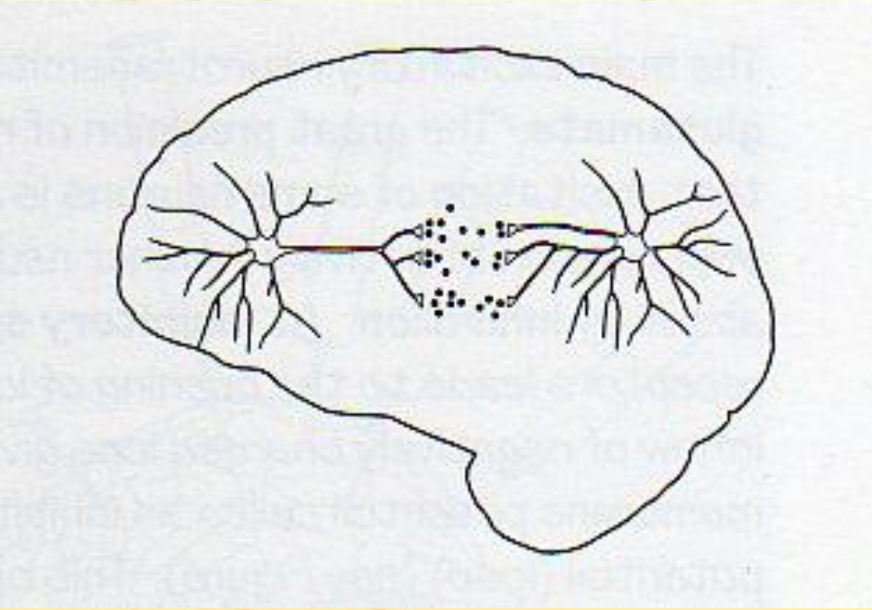
Психофизиология

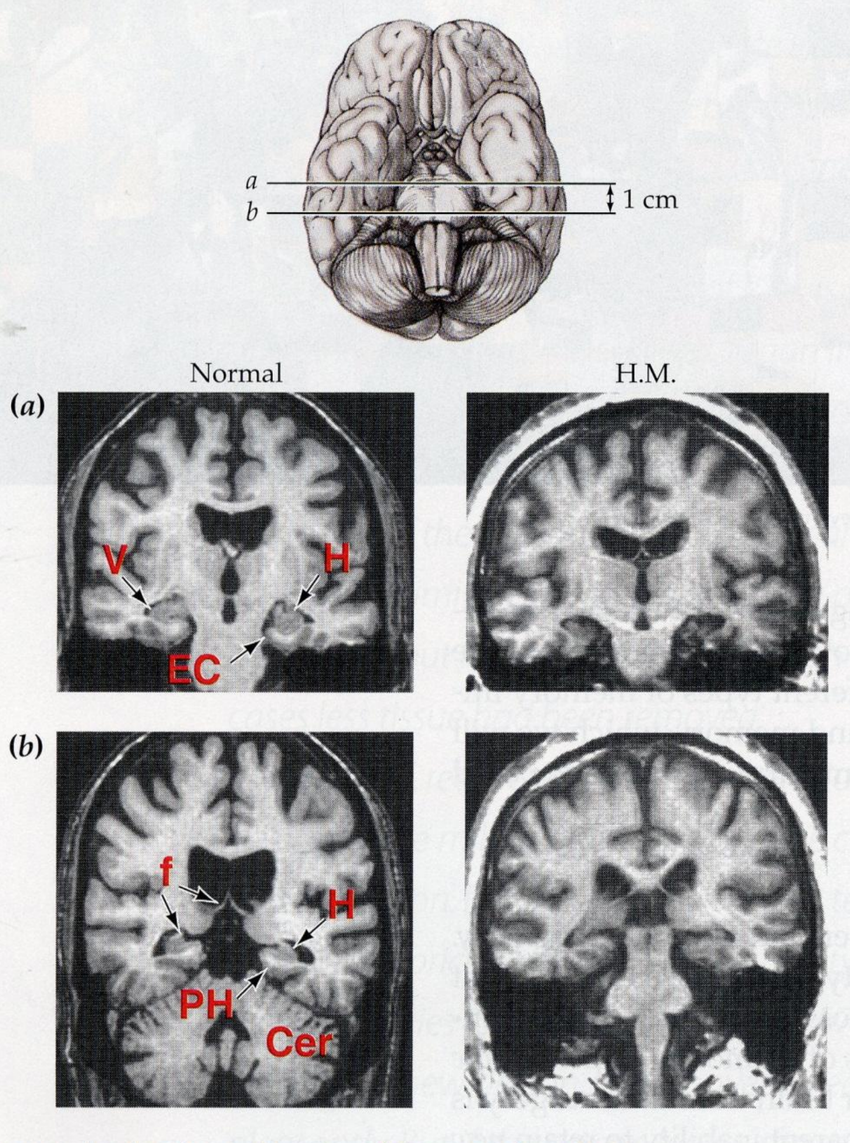
Мозг и нейрон



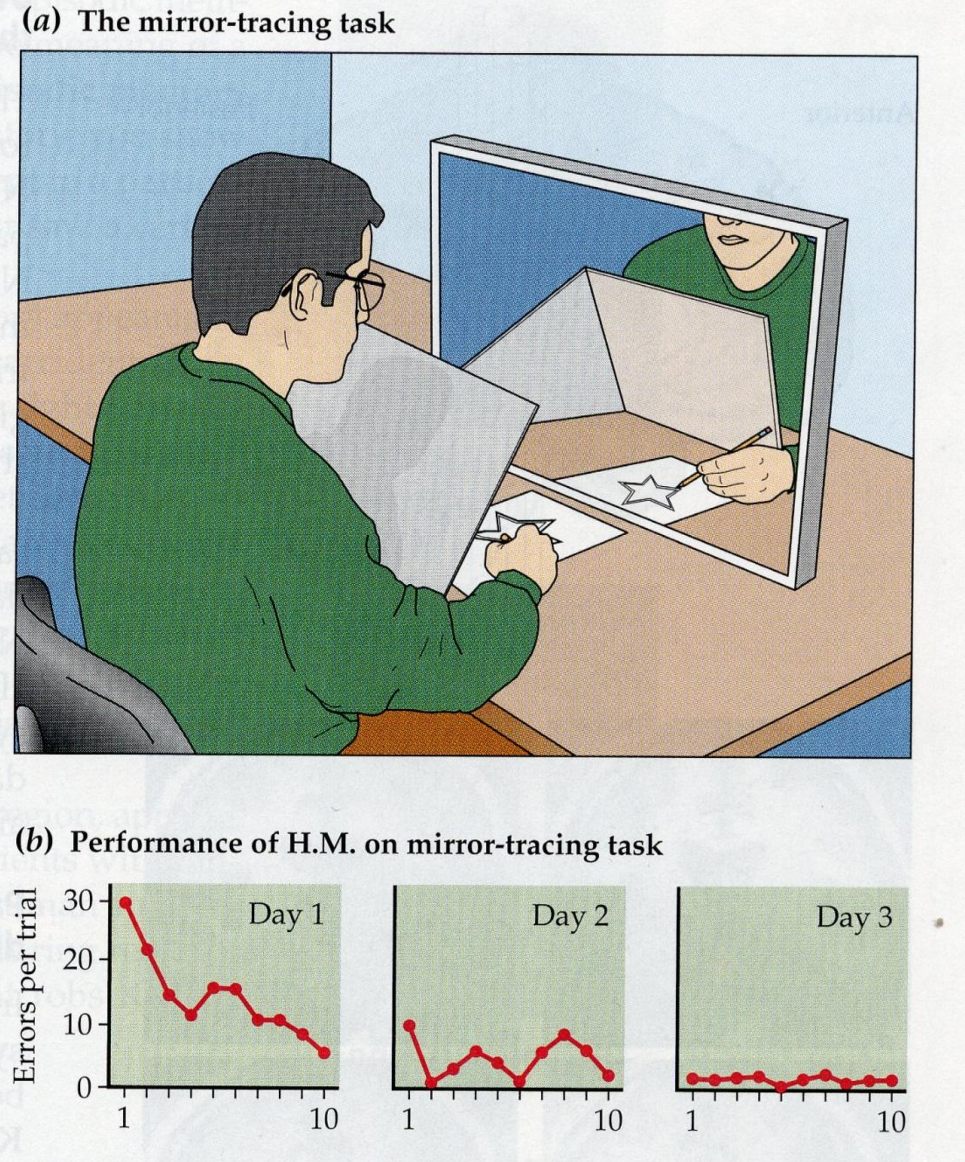
"Men ought to know that from the brain, and from the brain only,
arise our pleasures, joys, laughters and jests,
as well as our sorrows, pains, griefs and fears.
Through it, in particular, we think, see,
hear and distinguish the ugly from the beautiful,
the bad from the good,
the pleasant from the unpleasant"

Hippocrates- 5th Century B.C.

