PIBB 生物化学与生物物理进展
Progress in Biochemistry and Biophysics
2016, 43(4): 367~373
www.pibb.ac.cn

脑功能原理：神经细胞编程和信息储存 *

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摘要 大脑采集感觉信息、整合认知和控制行为过程，这些任务的实现依赖于神经细胞及其环路的信息储存与编程. 澄清神经信息编程与储存的原理是研制拟脑计算机的基础. 本文将基于神经细胞的模拟 - 数字信号转换、数字信号兼容式输出以及新信息储存与提取等方面的研究揭示脑认知原理.

关键词 神经元编码，记忆细胞，神经元，突触和神经环路
学科分类号 Q42 **DOI**: 10.16476/j.pibb.2016.0079

脑的基本单元是神经元和神经胶质细胞. 神经细胞之间以及神经细胞群集核团之间的协调是基于神经网络和细胞程序语言的有效沟通，是脑功能完成的基础. 神经细胞语言分为化学和电学两类，它们可以互相触发并转换. 化学语言是以细胞内信使和细胞间递质为基础的，电学语言是以神经细胞电活动和突触电信号传递为基础的. 化学语言是分子的群体行为，目前缺乏对这些分子过程的定量分析手段，本文的重点将放在神经细胞电学语言的编程原理.

神经细胞电学语言的本质是膜电位脉冲. 阈下电位可被理解为细胞编制的连续式模拟信号，包括突触信号传递的突触电位和神经元自发活动的起搏电位等. 动作电位可被理解为细胞编制的离散式数字脉冲信号，后者类似计算机核心处理器产生的 1 和 0 数字信号. 换句话说，除了编程类似核心处理器的数字信号，神经元还能编程模拟信号和控制模拟 - 数字信号转换. 神经细胞程序比计算机复杂是目前脑功能不能被人工智能取代的原因.

1 神经细胞信号编程

神经元的亚细胞结构包括接受突触输入信号的树突，整合模拟信号并使之转换为动作电位的胞体和动作电位输出的轴突及其分枝[1-3]. 接收、整合和输出神经信号的规律与稳态是神经元编程的基础.

1.1 突触模拟信号

化学突触传递过程包括突触前末梢动作电位触发的神经递质释放、递质作用于突触后膜受体、受体介导离子通道开放以及带电离子在电化学势能驱动下跨膜流动，进而产生突触后膜电位波动. 突触模拟信号的幅度与时程受到递质释放量、递质释放模式(囊泡释放及其同步性)、受体反应性、受体密度数量以及离子电化学驱动力等因素的影响. 这些因素的综合作用使得突触传递动力学表现为突触传递易化 (synaptic facilitation) 和突触传递抑制 (synaptic depression)[4-5].

1.2 突触模拟信号整合与神经元数字信号编程的规律

每个神经元接受成百上千的兴奋性和抑制性突触输入，突触传递多脉冲信号的模式表现为渐进性易化和衰减性抑制(图 1). 单个突触在不同的时相可表现这两种传递模式的交替，调节神经递质释放

* 国家自然科学基金(81471123)和国家重点基础研究发展计划(2013CB531304)资助项目.
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收稿日期：2016-03-11，接受日期：2016-03-17

和受体反应性可以使突触传递交替转化模式变为相对单一的模式[6-7]．在神经递质是否为量子式释放，递质释放概率的高低和受体反应性的强弱等因素的作用下，突触传递动力学有很大的变异范围[4-6]．由此导致来自众多兴奋和抑制性突触模拟信号的线性和(/或)非线性整合是相当复杂的．再结合神经元的内在特性[8-9]，整合信号驱动突触后神经元编程数字动作电位信号的模式是相当广谱的．这些神经元编程 1 和 0 组合码的多样性是神经细胞语言编程既丰富又精确的基础．

