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# Progress in defining heterogeneity and modeling periglomerular cells in the olfactory bulb

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In recent years the evolution of olfactory bulb periglomerular cells, as well as the function of periglomerular cells in olfactory encoding, has attracted increasing attention. Studies of neural information encoding based on the analysis of simulation and modeling have given rise to electrophysiological models of periglomerular cells, which have an important role in the understanding of the biology of these cells. In this review we provide a brief introduction to the anatomy of the olfactory system and the cell types in the olfactory bulb. We elaborate on the latest progress in the study of the heterogeneity of periglomerular cells based on different classification criteria, such as molecular markers, structure, ion channels and action potentials. Then, we discuss the several existing electrophysiological models of periglomerular cells, and we highlight the problems and defects of these models. Finally, considering our present work, we propose a future direction for electrophysiological investigations of periglomerular cells and for the modeling of periglomerular cells and olfactory information encoding.

**periglomerular cell, patch-clamp, modeling and simulation, heterogeneity**

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Research into the mechanism of olfactory information coding is important to explore and understand the sensory nervous system, mechanisms of information coding in the brain and mechanisms of memory [1]. In the olfactory neural system, as the first synaptic junction relay station in the olfactory pathway, the olfactory bulb is an important structure for the integration and coding of olfactory information. Among the many types of olfactory bulb cells, periglomerular (PG) cells are often ignored because of their small size, the difficulty in obtaining them and their lack of special markers. In the evolution of the olfactory bulb, PG cells first appeared in amphibians but only in small quantities. However, when amphibians developed into reptiles and mammals, the number of PG cells increased rapidly, implying that the appearance of PG cells may be related to recognition of odor in the terrestrial environment, one which is quite different from the aquatic environment. Odorous chemicals in the terrestrial environment are hydrophobic and unstable [2]. Regardless, the evolution and function of PG cells in olfactory information processing remains very unclear [3].

In studying the mechanisms of physiological systems, physiological system modeling and simulation play an important role because they can simulate conditions that cannot be achieved in a physiological experiment. In the field of neuroinformatics, the modeling and simulation of the electrophysiological characteristics of neurons are of great significance to the coding of neural information. For example, Laurent *et al*. [4] and Bazhenov *et al*. [5] studied syn-

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chronous oscillation in insect olfactory electrophysiological activities by developing an anatomical model of locust antennae. Brody *et al.* [6] built a simple network model according to the properties of animal olfactory systems in order to verify how the olfactory system distinguishes different odors by peak synchronization. Similarly, during the process of identifying the impact of peak synchronization on invertebrate olfactory information coding, Linster *et al.* [7] were successful in adjusting uncontrollable variables in a physiological experiment. Therefore, building a sophisticated electrophysiological model of PG cells in order to study the evolution of PG cells and their effect on olfactory information coding is crucial.

Recently, through the study of PG cell modeling, researchers have found that when olfactory sensory neurons are subjected to weak odor stimulation, the feedforward inhibition effects of PG cells on mitral cells play a leading role in olfactory information coding. However, when subjected to strong odor stimulation, the excitatory effects that olfactory sensory neurons have on mitral cells play a leading role. In addition, PG cells enhance the contrast of the coded information between the first level and second level neurons [8,9], similar to contrast enhancement of the retina in the visual nervous system. Although the PG cell models used in the research above are imperfect, these preliminary results conform to the basic laws of neurophysiology. Moreover, they encourage scientists to further their research on the physiological mechanism of PG cells.

## 1 Anatomical structure of the olfactory system and the mechanism of olfactory information coding

As shown in Figure 1, the mammalian olfactory system consists of an olfactory epithelium, an olfactory bulb and an olfactory cortex, all of which have a laminar organization [10]. The primary neurons in olfactory bulbs include mitral and tufted cells. The neurons of the glomerular shell are referred to as juxtaglomerular (JG) neurons [11,12]. The JGs neurons can be morphologically classified as one of three types: periglomerular (PG) cells, slightly larger external tufted cells and short axon cells. Granule cells are a kind of interneuron and constitute the largest population in the olfactory bulb. Compared with primary neurons and granule cells, PG cells are small with a soma 5–8 μm in diameter. They are distributed around the glomeruli and their dendrites project to a single glomerulus or to several adjacent glomeruli. Their axons extend further into several glomeruli. Generally, the membrane capacitance of rat PG neurons is (7.2±0.2) pF. The resting potential is (−52±7) mV and membrane resistance is (750±63) MΩ [2]. Figure 2A shows the olfactory bulb cells of a postnatal SD rat culture after 7 d *in vitro*. Figure 2B is a picture of PG neurons under an optical microscope.