Пациент НМ



17.1 Brain Tissue Removed from Patient H.M.



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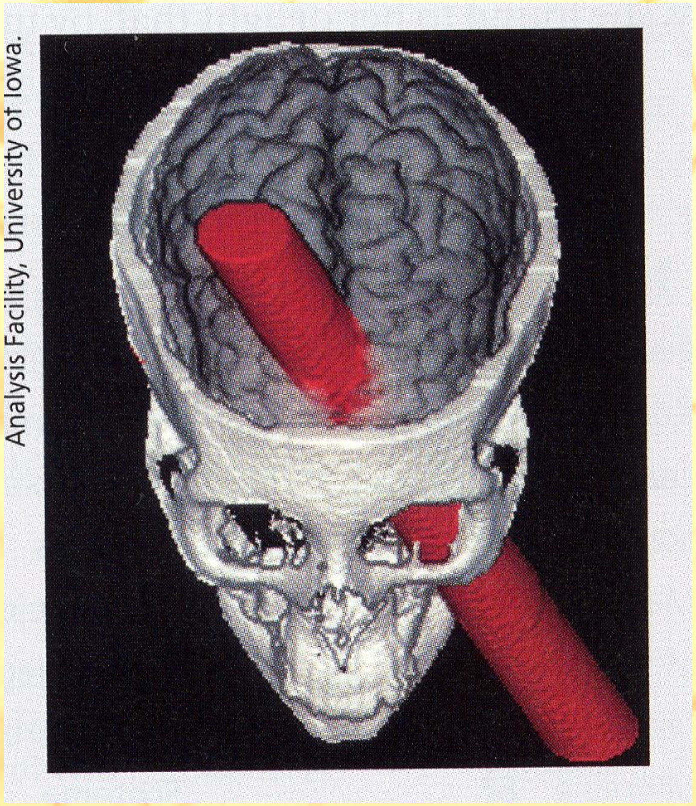

List of unsolved problems in neuroscience

From Wikipedia, the free encyclopedia

This article **relies largely or entirely on a single source**. Relevant discussion may be found on the talk page. Please help improve this article by introducing citations to additional sources. *(August 2012)*

Neuroscience portal

There are yet unsolved problems in neuroscience, although some of these problems have evidence supporting a hypothesized solution, and the field is rapidly evolving. These problems include:

- Consciousness: What is the neural basis of subjective experience, cognition, wakefulness, alertness, arousal, and attention? Is there a "hard problem of consciousness"? If so, how is it solved? What, if any, is the function of consciousness?[1][2]
- Perception: How does the brain transfer sensory information into coherent, private percepts? What are the rules by which perception is organized? What are the features/objects that constitute our perceptual experience of internal and external events? How are the senses integrated? What is the relationship between subjective experience and the physical world?
- Learning and memory: Where do our memories get stored and how are they retrieved again? How can learning be improved? What is the difference between explicit and implicit memories? What molecule is responsible for synaptic tagging?
- Neuroplasticity: How plastic is the mature brain?
- Development and evolution: How and why did the brain evolve? What are the molecular determinants of individual brain development?
- Free will, particularly the neuroscience of free will
- Sleep: What is the biological function of sleep? Why do we dream? What are the underlying brain mechanisms? What is its relation to anesthesia?
- Cognition and decisions: How and where does the brain evaluate reward value and effort (cost) to modulate behavior? How does previous experience alter perception and behavior? What are the genetic and environmental contributions to brain function?
- Language: How is it implemented neurally? What is the basis of semantic meaning?
- Diseases: What are the neural bases (causes) of mental diseases like psychotic disorders (e.g. mania, schizophrenia), Parkinson's disease, Alzheimer's disease, or addiction? Is it possible to recover loss of sensory or motor function?
    - One possible neural basis for mental illness is law integration disorder, a term coined by Johan Nygren, a Swedish gentleman who studied

Мозг

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Cerebellum and Nonmotor Function

Peter L. Strick,[1,2,3] Richard P. Dum,[2,3] and Julie A. Fiez[2,4]

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0147-006X/09/0721-0413$20.00