就突触整合信号驱动神经元编程数字动作电位的规律(或者说是神经元分析突触模拟信号使之转化为动作电位数字信号的规律)，目前研究提示的要点如下：a．突触后受体反应性的增加使得突触传递的波动模式转化为单一的抑制型模式，依据该单一模式整合的模拟信号能够增强神经细胞编程能力和精确性[6]．b．突触前神经递质的量子式释放可以增强整合的模拟信号驱动神经细胞编程能力和精确性[10]．c．神经递质释放概率的增加可以增强整合的模拟信号驱动神经元编程能力和精确性[7]．d．低强度的抑制性突触信号可以增加整合的模拟信号驱动神经元编程能力和精确性，较强的抑制性突触信号则降低整合的模拟信号驱动神经元编程能力和精确性[9, 11]．e．突触数量以及兴奋 / 抑制性突触的比例与模拟 - 数字信号转换能力成正相关．f．突触输入信号强度和神经元胞体编程能力之间具有代偿互补关系，从而维持神经元编程及输出的稳态，这有利于记忆信息的保持[11]．

1.3　神经元数字信号编程的起源部位

研究显示，短脉冲驱动神经元产生单个动作电位是起源于轴突起始段[12-18]．这个结论是否也适用于数字式序列动作电位？研究提示，生理性突触整合信号驱动神经元胞体产生数字式序列动作电位，长时程模拟信号驱动神经元胞体产生序列动作电位，短脉冲驱动神经元轴突产生单个动作电位(图 1)，这种依据输入信号模式而决定动作电位起源部位之目的是在于节省细胞能源消耗[19-20]．由于脑内突触整合信号均是长时程的，神经元发放的是序列动作电位，因而神经元编程数字信号是起源于细胞体的．轴突始段的高密度钠离子通道可能是用来放大幅度不完整的动作电位[21]．

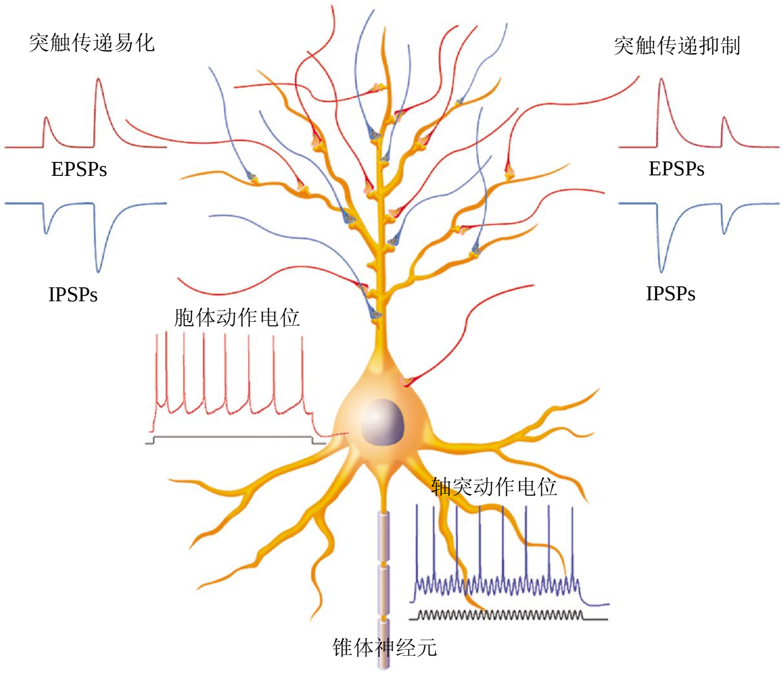

Fig. 1　The reception and integration of synaptic inputs in a pyramidal neuron

图 1　神经元接受与整合突触输入信号

红色轴突和曲线分别表示参与兴奋性突触形成和兴奋性突触后电位；蓝色轴突和曲线分别表示参与抑制性突触形成和抑制性突触后电位．连续脉冲诱导突触反应的递增被称之为突触传递易化；连续脉冲诱导突触反应的递减被称之为突触传递抑制．整合的长时程信号诱导胞体产生动作电位；短时程波动信号诱导轴突始段产生动作电位．

1.4 轴突输出数字动作电位信号的特征

对活体动物的研究显示，序列动作电位的幅度是变化的[22]．动作电位的幅度是否也携带神经信号编码呢？研究发现，胞体产生的低幅度动作电位在经过轴突传向其末梢时可以被放大，使得神经末梢的序列动作电位趋于等幅度(图 2)，触发下一级神经元突触信号近似等高度[21]．计算机模拟研究支持这一结论[23]，即轴突放大功能使得神经元输出数字信号编码．另一方面，轴突对高频动作电位有限频作用，即高频动作电位传导过程中的频率衰减[24-26]，这可以防止下一级神经元受到上一级神经元的强脉冲信号的冲击．