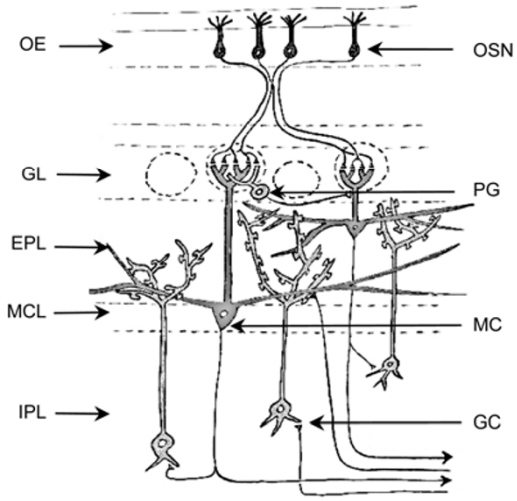



**Figure 1** Principal neurons of the olfactory epithelium and olfactory bulb, their connections and locations. Abbreviations: OE, olfactory epithelium; GL, glomerular layer; EPL, external plexiform layer; MCL, mitral cell layer; IPL, internal plexiform layer; OSN, olfactory sensory neuron; PG, periglomerular cell; MC, mitral cell; GC, granule cell.

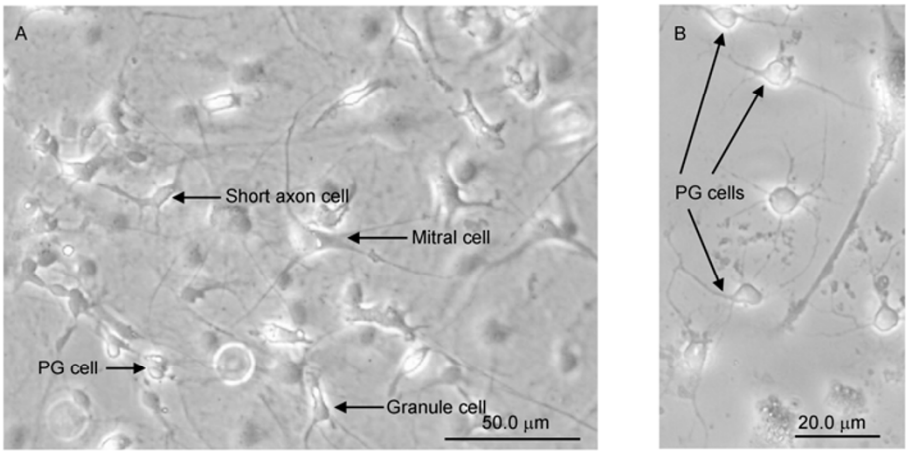



**Figure 2** Olfactory bulb cells. A, Olfactory bulb cells of a postnatal SD rat culture after 7 d *in vitro*. Mitral cells, granule cells, PG cells and short axon cells can be distinguished morphologically. B, PG cells.

Synaptic connections in the olfactory bulb can be classified into two types. One is the connection between mitral cells and granule cells, and the other is the connection between mitral cells and the interneurons around the glomeruli [13]. Connections between mitral cells and granule cells, including two kinds of dendrite-dendrite connection, were understood quite clearly. They are the direct connections between mitral cells and granule cells, and the indirect connections in the feedback loop between mitral cells, cortical neurons granule cells and the mitral cell pathway. Granule cells generally have a depressive effect on mitral cells and tufted cells. However, some studies suggest that a proportion of the mitral cells have excitatory connections with mitral cells and tufted cells [14]. The mechanism of the synaptic connection between mitral cells and interneurons around the glomeruli is not completely understood. The glomeruli contain the axon terminals of olfactory sensory neurons as well as the dendrites of mitral cells, tufted cells and PG cells. The olfactory sensory neurons are glutamatergic and have excitation effects on PG cells, mitral cells and tufted cells. All mitral cells, tufted cells and PG cells have NMDA receptors and non-NMDA receptors. PG cells generate synaptic connections with the primary dendrites of mitral cells. PG cells are GABAergic and have a depressive effect on mitral cells and tufted cells. However, some studies have indicated the presence of excitatory connections between these cells [15]. The properties of the synaptic connection between PG cells and primary neurons need to be studied further.