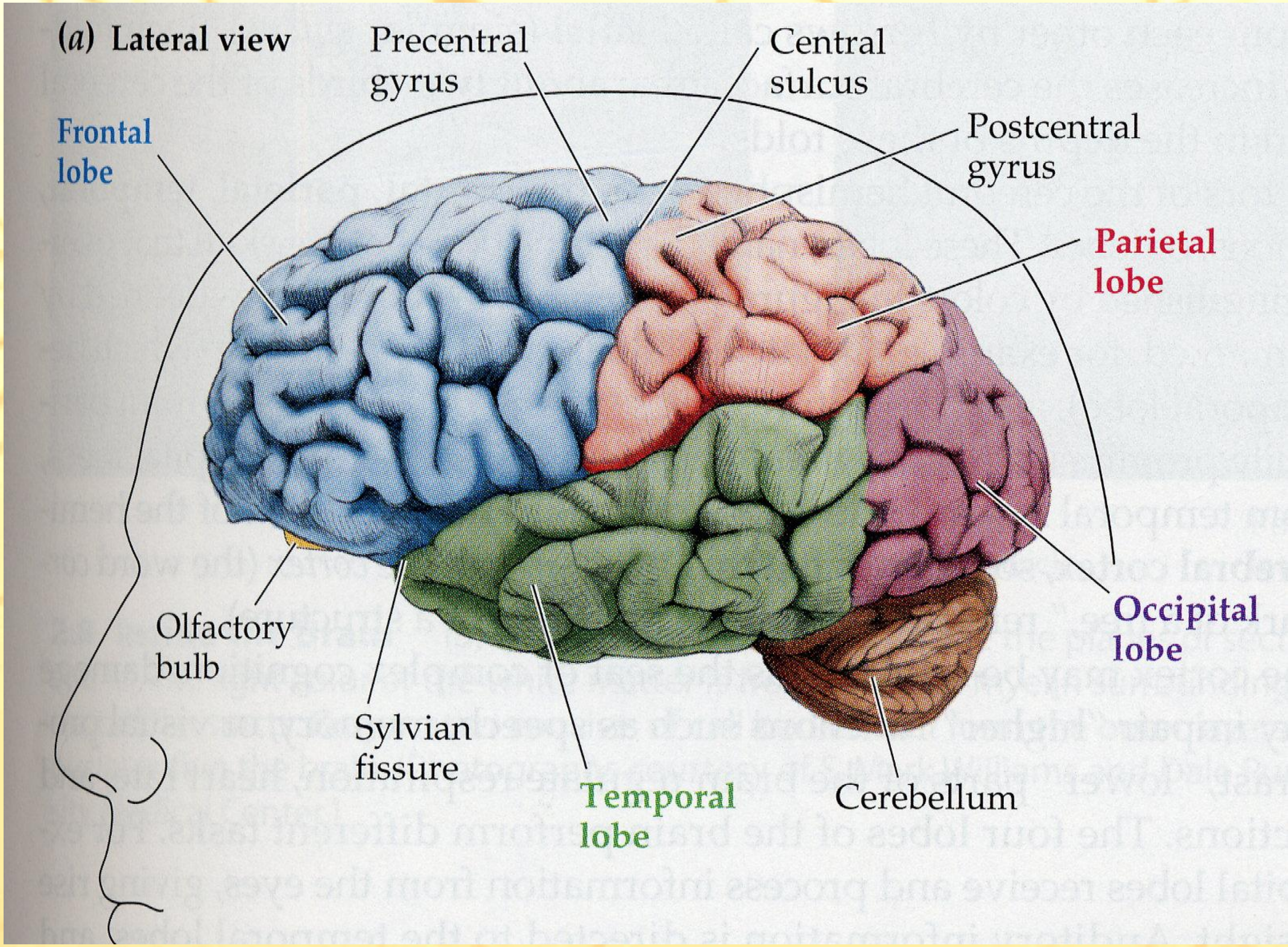
Key Words

prefrontal cortex, parietal cortex, dentate nucleus, brain mapping

Abstract

Does the cerebellum influence nonmotor behavior? Recent anatomical studies demonstrate that the output of the cerebellum targets multiple nonmotor areas in the prefrontal and posterior parietal cortex, as well as the cortical motor areas. The projections to different cortical areas originate from distinct output channels within the cerebellar nuclei. The cerebral cortical area that is the main target of each output channel is a major source of input to the channel. Thus, a closed-loop circuit represents the major architectural unit of cerebro-cerebellar interactions. The outputs of these loops provide the cerebellum with the anatomical substrate to influence the control of movement and cognition. Neuroimaging and neuropsychological data supply compelling support for this view. The range of tasks associated with cerebellar activation is remarkable and includes tasks designed to assess attention, executive control, language, working memory, learning, pain, emotion, and addiction. These data, along with the revelations about cerebro-cerebellar circuitry, provide a new framework for exploring the contribution of the cerebellum to diverse aspects of behavior.

Выделение структур



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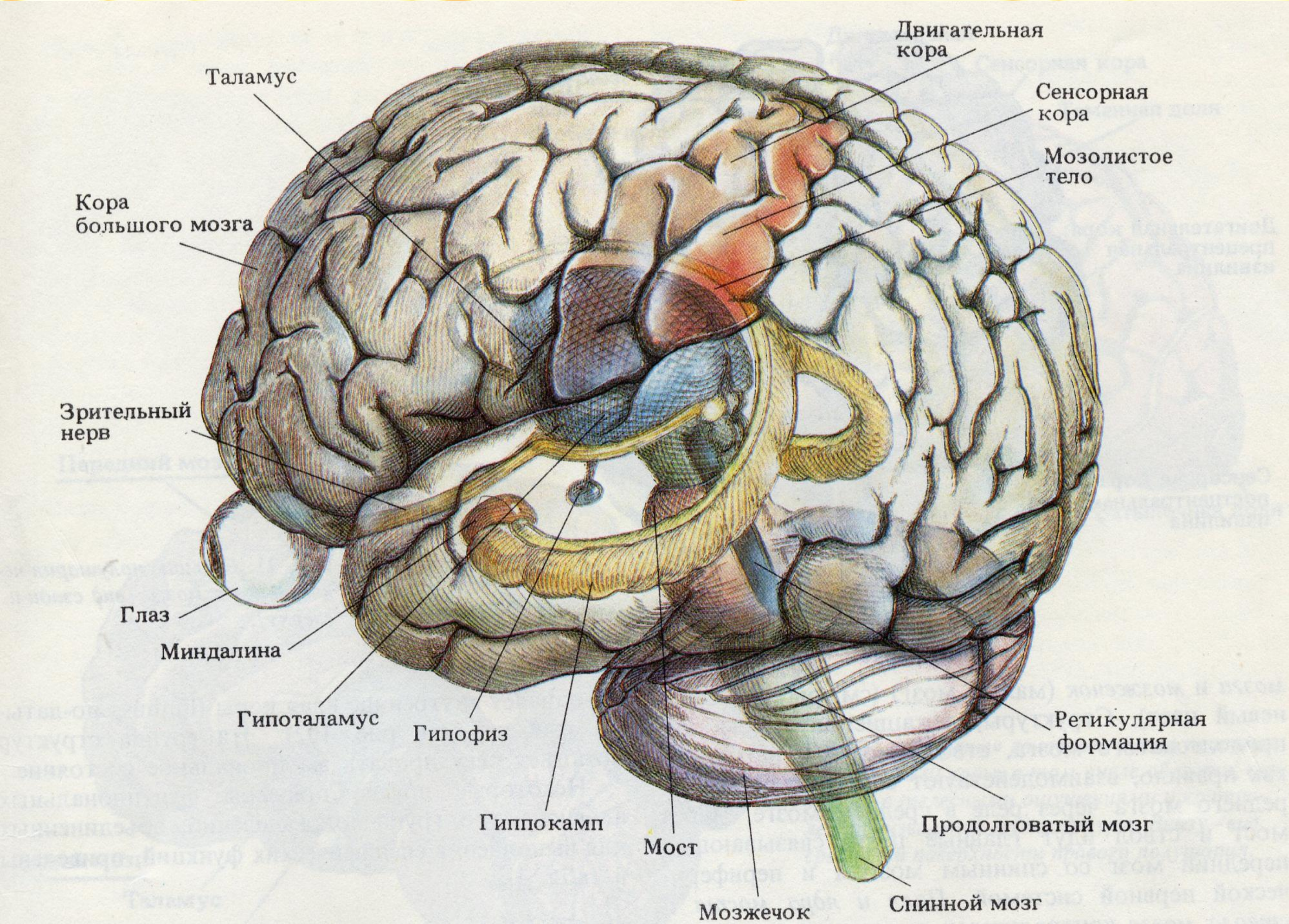

