Reactive Gliosis

►Glial Scar

Reactive Oxygen Species: Superoxide Anions

►Neuroinflammation: Modulating Pesticide-Induced Neurodegeneration

Readily Releasable Secretory Vesicles

►Neurotransmitter Release: Priming at Presynaptic Active Zones

Reafference

Definition

Sensory input resulting from an animal's own motor output.

►Reafferent Control in Electric Communication

Reafferent Control in Electric Communication

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Synonyms

Electrocommunication; Electrical communication

Definition

Every motor act that an animal produces will elicit sensory input from its own receptors [1]. Termed ►reafference, this self-generated sensory input can be quite useful. For example, bats listen to the echoes of their own ultrasonic calls to navigate through the night, and sensory feedback from skeletal muscles can be used to improve motor control. On the other hand, reafferent input is often not informative, and it can even interfere with the detection of external sensory input. A major problem faced by all animals is distinguishing reafferent sensory input from external sensory input. This issue is particularly relevant to the subject of animal communication. A communicating animal must produce its own signal as well as detect the signals produced by other individuals. A central question in the neurobiology of communication behavior is how sensory systems are able to discriminate self-generated from externally produced signals.

Consider the problem of reafference for visual perception. Any movement of the eyes, either directly or indirectly, due to movements of the head or body, causes the visual input to the retina to shift dramatically. How does the visual system compensate for this shift and maintain sensitivity to external visual stimuli? Early experiments suggested that every time a motor command that induces eye movement is issued, a copy of that command is also sent to the visual system, which generates a negative image of the visual input expected to result from that movement [1,2]. Combining this negative image with actual visual input eliminates any self-induced changes. As a result, the perceived visual world maintains its stability and only externally generated visual inputs are detected.

This basic mechanism relies on two distinct features. First, the timing of motor output must be relayed to the sensory system through what is referred to as a ►corollary discharge [2]. Second, the corollary discharge must activate a negative image of the reafferent input, a so-called ►efference copy [1]. Research on weakly electric fish has provided insight into the neuronal implementation of these two features [3,4].

Characteristics

Quantitative Description

African mormyrid fish possess an electromotor system that generates weak electric signals from a specialized ►electric organ, as well as an electrosensory system for detecting these signals (Fig. 1a). This unique sensorimotor system serves two functions. Through ►active electrolocation, mormyrids are able to detect distortions in their own electric field caused by nearby objects and thereby locate and identify various features of those objects, as well as navigate through their environment. By sensing the electric signals generated by other individuals, mormyrids are also able to communicate within the electric modality.

Electric signals in mormyrids consist of a fixed ►electric organ discharge (EOD) separated by a variable ►sequence of pulse intervals (SPI) (Fig. 1b). The EOD waveform conveys several aspects of the sender's identity, such as its species, sex, dominance, and possibly even its individual identity [5]. The total duration of the EOD is a particularly salient variable across species, ranging from as little as 100 µs to over 10 ms, and it may also exhibit sex- and status-related differences, with dominant males having a two- to three-fold longer EOD than females. By contrast, the SPI is involved in communicating contextual information about the sender's behavioral state and motivation. A variety of different patterns in the SPI have been linked with behaviors such as courtship and aggression [5].

In order for mormyrids to utilize the information available to them in these electric signals, however, they must first be able to distinguish their own EODs from those of other individuals. This distinction is made possible by a corollary discharge pathway that relays the timing of EOD production to central electrosensory regions (Figs. 1a and 2). By comparing incoming electrosensory information with an internal copy of their electromotor commands, they are able to distinguish their own electric signals from those of other nearby fish [4].