The release of neurotransmitters as well as the opening and closing of ion channels in the neural network described above result in synchronous oscillations of the olfactory sensory neuron cluster [16,17]. Neuron cluster coding analysis is currently a primary means of studying the mechanism of neural information processing, which includes frequency coding and space-time coding [18]. In addition, information entropy analysis provides a new approach to investigate neural information coding. Information entropy analysis of neural network firing sequences allows us to verify how neural information coding adapts to changes in input of sensory information from a systematic and holistic perspective. It also allows for the study of problems in neural information transmission, including the efficiency of transmission [19].

## 2 Heterogeneity of periglomerular cells

Early studies generally agreed that periglomerular cells were homogeneous [20]; however, recent experiments and studies have shown that periglomerular cells are heterogeneous [11,21–24]. Periglomerular cells have a variety of subpopulations. The main classification methods include chemical heterogeneity, the morphology of synaptic connections and electrophysiological experiments.

The first classification is based on immunochemical reactions. There are six molecular markers in the periglomerular region of the rodent main olfactory bulb: four neuroactive substances, namely GABA or its key synthesizing enzyme glutamic acid decarboxylase (GAD), dopamine or its key synthesizing enzyme tyrosine hydroxylase (TH), enkephalin (ENK) and thyrotropin-releasing hormone (TRH). The remaining two markers are calcium-binding proteins, namely calretinin (CR) and calbindin D28K (CB). Kosaka *et al*. [11] classified periglomerular cells into three distinct groups: GABA-like immunoreactive (LIR) and/or GAD immunoreactive (IR), CR-IR and CB-IR cells. They constitute 20%, 20% and 10% of periglomerular cells, respectively. Furthermore, TH-IR, TRH-IR and ENK-IR neurons are regarded as subpopulations of each group.

The second classification method is based on the morphology of synaptic connections. Kosaka *et al*. [11] classified glomeruli into two compartments, the olfactory nerve (ON) zone and the non-ON zone. The ON zone is the site where olfactory sensory cells make synapses on their targets. The non-ON zone is where dendrodendritic interactions between intrinsic neurons occur, as shown in Figure 3B. Type 1 PG cells send their intraglomerular dendrites into the ON and non-ON zones. Type 2 PG cells send their intraglomerular dendrites into the non-ON zone only. Type 1 PG cells include GABA-LIR and/or GAD-IR and TH-IR cells, whereas type 2 PG cells include CB-IR and CR-IR cells [25]. How-

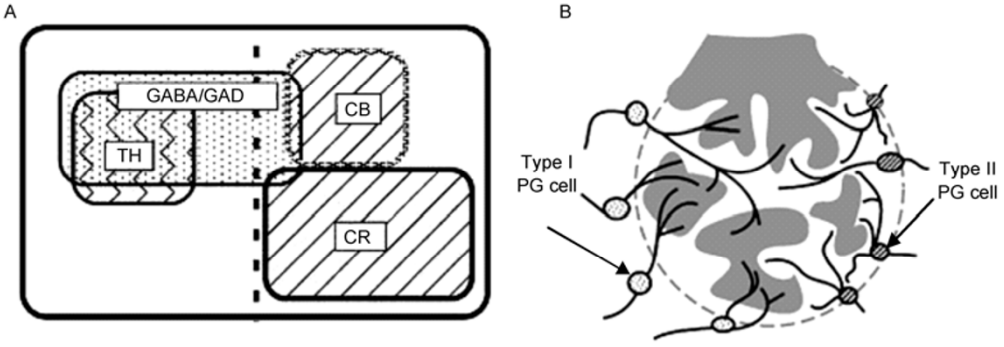



**Figure 3** Classification of PG cells. A, The ratio of different kinds of PG cells classified according to their immunochemical reactivity. B, Distribution of type I and type II PG cells. The gray area indicates olfactory sensory neurons, while the white area indicates non-olfactory sensory neurons.

ever, not all GABA-LIR and/or GAD-IR and TH-IR cells are Type 1 PG cells.

From the perspective of electrophysiological modeling, these two classification methods do not have much to do with the modeling of PG cells. However, there is a high reference value in the accurate modeling of the olfactory bulb network. For example, defining the proportion of different PG cell subpopulations in a network according to the actual anatomical structure helps to increase the authenticity of the network model.