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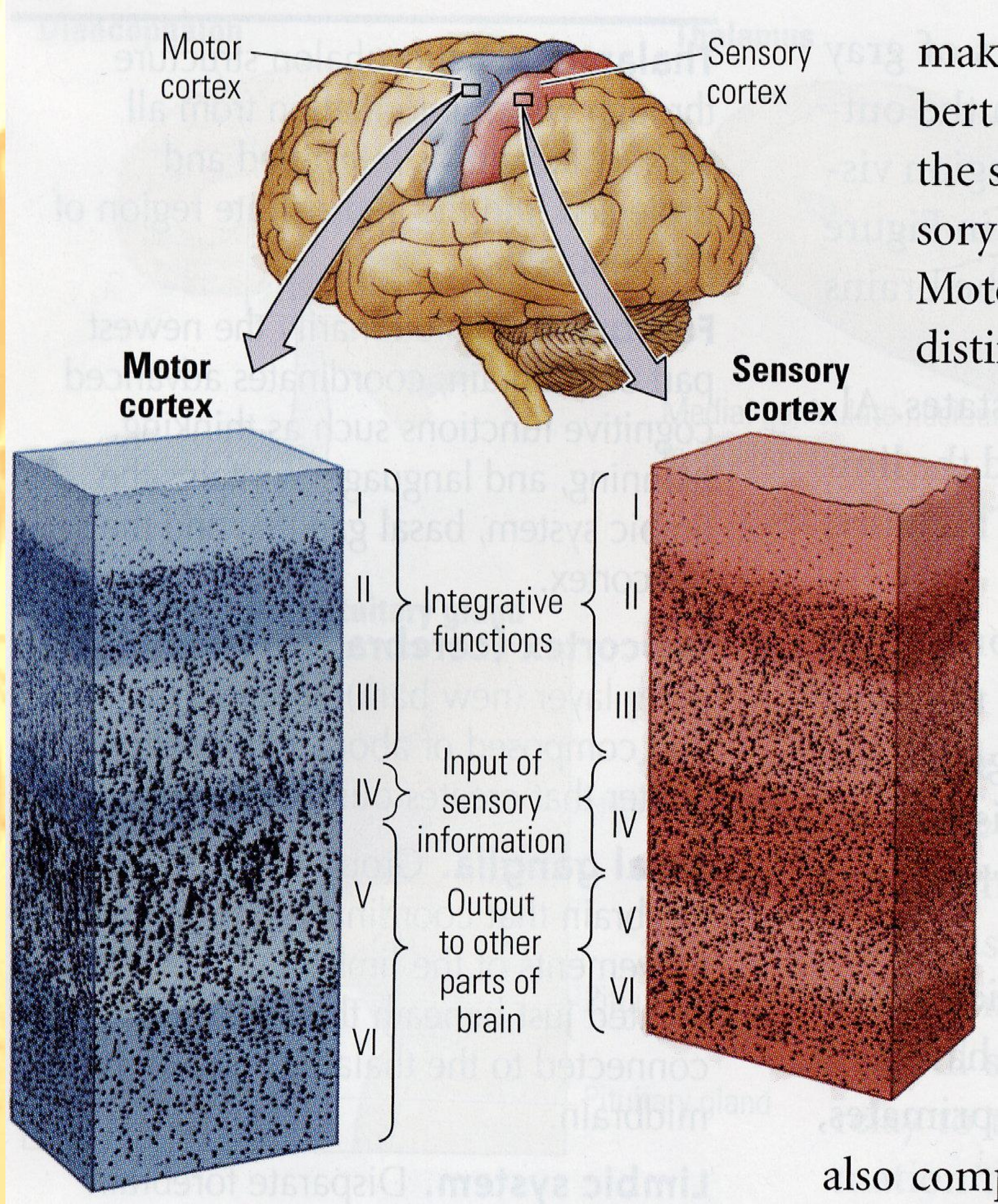
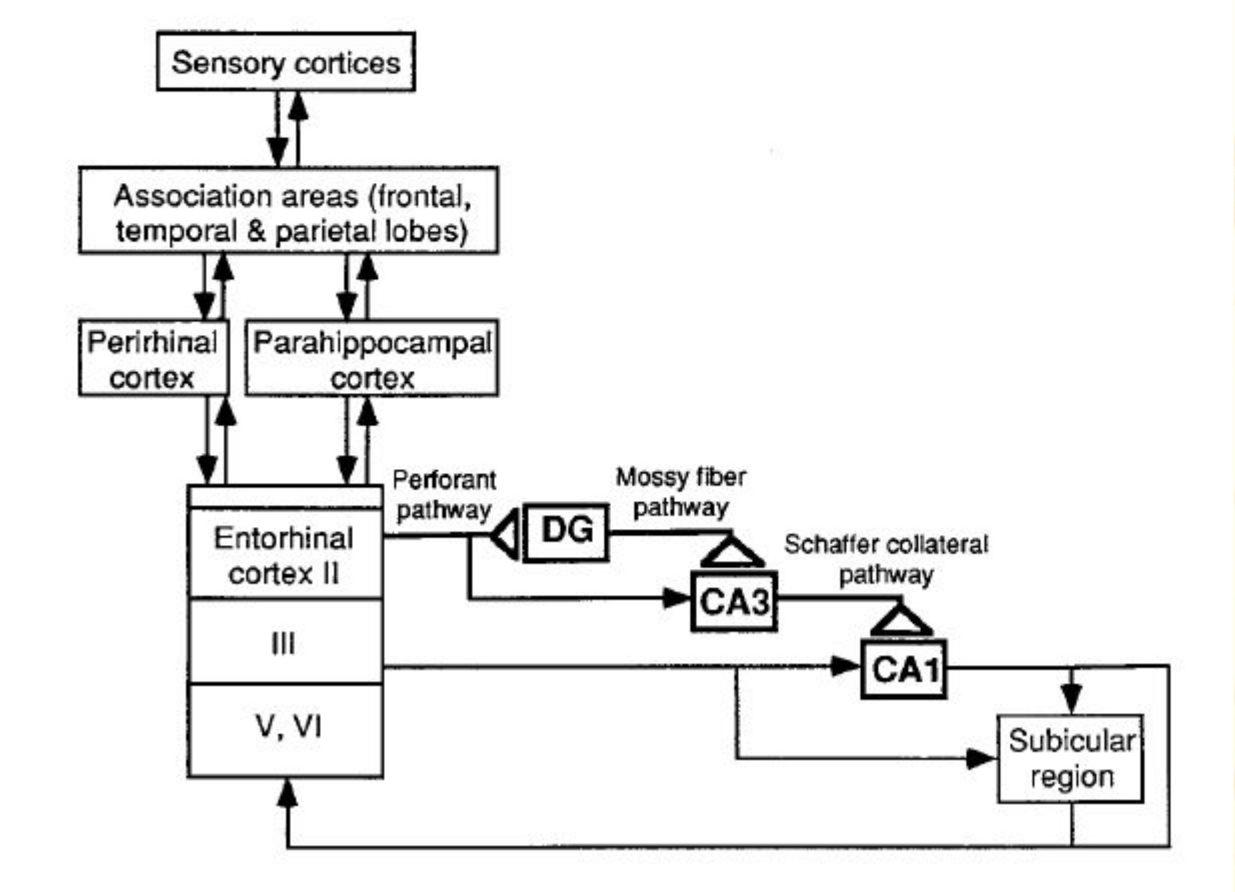
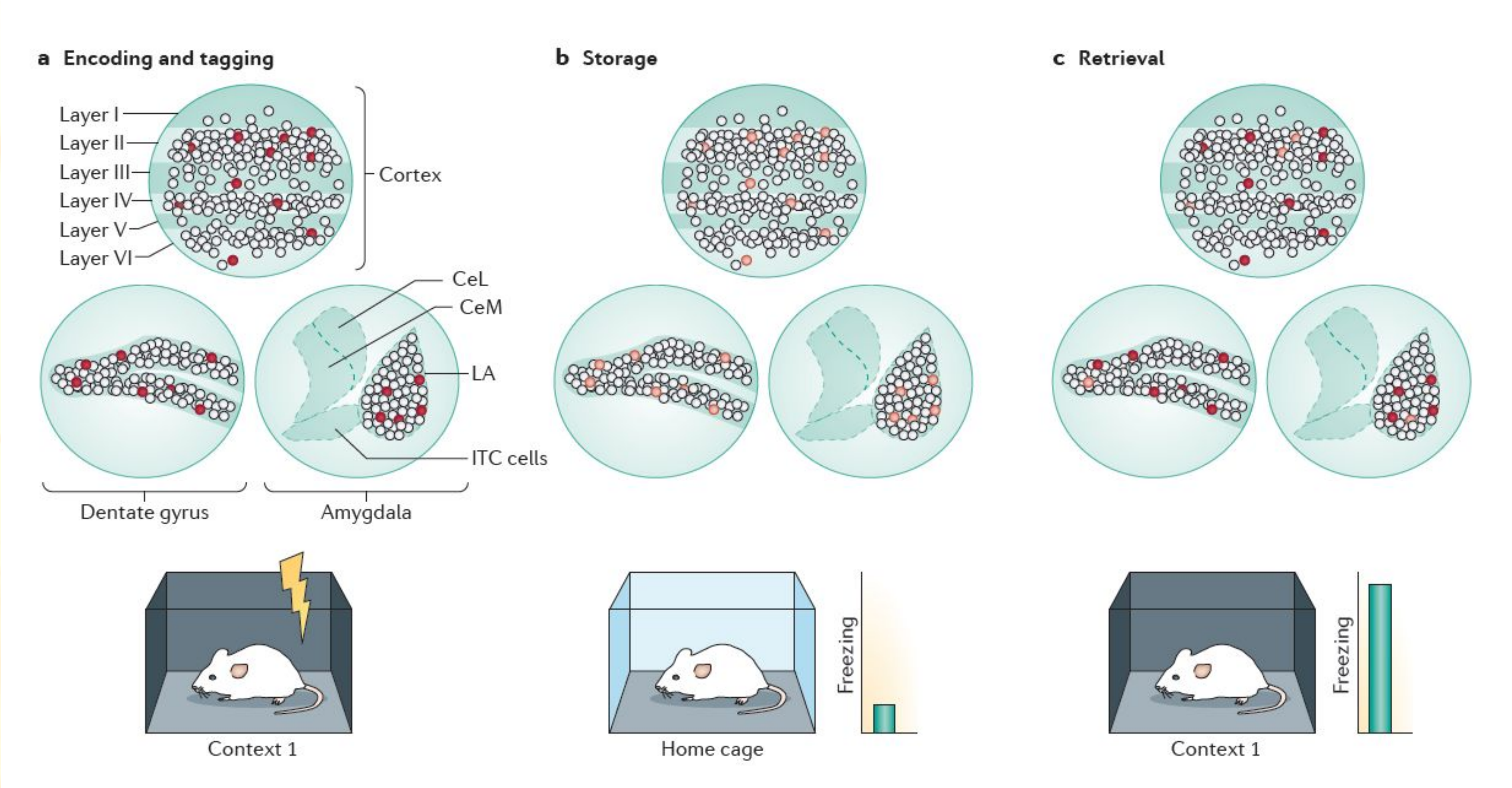