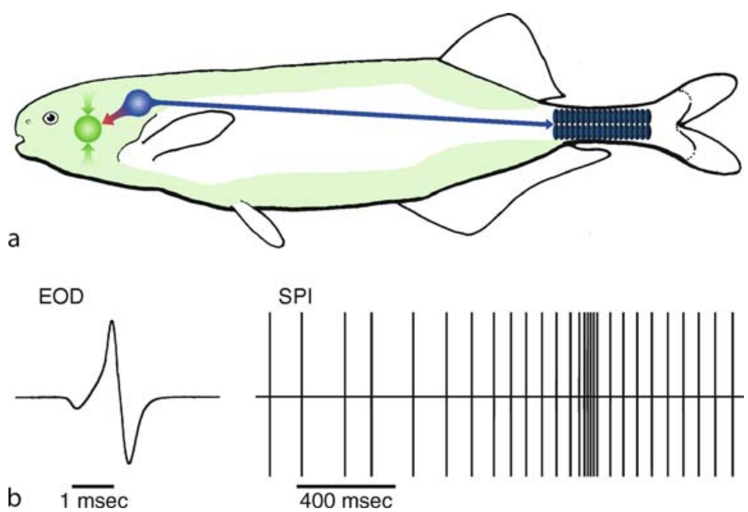
Higher Level Structures

Electromotor Pathway

Each EOD is initiated by a group of neurons in the ventral hindbrain that together constitute the electric organ ►command nucleus (CN) [5]. The neurons in the CN project both directly and indirectly to an adjacent group of neurons that make up the medial relay nucleus (MRN). The neurons in the MRN receive the command from the CN and relay it down the spinal cord to electromotor neurons that drive the electric organ (Fig. 2). The activity in the CN, and therefore the SPI, is determined by a number of descending inputs, foremost of which is a precommand nuclear complex (PCN) consisting of two adjacent, but physiologically and anatomically distinct neuronal populations [5].

Electrosensory Pathway

The electrosensory system of mormyrids consists of three distinct pathways, one of which is relevant for electric communication (Fig. 2). The primary sensory afferents in this pathway receive input from so-called ►knollenorgan electroreceptors, and project to a region of the dorsal hindbrain termed the nucleus of the electrosensory lateral line lobe (nELL) [6]. The neurons in the nELL relay this electrosensory input to a large midbrain structure termed the ►torus semicircularis, a sensory processing region considered homologous to the inferior colliculus of mammals.



Reafferent Control in Electric Communication. Figure 1 (a) Schematic of the electric communication system in the mormyrid *Brienomyrus brachyistius*. The electric organ, shown in blue, is controlled by a command center in the hindbrain. Each descending command drives the production of a single electric organ discharge (EOD). External electric fields are detected by electroreceptors, whose distribution on the body surface is indicated by turquoise shading. Input from the electroreceptors converges onto an electrosensory region in the hindbrain, which also receives input from the electric organ command center. (b) Structure of electric signals in mormyrids. Head positive voltage is plotted upward. The electric organ discharge (EOD) has a fixed, characteristic waveform, while the pattern of EOD production, indicated by the sequence of pulse intervals (SPI), is variable.

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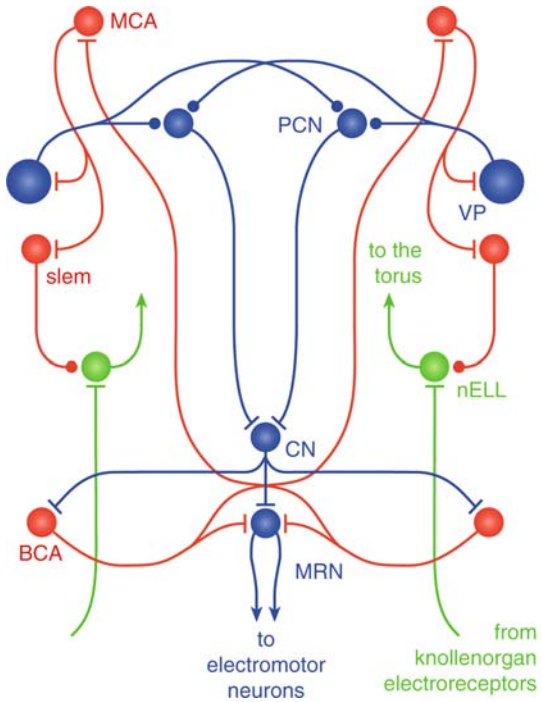