The third classification method is based on the characteristics of $K^+$ conductance. Whole-cell recordings were established in 132 PG cells by Puopolo and Belluzzi [26]. Patch-clamp experiments show that one group of PG cells displays a long plateau potential after an action potential and shows an usual outward rectifying behavior at depolarized potentials. This group, defined as R, displays an outward rectification at depolarized potentials. This neuronal population has two distinct potassium channels: a fast, transient A-type conductance, and a classical delayed rectifier $K^+$ conductance. The A-current is larger than $I_{KV}$, but the two maximal conductances are not very different ($g_A/g_{KV}$= 1.5). The second cell type, defined as N, displays a prominent A-current (9 nS), with a delayed rectifier conductance that is very small or completely absent ($g_{KV}$=0.63 nS, $g_A/g_{KV}$=14.5). A third cell type displays mixed properties. The various cell types are present in approximately equal proportions at all ages studied (36.3% for R-type, 34.7% for X-type and 29% for N-type). Basically, under current-clamp conditions, these cells rectify in an outward direction, but more slowly than and not as thoroughly as R-types. The three cell types have no obvious differences in passive membrane properties ($R_m$ and $C_m$) or morphology. Additional observations show that the total $K^+$ conductance appears to be much the same in all cell types, and that all cell types respond with a single action potential to prolonged depolarization [26].

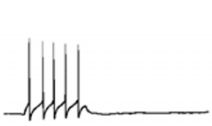
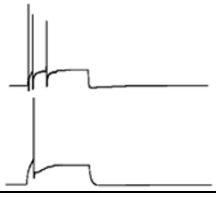
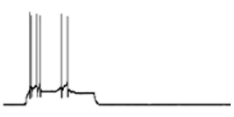
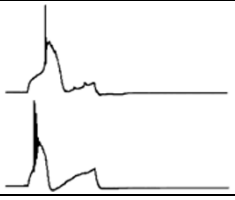
The fourth classification method is based on the response to depolarizing pulses. Different subpopulations of cells vary in the type, number and distribution of ion channels on the cell surface, and therefore respond to the same depolarizing current pulse stimulation with different action potentials. These differences are mainly reflected by the amplitude and the frequency characteristics of single cells. In neural networks, these differences can also be embodied in synchronization and intermittent interaction effects. Differences in the action potentials produced may indicate different types of nerve cells or neural networks.

The firing of periglomerular cells contains spontaneous activity and responses to depolarizing pulses. Puopolo [27] and Pignatelli [28] examined the spontaneous activity of PG cells of mice. They found that TH-IR PG cells are the only type that fire with a spontaneous rhythmical activity. The persistent $Na^+$ current and T-type calcium current play vital roles in this spontaneous activity. McQuiston and Katz [29] studied the responses of PG cells in mouse slices to depolarizing pulses using whole cell patch-clamp techniques. Based on their response to depolarizing pulses, PG cells could be divided into two physiological classes: bursting and standard firing (Table 1). Standard firing cells accounted for 33.3% of the PG cells and bursting cells for 66.7%. When depolarized, the standard firing neurons exhibited a range of responses: accommodating, non-accommodating, and irregular firing patterns of action potentials. Bursting neurons produced a calcium-channel-dependent low-threshold spike (LTS) when depolarized by either current injection or spontaneous or evoked postsynaptic potentials [29].

Comparison between the results of Puopolo and McQuiston reveal obvious differences. Electrophysiology studies prior to those of McQuiston, for example, by Bardoni *et al.* on frog periglomerular slices [30] or patch-clamp experiments on rat olfactory bulb slices performed by Puopolo and Belluzzi [31], failed to discover the LTS. In these studies, PG cells fired single or multiple action potentials under a depolarizing current input. However, PG cells in olfactory bulb slices of young rabbits did not fire action potentials [32]. McQuiston and Katz [29] found that the LTS is quite sensitive to recording time and temperature. To sum up these studies, the reason Belluzzi *et al.* failed to find the LTS is possibly because of differences between species or in experimental conditions (temperature, recording time, solutions, and the patch-clamp equipment).

Overall, the last two classifications are based on microscopic ion channels and macroscopic action potentials. These two classifications are somehow related, so the modeling of PG cells may include an inherent unity.