神经元轴突通常有许多分枝，轴突分枝支配到不同的神经元；受支配的突触后神经元具有不同的兴奋性[6, 27]．这就要求轴突分枝有不同的功能状态以维持每一突触前分枝与突触后神经元伴侣的功能匹配．研究显示，轴突分枝在动作电位传导能力上是分化的，并且与其突触后神经元伴侣产生动作电位的能力呈线性相关(图 3)，这种突触前后伴侣的功能兼容匹配可以防止某些伴侣的功能沉默或者亢进，从而构成神经网络连接的基本原则[28-30]．

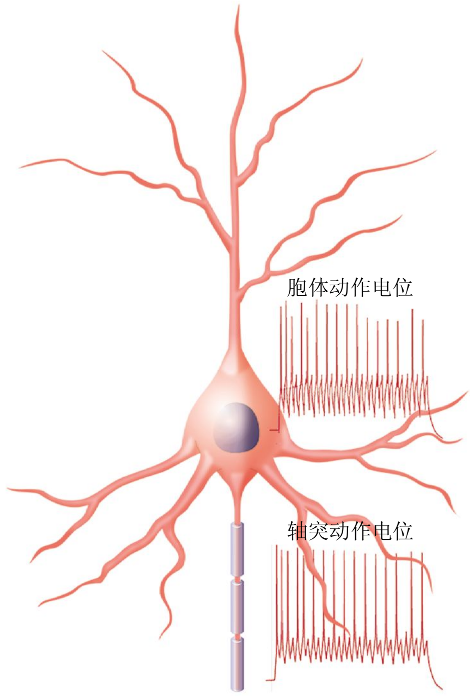

Fig. 2 Somatic spikes are amplified at the axon

图 2 轴突放大神经元胞体产生的动作电位

在细胞体和轴突的配对胞内电生理记录显示，神经元胞体产生的动作电位在幅度上是变异的，这些动作电位在传导到轴突后则是完整而等幅度的．

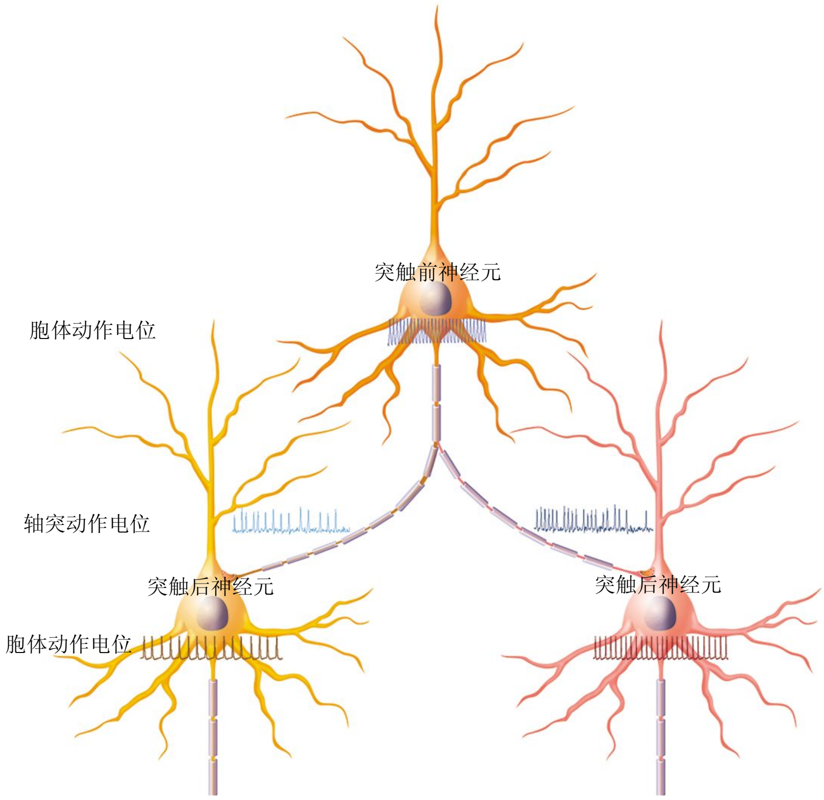

Fig. 3 Functional compatibility between presynaptic axon branches and postsynaptic nerve cells