Reafferent Control in Electric Communication. Figure 2 Electric communication pathways in mormyrids. The electromotor pathway is shown in blue, the electrosensory pathway in green, and the corollary discharge pathway in red. Excitatory connections are indicated by flat lines, inhibitory connections by solid circles. Abbreviations: *BCA*, bulbar command-associated nucleus; *CN*, command nucleus; *MCA*, mesencephalic command-associated nucleus; *nELL*, nucleus of the electrosensory lateral line lobe; *PCN*, precommand nuclear complex; *MRN*, medial relay nucleus; *slem*, sublemniscal nucleus; *VP*, ventroposterior nucleus.

Electric Organ Corollary Discharge Pathway

The EOD command issued by the CN is relayed not just down the spinal cord to the electric organ, but also to higher brain centers that provide a precise timing reference of EOD production (Fig. 2) [3,5]. This electric organ corollary discharge (EOCD) pathway plays an important role in electric communication. For electrosensory processing in the knollenorgan pathway, it gives rise to an inhibitory input to the nELL that serves to block responses to reafferent electrosensory input (Fig. 2) [4]. In addition, the EOCD pathway helps regulate EOD production, as it projects to an electromotor region that provides inhibitory input to the PCN (Fig. 2). As a result, the region that drives the CN to fire is inhibited each time an EOD is generated. This negative feedback, referred to as recurrent inhibition, plays a critical role in controlling the SPI [5].

Lower Level Components

Electric Organ

The electric organ of mormyrids is located at the base of the tail and consists of a homogenous population of disc-shaped, modified muscle cells called ►electrocytes (Fig. 1a) [7]. When they are activated in synchrony by input from spinal electromotor neurons, their individual electrical potentials summate and give rise to the EOD, the amplitude of which is typically a few volts. Differences in the EOD waveform across species and between the sexes are directly related to variations in electrocyte morphology [7].

Electroreceptors

The knollenorgans involved in electric communication typically contain a few receptor cells that are housed together within a single large capsule [8]. Knollenorgan receptors are broadly tuned to the spectrum of the species-specific EOD and are extremely sensitive, with thresholds as low as 0.1 mV. In response to outside positive-going voltage steps, they fire a single spike at a short fixed latency. This phase-locked activity is relayed by primary sensory afferents to the nELL.

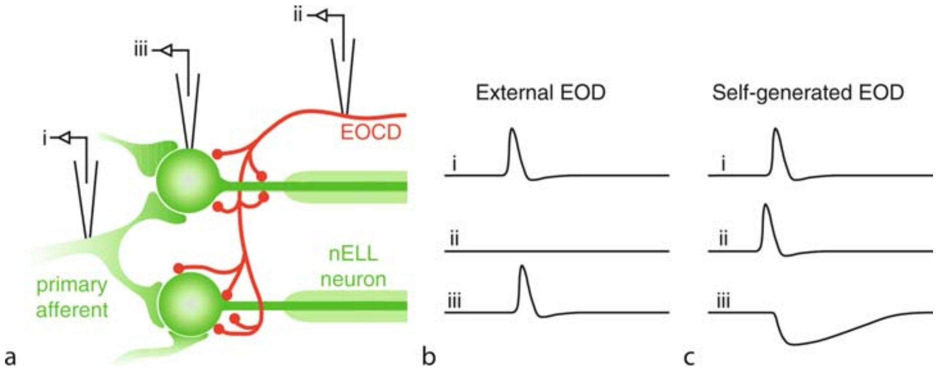
Specialized Features of Time-Coding Circuitry

The electromotor and electrosensory pathways of mormyrids are characterized by several unique anatomical specializations. Both pathways contain high levels of calcium-binding protein and consist of large, spherical, adendritic cell bodies that give rise to thick, heavily myelinated axons. Synapses in both pathways are typically mixed chemical-electrical, and often form large terminals that envelope a significant portion of the postsynaptic soma. Unlike most brainstem nuclei that occur in bilateral pairs, the CN and MRN form unpaired, midline nuclei. All of these features have been associated with neural circuits in which spike timing precision is of the utmost importance [9]. For the electromotor system, this precision is critical for activating the electrocytes in synchrony and thereby maintaining a constant EOD waveform. For the electrosensory system, it is involved in accurate temporal coding of the EOD waveform.