**Table 1** Action potential pattern of rat periglomerular cells under depolarizing current injection

| Standard (33.3%) | | | Bursting (66.7%) |
|---|---|---|---|
| Non-accommodating (9.5%) | Accommodating (14.3%) | Irregular firing (9.5%) | Low-threshold spikes |
|  |  |  |  |

## 3 Modeling of periglomerular cells

Simplified neuron modeling methods have been widely used in neural computational simulation modeling to improve computing speed. Generally, there are two kinds of simplified methods. The first focuses on the electrophysiological properties of the cells by keeping constant the membrane time and input impedance while reducing the number of compartments. The second is to abstract electrophysiological characteristics of cells by reducing the number of compartments and ion channels on the premise of maintaining the same reaction output. It is hard to acquire physiological data from periglomerular cells in patch-clamp experiments because of their small size. To date, no complete model of periglomerular cells has been established and no model has been established according to their heterogeneity. This section lists three simplified models of periglomerular cells and analyzes their advantages and disadvantages.

The first model is a single-compartment model established by Pignatelli [28] on the basis of patch-clamp experiments. The model contains five kinds of ion currents: a fast transient sodium current, $I_{Na(F)}$, a persistent sodium current, $I_{Na(P)}$, a delayed rectifier potassium current, $I_{Kr,}$ an L-type calcium current, $I_{Ca(L)}$, and a T-type calcium current, $I_{Ca(T)}$. The model studied the spontaneous activities of mouse TH-IR periglomerular cells. The simulation results are shown in Figure 4A. The model fires a single action potential in response to a depolarizing current pulse. Both $I_{Na(P)}$ and $I_{Ca(T)}$ are necessary to sustain spontaneous firing as the selective blocking of one or both will abolish spontaneous activity. The interactions of these subthreshold currents lead to the spontaneous activities of periglomerular cells. These models help to guide electrophysiological experiments of periglomerular cells. Calcium currents contain several components. The larger of these components is the L-type calcium channel current, while low-threshold T-type calcium currents play an essential role in the autorhythmic process. Moreover, some studies reveal that the T-type calcium channel is also a key factor in determining the LTS of periglomerular cells. In addition, the model partly reveals the influence of periglomerular cells in olfactory information coding. First, this kind of cell is a Category I periglomerular cell, according to the morphology of synaptic organizations. Combined with the simulation analysis results, the TH-IR periglomerular cells have been shown to connect the olfactory sensory neuron zone to the non-olfactory sensory neuron zone of the glomeruli in the olfactory signal transduction pathway. The dendrites of these cells receive excitatory input from the axon terminals of olfactory nerve cells and the activation of TH-IR periglomerular cells will reduce the excitability of primary neurons through synaptic connections. Second, the spontaneous action potential of TH-IR periglomerular cells means a continuous release of dopamine to a certain area, thus inhibiting the olfactory sensory neurons. Thus, TH-IR periglomerular cells impact the process of olfactory information encoding on two levels.

However, the model still has some inadequacies. First, the source of data in the model is not complete. Because of the technical limitations of electrophysiological experiments with periglomerular cells, the model fails to fit the inactivation parameters of T-type calcium currents, and some of the ion channels and passive parameters are obtained from external tufted cells instead of from periglomerular cells. Second, the application of the model is quite limited. It studies the spontaneous characteristics of the TH-IR periglomerular cells, but this kind of periglomerular cell is only a small subpopulation of periglomerular cells. The model ignores the potential response of periglomerular cells under synaptic input.

The second model is a five-compartment mammalian model created by Arruda *et al.* [33]. The model was adapted from that of Davison [34] and abstracted the periglomerular cells into five compartments: soma, primary dendrites, secondary dendrites, axon and dendritic spines. A sodium current, $I_{Na}$, exists in the soma and axon, and the transient potassium current, $I_A$, the rectifier potassium current, $I_{KV}$, hyperpolarization-activated cation current, $I_h$, the low threshold T-type calcium current, $I_{Ca(T)}$, and the calcium diffusion mechanism exist in the soma, dendrites and dendritic spines. The simulation results are illustrated in Figure 4B, which shows the potential fire mode of accommodating PG cells. First, the model has more compartments compared to the first model and the accuracy of the morphology and passive parameters are increased significantly compared to the single compartment model, allowing the model to better fit