图 3 突触前轴突分枝与其支配突触后神经元的功能匹配

一个突触前神经元通过其轴突分枝支配许多功能不同的突触后神经元．突触前神经元的动作电位沿着其轴突分枝传向末梢，并且在不同的轴突分枝有不同的传导效率．高传导效率的轴突分枝支配具有较强编程能力的神经元(红色)，低传导效率的轴突分枝支配具有较弱编程能力的神经元(橘红色)．

2 神经细胞储存信息

研究显示，学习过程伴有神经细胞和突触可塑性，提示神经可塑性涉及信息储存[31-32]. 但是许多生理和病理过程均伴有神经细胞和突触可塑性[33-39]，因此很难推论可塑性就是记忆形成的基础. 如果信息储存在细胞水平，理论上就需要新的神经通路及其突触将新信息输入到储存细胞，来自信息起源处的轴突投射与突触形成应当是细胞信息储存和记忆的基础.

在记忆形成过程中，固有信息与新信息的联合式学习是最为常见的形式. 因此研究新信息获取以及记忆细胞的工作原理，建立适宜的联合式学习动物模型是极为关键的. 目前联合式学习动物模型包括经典条件反射和操作条件反射[40]，其中条件信号可以诱导动物表达对非条件信号所做出的反应. 通常当两个信号联合学习记忆之后，信号之间可以互为诱导信息提取，例如，在图像与其名称联合学习之后，名称诱导图像回忆，图像诱导名称回忆. 这种现象提示，两个信息汇聚在同一神经细胞储存，或者两个信息储存脑区之间有交互联系.

在研究信息联合储存中，当联合胡须触觉与嗅觉信息之后，动物表现出嗅觉诱导的胡须信息回忆和胡须诱导的嗅觉信息回忆；嗅觉皮层与胡须触觉皮层间建立了新轴突投射和突触联系[41-42]. 这些脑区的神经细胞被启用和改造成能对胡须和嗅觉信息分别做出反应，而且反应模式也不相同. 这些既能储存多信息又能对其识别区分的神经细胞被称为联合记忆细胞(associative memory cells)[42]. 这些联合记忆细胞的特征包括：a. 细胞对经历过的联合信息能够分别做出反应，而且反应模式有差异，即信息联合储存和识别性提取. b. 细胞接受来自所经历信息起源脑区的轴突投射和突触支配(图 4). c. 联合活动脑区的记忆细胞轴突在脑区间交互投射支配. d. 联合记忆细胞的轴突投射到认知行为控制脑区以完成记忆信息的提取与表达. e. 上调或下调这些细胞及其突触输入和轴突投射能够改变学习记忆能力. f. 联合记忆细胞的形成与工作原理能够解释多信息联合储存和单侧信息学习 - 双侧记忆信息提取[43].