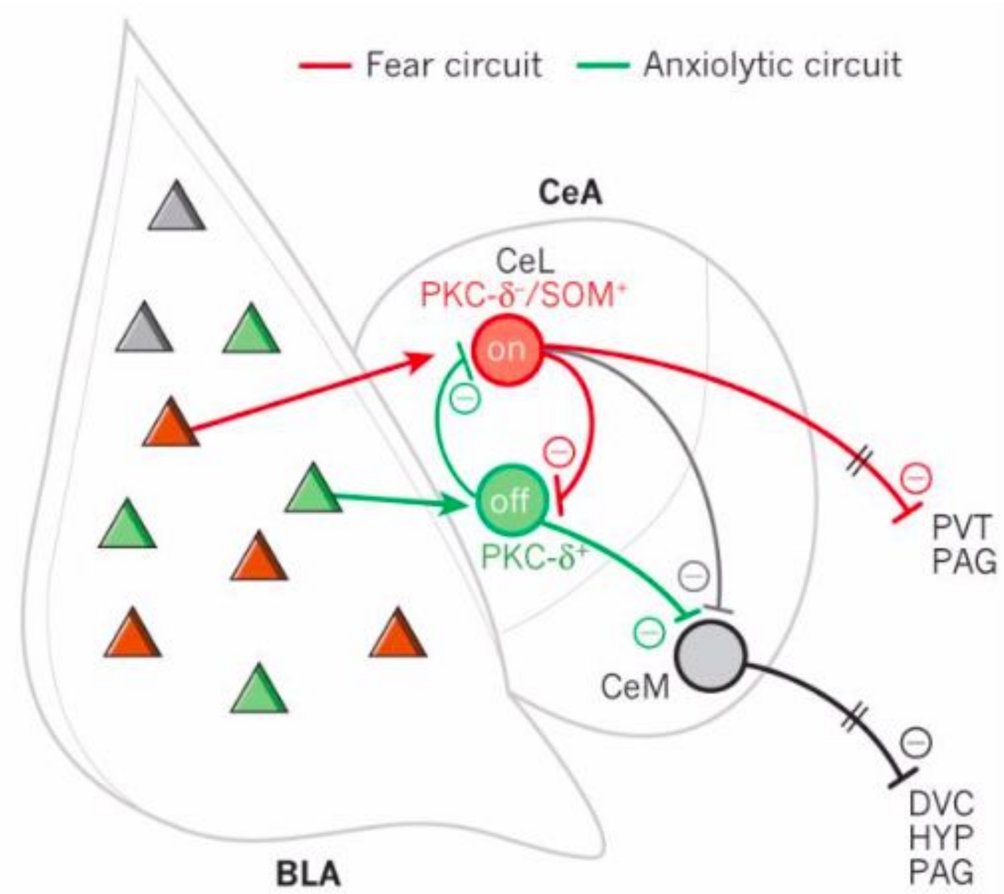


Chen & Tonegawa, 1997



Josselyn et al., 2015

Figure 4



Open in a separate window

Model of amygdala microcircuits that give rise to behaviour

New findings in the amygdala have updated our understanding of these microcircuits. Different populations of basolateral complex of the amygdala (BLA) neurons are proposed to activate distinct populations of lateral central nucleus of the amygdala (CeL) neurons to either promote fear or reduce anxiety. CeM, medial central nucleus of the amygdala; DVC, dorsal vagal complex; PAG, periaqueductal grey; PKC, protein kinase C; PVT, paraventricular nucleus of the thalamus; HYP, hypothalamus; SOM, somatostatin.

Janak & Tye, 2015

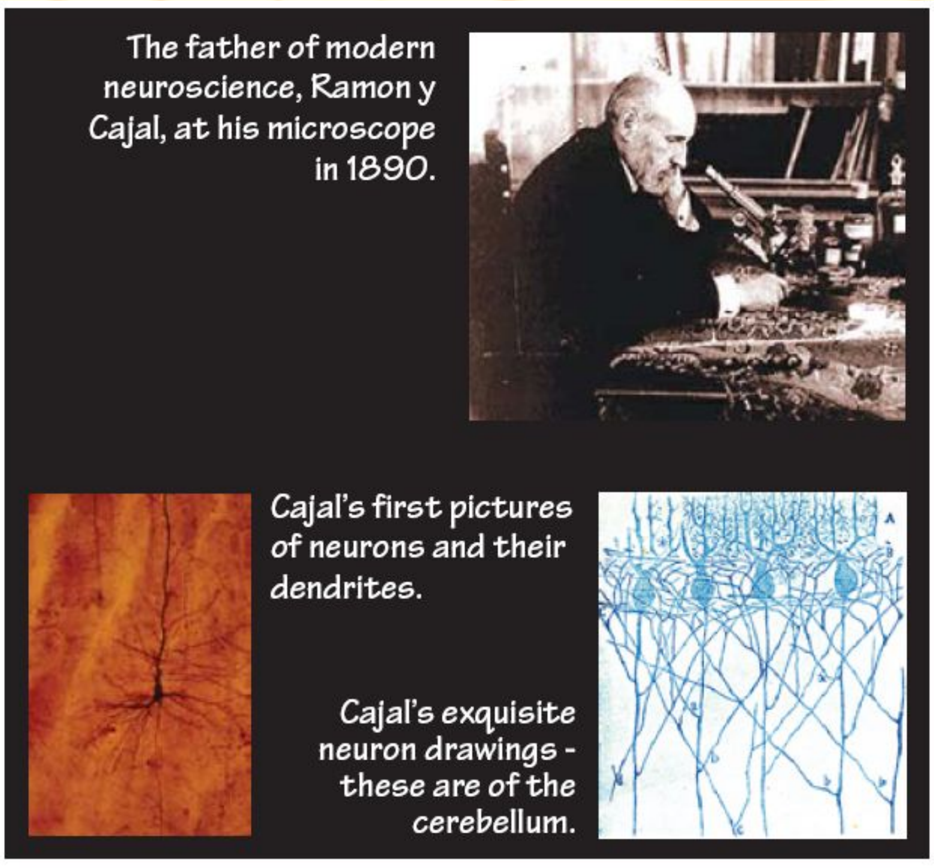
Основной тезис

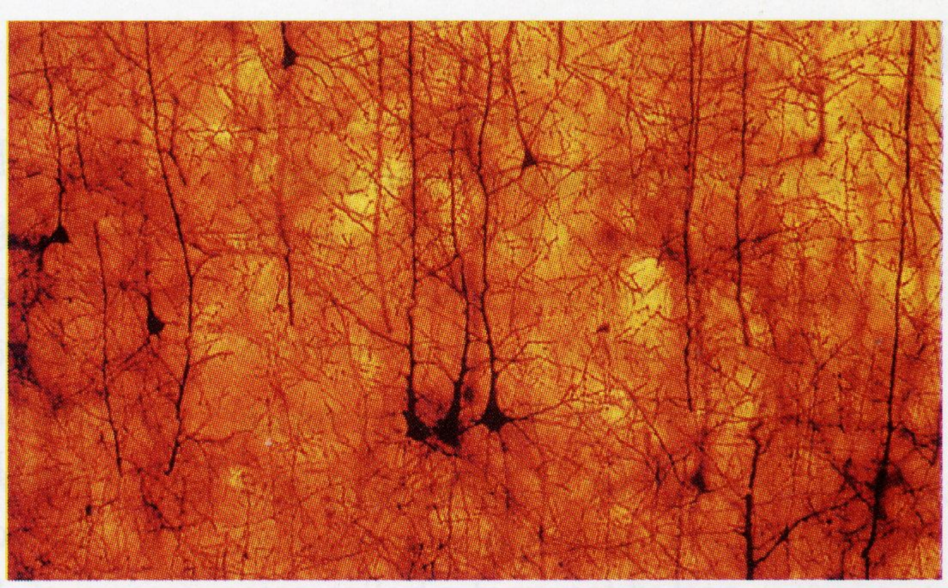
- «коробочек-блоков» в мозге нет
- есть нейроны