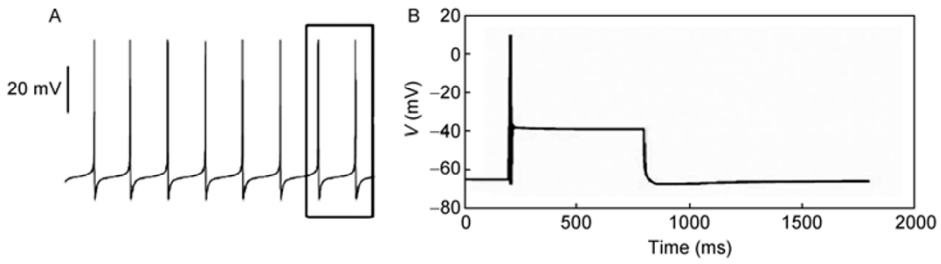



**Figure 4** The results of modeling PG cells. A, Simulation results of rat spontaneous TH-IR PG cells. B, Voltage response of the five-compartment model in mammalian PG cells.

physiological conditions. Second, these two models have slight differences in the choice of ion channel types. This difference may be attributable to the different species or to the heterogeneity of periglomerular cells. $I_h$ was not inserted into the first model. Based on experimental studies, $I_h$ does not exist in the TH-IR periglomerular cells of mice and it was not the cause of spontaneous activities. $I_h$ was added in the second model, and according to Cadetti, $I_h$ contributes to the resting potential and to the synchronous oscillation of periglomerular cells in the olfactory bulb network [35]. Therefore, the presence of $I_h$ and its role in the olfactory coding process will become a focus of electrophysiological studies.

However, the above model still has several shortcomings. First, the kinetics of the five ion channels inserted into the model do not fit with data obtained through electrophysiological experiments of periglomerular cells but instead are adapted from corresponding ion channels of other neurons (such as the hippocampal CA3 vertebral neurons). Second, the model does not consider the heterogeneity of periglomerular cells, but only covers the accommodation of periglomerular cells. Furthermore, the model does not analyze the role periglomerular cells play in the olfactory information encoding process. These issues are further studied and discussed in the author's doctoral dissertation [36].

The third model is a single-compartment model of GABA-LIR periglomerular cells established by the research group of the National Biosensor Laboratory of Zhejiang University [37]. The model contains four ion currents: the sodium current, $I_{Na}$, delayed rectifier $K^+$ current, $I_{Kr}$, transient potassium current, $I_A$, and transient calcium current, $I_{Ca.}$ As shown in Figure 5A, varied depolarizing current pulses (10, 40, 70, and 100 pA) were used to test the model. The firing frequency increased with the stimulus intensity. With the action potential time interval kept constant, under certain stimulus intensities, the simulation results of the model are consistent with physiological experiments (Figure 5B). These cells belong to the non-accommodation periglomerular cells.

However, this model is also not complete. First, the data the model uses combines the electrophysiological parameters of frogs, rats and other species because of a lack of supporting evidence from electrophysiological experiments. Second, unlike the previous two models, the choice of ion channels remains to be improved. The T-type calcium current has been shown to play an important role in the electrophysiological properties of periglomerular cells and hyperpolarization-activated cation currents also affect the olfactory network coding process, but this model does not incorporate the two ion currents. Finally, the model simulates a single subpopulation of periglomerular cells without considering the heterogeneity of periglomerular cells.

## 4 Outstanding problems and future research on periglomerular cells

In summary, our understanding of the electrophysiological heterogeneity and simulation modeling of PG cells is not yet mature, and the role PG cells play in olfactory pathways and their effects on olfactory information coding are still not fully explained. This section discusses the remaining problems in PG cell research and highlights future studies.

### 4.1 Methods for identifying periglomerular cells

To identify PG cells in cultured slices, target cells can be identified according to the anatomical structure of the olfactory bulb and the membrane capacitance of PG cells, but the electrophysiological signal collected may be affected by synapses of the surrounding cells. After culturing scattered nerve cells for a period of time to allow the regeneration of