Higher Level Processes

Distinguishing Self-Generated EODs from External EODs

Knollenorgan receptors respond equally to any EOD that is above threshold, whether it is generated by the fish's own electric organ or that of another fish. In both cases, primary knollenorgan afferents generate a single spike that gives rise to an excitatory input to nELL [4]. However, the neurons in nELL also receive inhibitory input from the EOCD pathway [4], which causes the nELL neurons to respond quite differently to self-generated and external EODs (Fig. 3).



Reafferent Control in Electric Communication. Figure 3 Corollary discharge-mediated inhibition of reafferent electrosensory input in the nucleus of the electrosensory lateral line lobe (nELL). (a) Primary knollenorgan afferents form large, excitatory, mixed chemical-electrical synapses onto the soma of large, adendritic spherical nELL neurons. The electric organ corollary discharge (EOCD) pathway also provides inhibitory input onto the soma and initial segment of nELL neurons. (b) Patterns of activity recorded from the electrode locations shown in (a) in response to an external EOD. (c) Patterns of activity recorded from the electrode locations shown in (a) in response to a self-generated EOD.

When knollenorgan afferents respond to an external EOD, the EOCD pathway is not active. As a result, the nELL neurons only receive the excitatory afferent input, which they relay to the midbrain (Fig. 3b). By contrast, when the fish generates its own EOD, the EOCD pathway also becomes active, providing inhibitory input to nELL neurons. This inhibition blocks the response of nELL neurons to afferent electrosensory input (Fig. 3c), and the signal therefore does not get relayed to the midbrain [4]. As the reafferent input for this system is simply a brief excitation, the corollary discharge-driven efference copy is simply a brief inhibition.

Temporal Coding of the EOD Waveform

The EOD of a neighboring fish will cause current to flow into one half of the body surface and out the other, meaning that knollenorgans on these two surfaces will be exposed to opposite stimulus polarities. As knollenorgans only respond to positive-going voltage steps, those located where current is entering the skin respond to the rising edge of the stimulus, while those located where current is exiting the skin respond to the falling edge. Thus, by comparing spike times from opposite sides of the body, a mormyrid can, in principle, determine the duration of the EOD waveform [6].

A primary projection site of nELL axons is the anterior exterolateral nucleus (ELa) in the torus semicircularis (Fig. 4a). Within the ELa, there are two distinct types of neurons, large cells and small cells, both of which receive excitatory input from nELL axons. Upon entering the ELa, the nELL axons immediately terminate onto 1 or 2 large cells, and then wind their way throughout the nucleus over distances of 3 to 4 mm before branching and terminating onto a large number of small cells [6]. The large cells project exclusively within the ELa, terminating on small cells with large inhibitory synapses [6]. Thus, the small cells receive phase-locked input from two different sources: excitatory input from nELL axons and inhibitory input from ELa large cells (Fig. 4b). However, the excitatory input is significantly delayed by the time it takes an action potential to propagate down the long, winding path of the nELL axon, suggesting an “anti-coincidence detection” model for comparing spike times from knollenorgans on opposite sides of the body [6].

As an example, the small cell shown in Fig. 4b receives delayed excitatory input in response to stimulus onset and inhibitory input in response to stimulus offset. For short duration stimuli, this delayed excitatory input will arrive during the inhibition, and the small cell will not fire (Fig. 4c). As stimulus duration increases, however, there will be a greater delay before the inhibitory input reaches the small cell. If the duration is long enough such that the delayed excitatory input arrives before the inhibitory input, then the small cell will fire (Fig. 4c). Thus, a given small cell will only respond to EODs that are longer than some threshold duration. Assuming that different small cells receive input from nELL axons of varying delays, each small cell will have a different threshold value, and EOD duration will be reflected in the total number of active small cells [6].