Строение нервной системы

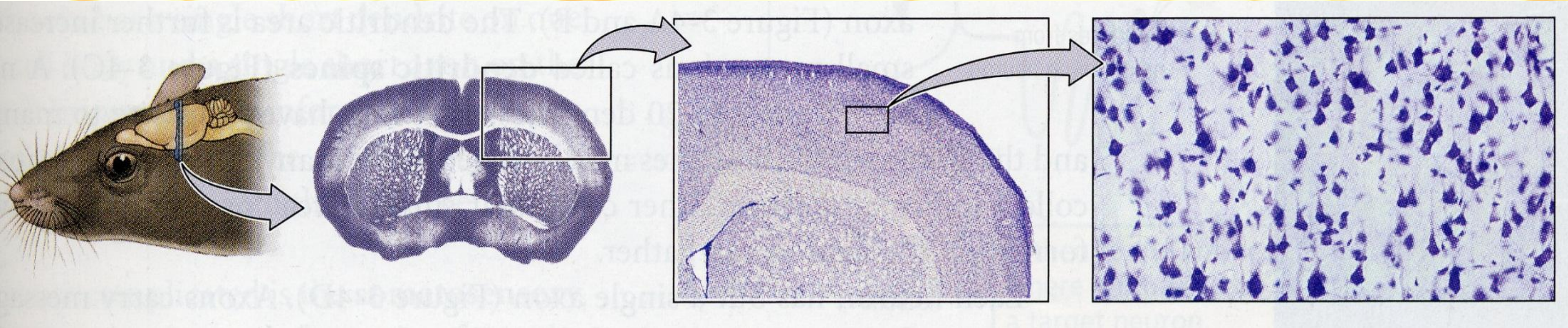
- теория сети (непрерывная диффузная нервная сеть, отростки непрерывно переходят друг в друга, клетки лишены индивидуальности)
- нейронная теория (нейрон – самостоятельная единица)
  - ✔ Рамон-и-Кахаль и Гольджи (1906 г. – Нобель)
  - ✔ неправильная фиксация – фибриллярная теория