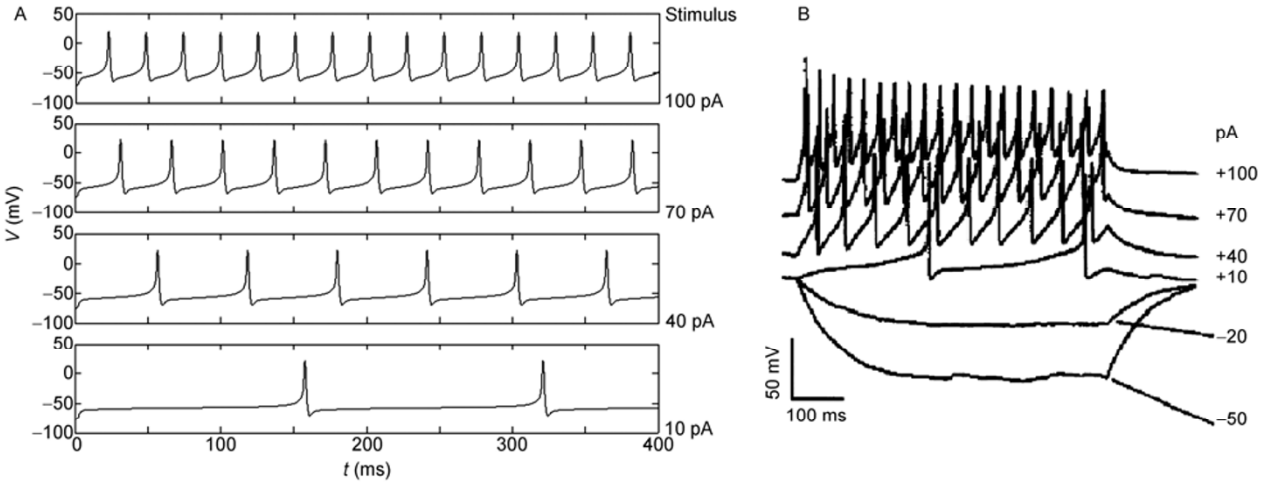



**Figure 5** Comparison of PG cell modeling results and the practical electrophysiology data. A, Voltage response of the single-compartment model for GABA-LIR PG cells. B, Voltage response of a PG cell to injected currents from a resting membrane potential of −70 mV.

neuron processes, single-cell patch-clamp experiments offer a more robust approach. However, because of the lack of specific markers, difficulties remain in the isolation, culture, and experimentation of PG cells. Thus, the identification of PG cells through molecular biological methods is a problem that needs to be solved.

### 4.2 Electrophysiological experiments and single-cell modeling of PG cells

First, the electrophysiological data source for PG cell modeling is quite limited, so collecting data from the same species remains a problem. Second, LTS is the main firing pattern among the four patterns. The LTS of the CA3 hippocampal vertebral nerve has been studied by Migliore *et al*. [38], while Destexhe *et al.* [39,40] have studied hypothalamic interneurons and thalamic reticular neurons, and Pinato [41] and Midtgaard [42] have studied granule cells. These studies have shown that the LTS may be related to T-type calcium currents and potassium currents. They also show that the distribution density of T-type calcium channels is not uniform, but is instead concentrated in the distal dendrites. Therefore, the experiments to determine the electrophysiological properties of PG cells will become a new focus of research. Furthermore, the pulsating electric field method is more effective for studying dendrite electrophysiology but this method has not yet been applied to PG cell research. In this regard, the future focus of the research team of Zhejiang University will be on PG cell patch-clamp experiments. We will collect complete electrophysiological data and further study the ion channel mechanisms of PG cell electrophysiological responses.

From the perspective of single-cell simulation modeling, the PG cells will be modeled according to their heterogeneity. As discussed in Section 2, we propose a new classification of PG cells based on a comprehensive consideration of potassium and calcium channels by dividing PG cells into six types: the LTS lacking cells, including N1-, R1- and the X1-types and those with LTS firing behavior, including N2-, R2-, X2-types. The mechanism of T-type calcium currents, potassium currents and the hyper-polarization activated action currents will be the focus of single-cell modeling research.

### 4.3 Investigating the cellular mechanisms of periglomerular cells based on a complete olfactory bulb network model

At present, research teams at the University of Sao Paulo, Brazil, and Zhejiang University are studying the functional mechanism of periglomerular cells under a complete olfactory bulb cell network model [36,37]. This study combines mitral cells and granule cells to build a three-layer olfactory network model that is then used to analyze the function of PG cells in olfactory bulb encoding. Our results show that PG cells influence the frequency of mitral cells less than that of granule cells, but that the interaction between PG cells and mitral cells decreases the synchronization of mitral cells in the network. This may be attributed to the release of inhibitory neurotransmitters from PG cells. As mentioned earlier, to explore the mechanism of PG cell evolution and its function in olfactory information coding, quantitative statistical methods can be introduced into future research. One example would be employing the information entropy method to evaluate the influence of PG cells on the output neurons in different network structure models (with or without PG cells, varied synaptic connections). In addition, more attention should be paid to the subpopulations of PG cells in the network model.