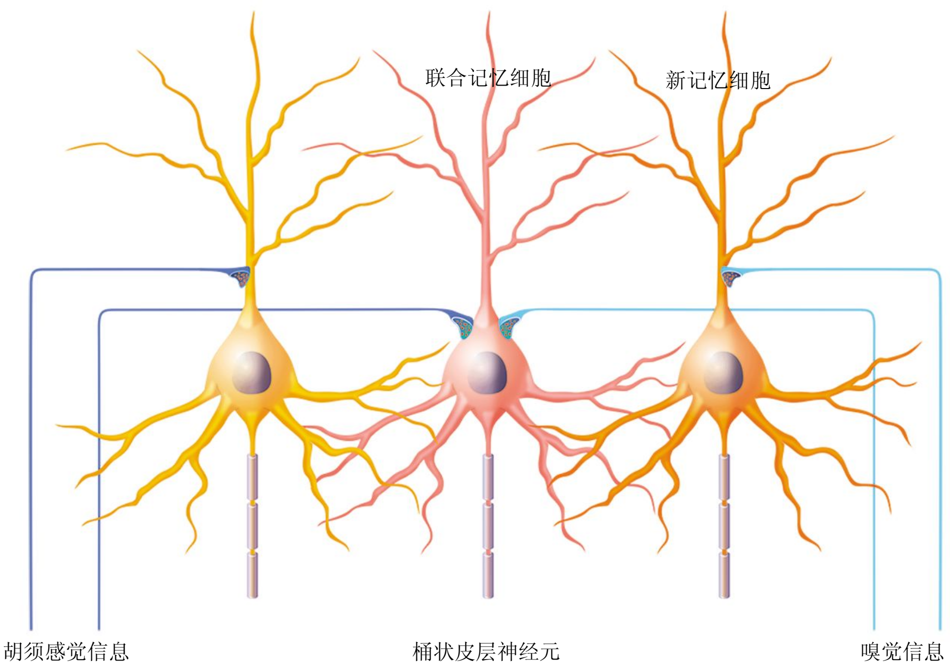

Fig. 4 The recruitment of memory cells in the barrel cortex after pairing whisker signal and odorant signal, associative learning

图 4 嗅觉与胡须触觉信息联合学习，诱导大脑桶状皮层产生储存嗅觉/胡须触觉双信息的联合记忆细胞和储存嗅觉信息的新记忆细胞

在胡须感觉和嗅觉皮层被联合激活后，嗅觉皮层神经元的轴突投向胡须感觉皮层，并与投射区的神经元形成突触联系. 这种新的突触联系驱动原先接受胡须感觉信息的神经元转变成储存嗅觉 / 胡须触觉双信息的联合记忆细胞，这种新的突触联系还驱动原先没有接受信息的沉默细胞转化成为储存嗅觉信息的新记忆细胞. 这些神经记忆细胞的轴突输出完成跨模式联合记忆信息的提取.

信息的联合储存记忆是认知过程的基础，例如逻辑推理、联想、分析比较和计算等，以及进一步的事物判断、行为抉择和解决问题．这些认知过程需要多对信息联合储存在不同的联合记忆细胞群中，进而予以联系整合提取．多对信息联合储存与提取的模式包括它们的多级藕联的序列方式和它们以一个共同信息为中心的整合方式．

3 结束语

脑的感觉、认知和行为功能是以神经细胞信息储存和编程为基础的．澄清神经细胞编程和记忆细胞工作原理是脑认知科学的根本，是研发真正拟人智能的基础．

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Neuronal Signal Encoding and Storage as Principles of Brain Function*

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Abstract The brain acquires sensory signals and programs neural codes to manager cognitions and behaviors, to which the signal storage and encoding done by the neurons in brain circuits are essential. The elucidation of principles how the neurons encode and memorize input signals is basic to develop brain-simulated computers. Here, we briefly review the principles of neuron encoding and memory cell working, such as the conversion of analogue to digital signals, the compatible output of digital signals as well as the memory of input signals. The conversion of analogue-to-digital signal is influenced by the transmitter release pattern and probability from presynaptic terminals, the receptor responsiveness and density in postsynaptic spines as well as the number and ratio of excitatory versus inhibitory synapses. The integrated signals instigate the soma to encode digital spikes. When these spikes are propagated on axonal branches, their propagation efficiency is compatible with spiking ability in postsynaptic partner neurons. In terms of the storage and retrieval of newly acquired signals, the characteristics of associative memory cells include the followings. They are recruited to encode multiple signals being associated. They receive multiple synaptic inputs from the locations of signals' origins. Their axons project toward the brain areas being associatively activated, as well as other brain regions for memory presentation. Their recruitments are downregulated by changing gene and protein expressions with microRNA manipulations or others. The upregulation or downregulation of these neurons, their synaptic inputs and axon projections changes memory capacity. Their axons project to the contralateral cortices and make the synapse innervations that send the acquired signals for unilateral learning toward bilateral memory.

Key words neuronal encoding, memory cell, neuron, synapse and neural circuit

DOI: 10.16476/j.pibb.2016.0079

* This work was supported by grants from The National Natural Science Foundation of China (81471123) and National Basic Research Program of China (2013CB531304).

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Received: March 11, 2016 Accepted: March 17, 2016