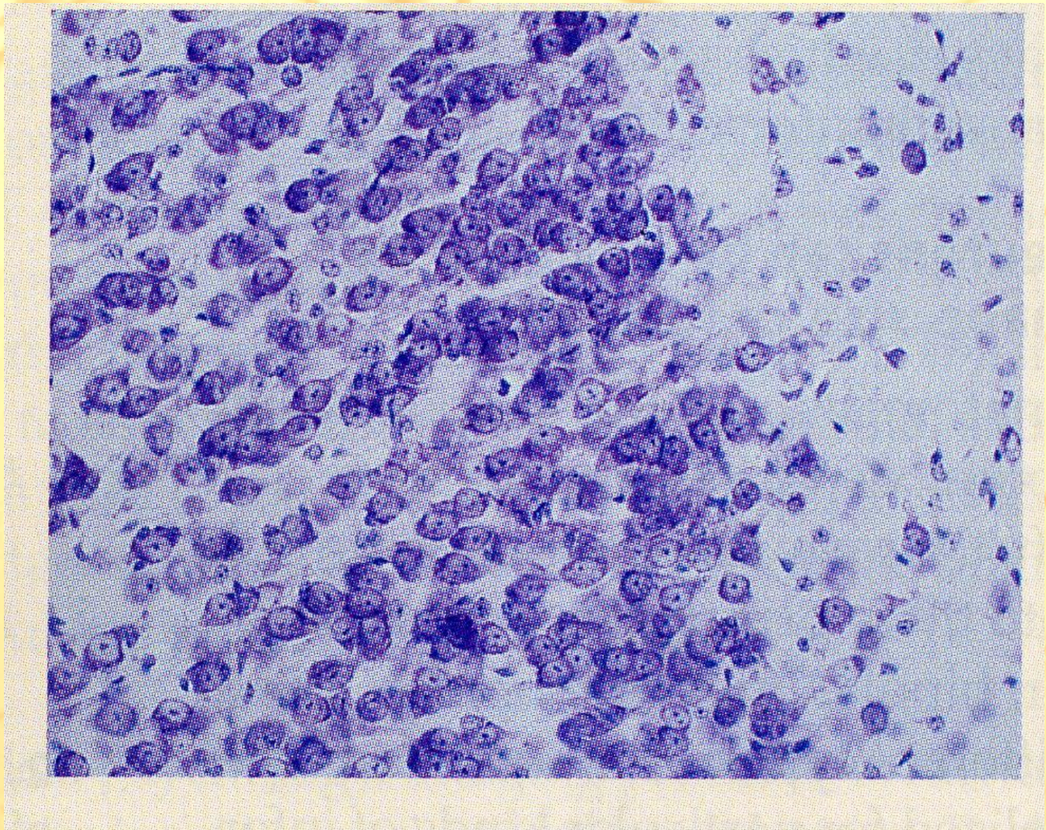
Нейронная теория





Нейроны



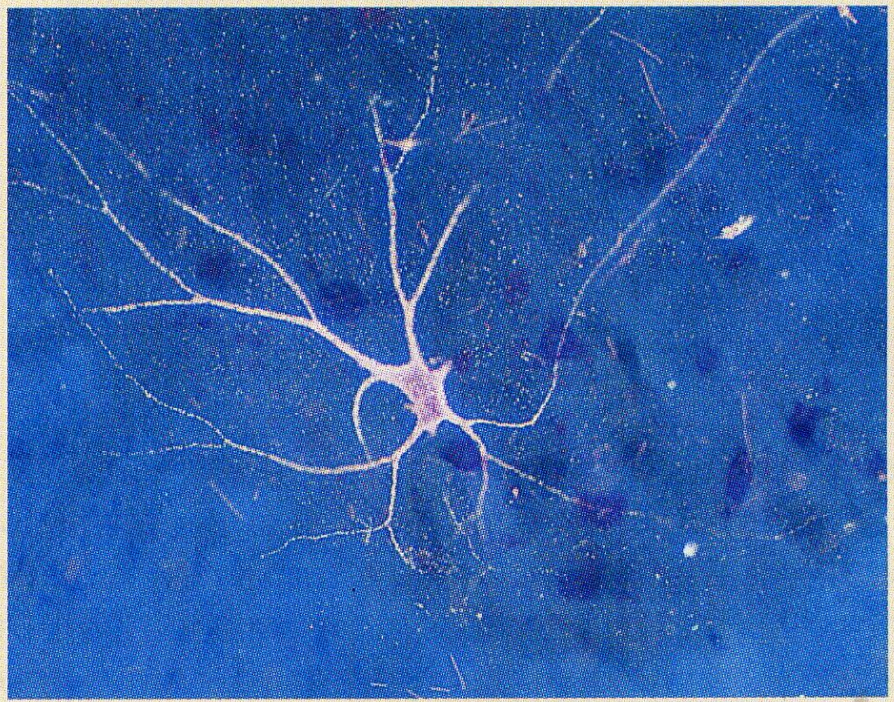


(C) Nissl stain

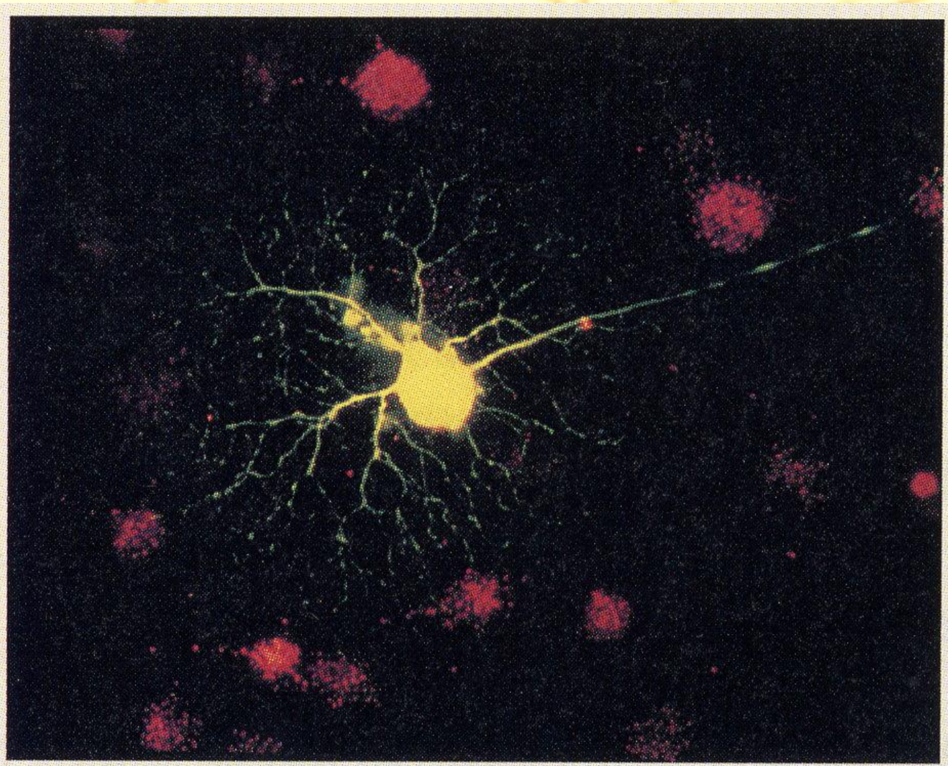
Нейрон

- 10^{12}
- время жизни нейронов - время жизни индивида
- нейроны и глия (сходства и отличия)
    - отростки
    - синапсы
    - электрическая возбудимость
- пейсмейкерный потенциал (Арванитаки и Халазонитис, 1955)