Function

The Reafference Principle

Dealing with reafferent sensory input is a problem faced by all animals [1]. In the communication system of mormyrid electric fish, this problem is solved by a very simple, yet effective solution: incoming sensory input is blocked by inhibition every time the fish produces a

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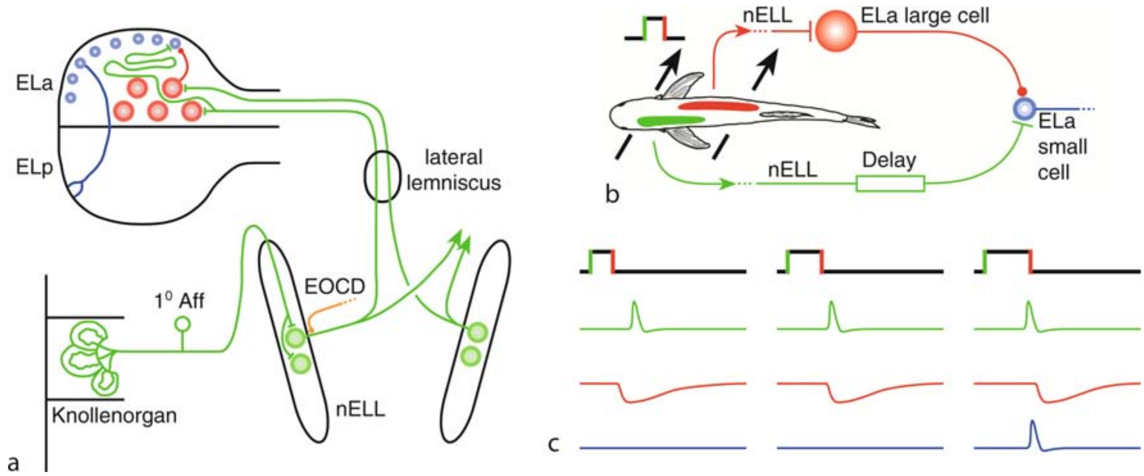

Reafferent Control in Electric Communication. Figure 4 Model of EOD waveform discrimination in mormyrids. (a) Neuroanatomy of the knollenorgan pathway. Excitatory connections are indicated by flat lines, inhibitory connections by solid circles. Primary afferents from knollenorgans project ipsilaterally onto the nucleus of the electrosensory lateral line lobe (nELL), which also receives inhibitory input from the electric organ corollary discharge pathway (EOCD). Axons from nELL ascend through the lateral lemniscus to project bilaterally to the anterior exterolateral nucleus (ELa) of the torus semicircularis, first onto large cells, then after winding throughout the nucleus, onto small cells. The large cells provide inhibitory input to the small cells. The small cells project ipsilaterally to the posterior exterolateral nucleus (ELp). (b) Schematic diagram showing the inputs to the small cell shown in (a) in response to a transverse square pulse. The ipsilateral side responds to the pulse onset, providing delayed excitatory input to the small cell, while the contralateral side responds to the pulse offset, providing inhibitory input to the small cell. c, Responses of the small cell shown in (b) to square pulses of varying duration. The green traces show the excitation provided by the nELL axon, while the red traces show the inhibition provided by the large cell. The blue traces show the resulting output of the small cell.

signal. Thus, the fish only senses the electric signals produced by other individuals. Recent studies have shown that this same strategy is used by singing crickets to block auditory responses to their own song [10]. Thus, corollary discharge-driven inhibition may be a widespread solution to dealing with the problem of reafference.

