stimulation. Physical Techniques in Biological Research, part A. New York: Academic. 23–44.

91. Chacron MJ, Lindner B, Longtin A (2007) Threshold fatigue and information transfer. Journal of Computational Neuroscience 23: 301–311.

92. Chacron MJ, Longtin A, Maler L (2005) Delayed excitory and inhibitory feedback shape neural information transmission. Physical Review E 72: 051917.

93. Ramchharit JR, Tan EW, Fortune ES (2005) Effects of global electro-sensory signals on motion processing in the midbrain of Eigenmannia. Journal of Comparative Physiology A-Sensory Neural & Behavioral Physiology 191: 865–872.

94. Vonderschen K, Chacron MJ (2009) Sparse Coding of Natural Communication Signals in Midbrain Neurons. Biomedical Central Neuroscience 10: O3.

95. Bastian J, Nguyenkin J (2001) Dendritic Modulation of Burst-like firing in sensory neurons. Journal of Neurophysiology 85: 10–22.

96. Saunders J, Bastian J (1984) The physiology and morphology of two classes of electrosensory neurons in the weakly electric fish Apteronotus Leptorhynchus. Journal of Comparative Physiology A 154: 199–209.

97. Chacron MJ, Maler L, Bastian J (2005) Feedback and Feedforward Control of Frequency Tuning to Naturalistic Stimuli. Journal of Neuroscience 25: 5521–5532.

98. Krahe R, Bastian J, Chacron MJ (2008) Temporal processing across multiple topographic maps in the electro-sensory system. Journal of Neurophysiology 100: 852–867.

99. Carr GE, Maler L (1985) A Golgi study of the cell types of the dorsal torus semicircularis of the electric fish Eigenmannia: functional and morphological diversity in the midbrain. Journal of Comparative Neurology 235: 207–240.

100. Manwani A, Koch C (1999) Detecting and estimating signals in noisy cable structure, I: neuronal noise sources. Neural Computation 11: 1797–1829.

101. Lewis JE, Maler L (2002) Dynamics of electro-sensory feedback: short-term plasticity and inhibition in a parallel fiber pathway. Journal of Neurophysiology 88: 1695–1706.

102. Lewis JE, Maler L (2004) Synaptic dynamics on different time scales in a parallel fiber feedback pathway of the weakly electric fish. Journal of Neurophysiology 91: 1064–1070.

103. Lindner B, Gangloff D, Longtin A, Lewis JE (2009) Broadband coding with dynamic synapses. Journal of Neuroscience 29: 2076–2087.

104. Harvey-Girard E, Lewis JE, Maler L (2010) Burst-induced anti-Hebbian depression acts through short-term synaptic dynamics to cancel redundant sensory signals. Journal of Neuroscience 30: 6152–6169.