### 4.4 Investigating cellular mechanisms of PG cells based on nerve cell chips

In recent years, neurobiology and molecular neurobiology have become two important branches of neuroscience. They are also the foundation and bridge to study neuroinformatics at the cellular and subcellular level. The tendency to work at smaller scales and to be more quantitative in analysis is becoming more important in today's neural information science. Examples include a 2010 publication in *Science* that claimed dendrites of cortical neurons can discriminate the spatial and temporal sequence of electrical input (based on the pulse mode information decoding hypothesis) [43], and a 2006 publication in *Science* showing electrophysiological modeling based on ion channels and neurotransmitters transmitting by synaptic connections [44].

Micro-electrode arrays (MEAs) can simultaneously record the action potentials of multiple cells or multiple neuronal synapses or organization propagation in a non-destructive manner, thus providing a powerful tool for these types of studies [45]. The Zhejiang University research group collects electrical signals by culturing olfactory nerve cells on the surface of MEAs and then analyzes their spiking rate, threshold and frequency. The results were published in *Biosensors and Bioelectronics* [46]. Part of the device is shown in Figure 6. Considering the current problems surrounding PG cell research, our next task is to develop integrated chips based on the MEA and directed growth of nerve cells. Chips produced by microfabrication technology can realize controllable growth and controllable synaptic connections and can be used in high-resolution electrophysiological testing of olfactory nerve cells. This device is shown in Figure 6D. We have applied for two national invention patents for this technology. Detailed and quantitative experimental research into the properties of PG cells can be carried out using this technology.

### 4.5 Simulation modeling of PG cells based on the olfactory bulb nerve cell chip

A reasonable neural network model is essential for neuro-

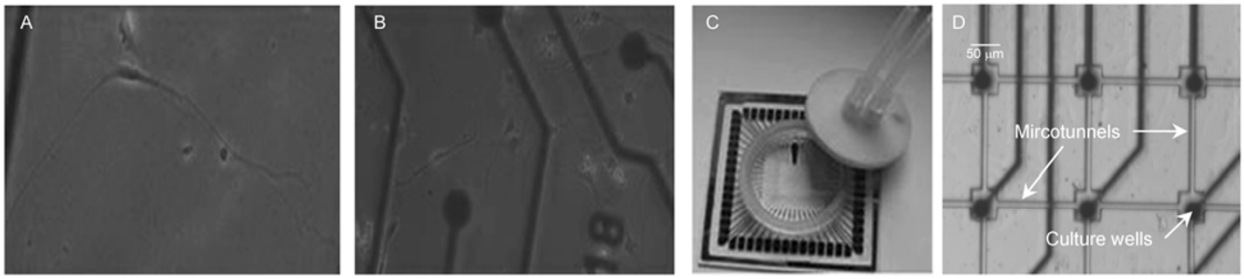



**Figure 6** The devices used for studies on the electrophysiology properties of PG cells. A, Individual olfactory sensory neurons on the surface of the MEA. The cilia are about 250 μm. B, Olfactory sensory neuron neural network on the surface of the MEA. C, Olfactory sensory neuron chip and the culture well. D, Growth direction controllable neuron culture chip composed of a PDMS device and an MEA.

science computation. The unit properties and connections of many established network models are set too subjectively. The building of network models based on real biological neural networks and cognitive function, including anatomical connections (taking into account the limit of space) and functional connections (taking into account the exchange of information and integration) deserves special attention in the future. With further research on nerve cell electrophysiology by neurobiologists and neural information scientists, controlled growth of neural circuits and precise emersion is necessary to study the dynamic behavior of neurons at a sub-cellular level. The above cell chip was based on microelectronic technology, which can control the orientation of cultured nerve cells and can overcome the difficulties in extracting the actual neural network structure caused by the uncertainty of neural network growth. This then provides a reliable experimental basis for controlled growth of neural circuits and precise emersion. On this basis, the electrophysiological signals of the chips recorded by the microelectrode array will yield much accurate and precise kinetic information on the propagation of nerve signals, which will be a great help for neural computation and also provide strong evidence for the validation of these models. Finally, this simulation modeling of PG cells based on the olfactory nerve cell chip provides a good way for people to explore the physiological mechanism of PG cells and their role in olfactory information encoding.

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