However, reafferent stimuli may often be much more complex, and the temporary blanking of responses afforded by simple inhibition may not be an effective solution. The earlier description of the effects of eye movement on visual processing is an illustrative example. Rather than brief excitation, the reafferent input in this case is a complex pattern of excitation and inhibition across many neurons over time, which is dependent on the specific eye movement undertaken. It is not sufficient to simply block incoming visual input during any movement, because this would result in complete blindness. In this case, rather than simple inhibition, the corollary discharge activates a spatiotemporally complex efference copy that cancels out the sensory input arriving from each portion of the visual field in response to the movement [1].

For active electrolocation in mormyrids, the fish's own EOD is the signal of interest, while those of other individuals constitute noise. Not surprisingly, then, the EOCD pathway provides excitatory, rather than inhibitory, input to the electrosensory pathway involved in active electrolocation and thereby facilitates reafferent sensory input [3]. However, much of this input is not informative, as it signals the presence of unchanging, or predictable, environmental features. In contrast to the hard-wired inhibition provided to the knollenorgan pathway, this corollary discharge-driven excitatory input can be altered through experience so that expected sensory input is nullified and only novel, informative input gets through [3]. This system provides an example of a modifiable efference copy, one that may be adjusted to compensate for changes in the sensory consequences of motor production.

Temporal Coding

Early research on electric communication in mormyrids focused on the SPI, because it was assumed that the EOD acted simply as a carrier signal for information encoded in a temporal pattern. The reasoning behind this was that EODs must be too brief to transmit any information. However, field recordings from mormyrids in the field revealed incredible species-specific diversity in the EOD waveform, as well as sex differences in many species [5]. Playback experiments in the field later demonstrated that these differences were behaviorally significant. In particular, EOD duration, or the relative timing of positive and negative voltage deflections were especially important [6]. These experiments therefore demonstrated that EOD recognition was mediated by a temporal code. In this chapter, we have seen a remarkable, yet simple, example of how the information contained within such a temporal code may be extracted through dedicated neuronal circuitry.

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Realism (Metaphysical, Internal, Common Sense, Naïve, Scientific)

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Definition

Realism is a metaphysical position concerning the status of objects, facts and properties which can be of the most different kinds. One may be a realist concerning objects in space and time like trees, rocks, and molecules, concerning abstract objects like numbers or values, properties like being red or facts like the fact that the earth is round. What does realism with respect to one or more of these types of items amount to? Unfortunately there is no shared view among the experts in the field as to how realism is best defined. The question is especially disputed among adherents of the various brands of realism and their critics, the so-called anti-realists. According to the definition shared by most (but not all) philosophers considering themselves realists, realism with respect to a certain item implies the following two claims: First, *the existence claim (EC):* The items in question exist. Secondly, *the independence claim (IC):* The items in question are neither themselves something mental (mere ►ideas or representations) nor is their existence in any way dependent on whether we represent them (that is, perceive them or think of them) in a particular way or not. If you believe, for example, that the earth exists independently of whether there is a being with mental states able to represent it then you are a realist about the earth. Realism is often restricted to certain types of items: one may be a realist concerning physical objects in space and time without being a realist concerning moral values. According to the two defining claims one might dispute realism concerning a certain item in two ways: by denying either (EC) or (IC). For example, realism about moral values can be denied either by denying that there are any such values in the first place or by admitting their existence but taking it to be completely dependent on our ability to devise such values.

According to the alternative definition put forward by anti-realists realism is not so much a theory about the nature of objects, facts or properties but a doctrine concerning the question of how the truth of sentences is best understood. The relevant conception of truth implies that truth is verification-transcendent, that is, a sentence might be true although we don't have the slightest possibility to find out that it is true. Anti-realists use this definition to criticize realism, because they take the verification-transcendent conception of truth to be at odds with their preferred accounts concerning the question of what is implied when a speaker understands a proposition [1]. Realists have objected to this characterization of their position that they see no need to commit themselves to any substantial notion of truth whatsoever by endorsing (EC) and (IC) [2]. This essay will therefore follow the first definition.

Description of the Theory

Realism cannot only be held with respect to different items, it can also be formulated with varying strength. These variations in strength are mainly due to the fact that (IC) can be interpreted in various ways. According