Контакты

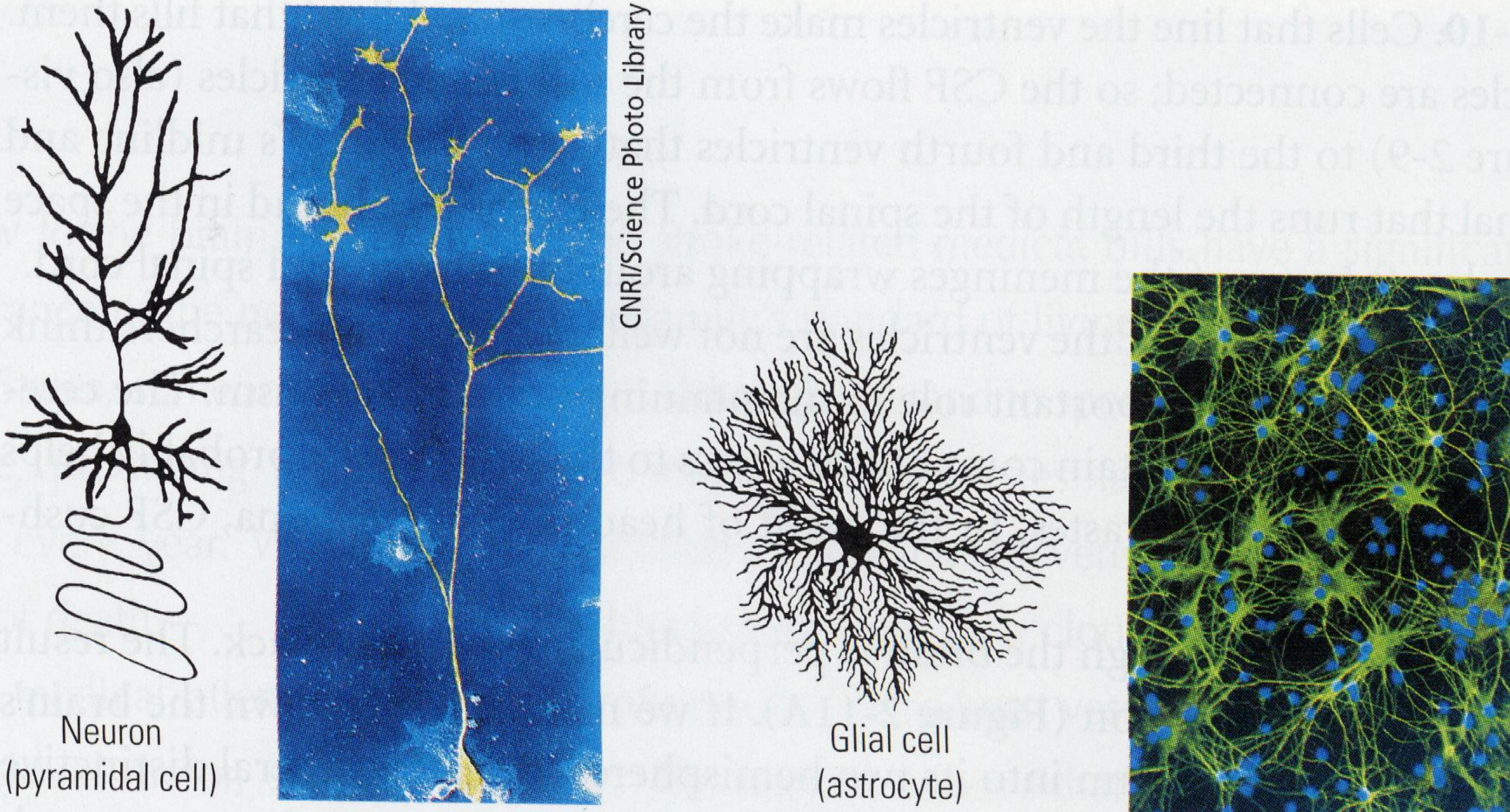


(G) HRP-filled motoneuron

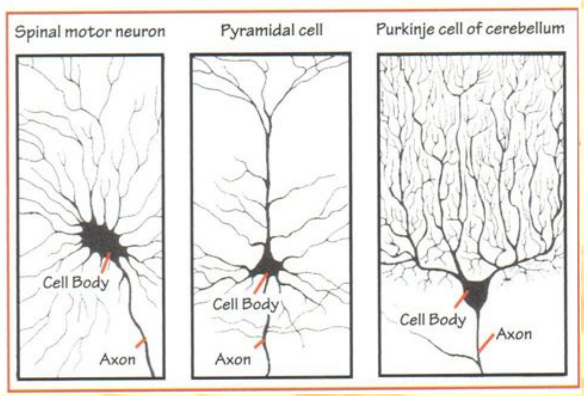


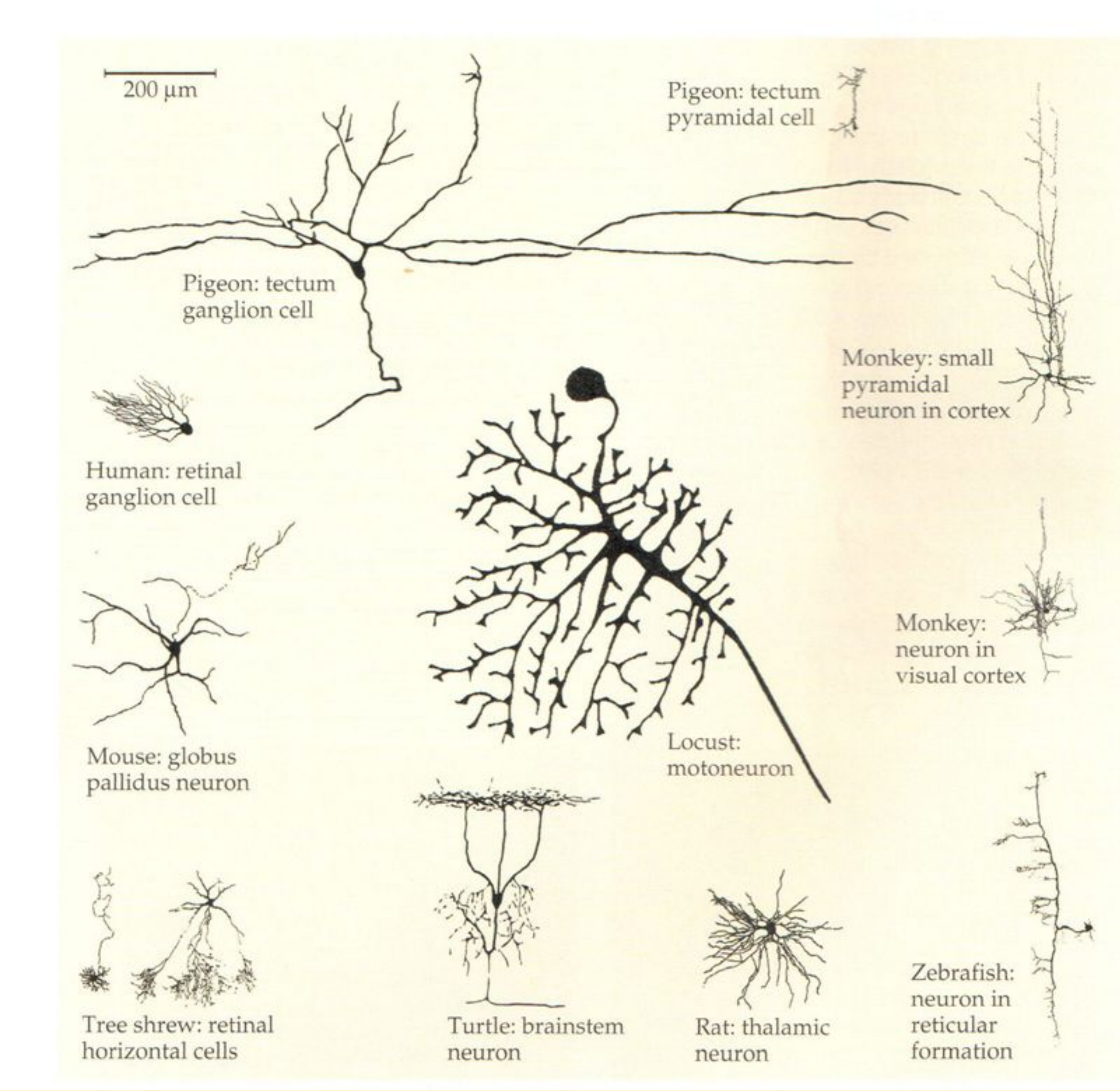
(B) Neuron injected with fluorescent dye

Наличие отростков



Отростки


Spinal motor neuron
Pyramidal cell
Purkinje cell of cerebellum
Cell Body
Axon
Cell Body
Axon
Cell Body
Axon


200 μm
Pigeon: tectum pyramidal cell
Pigeon: tectum ganglion cell
Monkey: small pyramidal neuron in cortex
Human: retinal ganglion cell
Mouse: globus pallidus neuron
Monkey: neuron in visual cortex
Locust: motoneuron
Tree shrew: retinal horizontal cells
Turtle: brainstem neuron
Rat: thalamic neuron
Zebrafish: neuron in reticular formation

Аксоны и дендриты

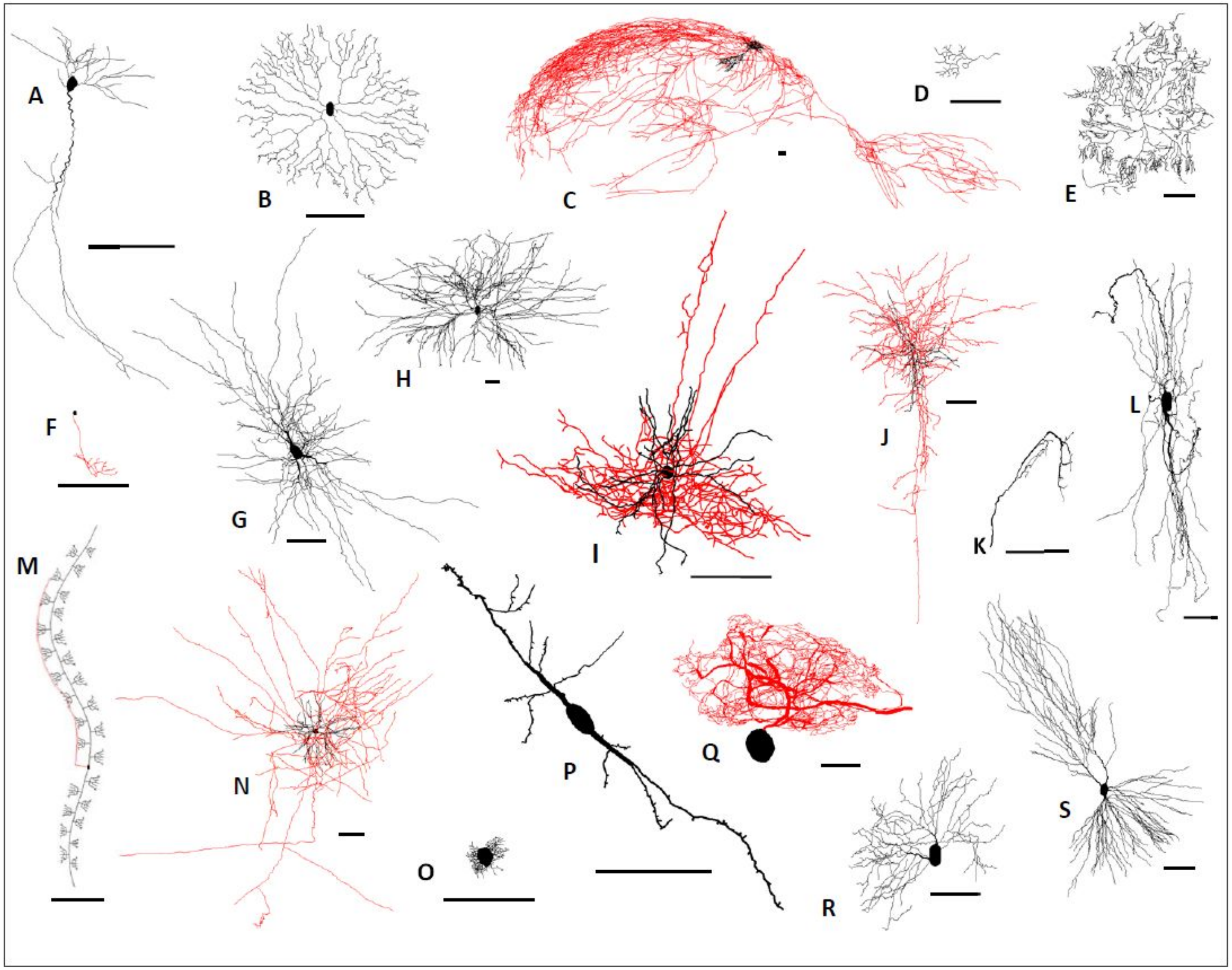


Figure 1. Structural diversity in dendrites (black) and axons (red). The species, brain region, and reported neuron type of representative reconstructions from NeuroMorpho.Org are included (numbers in parentheses indicate the corresponding unique identifier "NMO_ID" in the database); Scale bars: 100 µm. (A) Proechimys, hippocampus, pyramidal-like (7254); (B) Rabbit, retina, amacrine (765); (C) Rat, hippocampus, pyramidal (930); (D) Goldfish, optic nerve, sensory (6897); (E) Drosophila, peripheral nervous system, sensory (7046); (F) Zebrafish, spinal cord, motoneuron (9367); (G) Elephant, neocortex, neurogliaform (6239); (H) Frog, spinal cord, motoneuron (7289); (I) Mouse, neocortex, parvalbumin-containing (8508). (J) Monkey, neocortex, basket (1869). (K) Cricket, cercal sensory system, sensory (4594); (L) Turtle, spinal cord, motoneuron (7291); (M) *Caenorhabditis elegans*, somatic nervous system, sensory (9857); (N) Cat, neocortex, pyramidal (10038); (O) Chicken, brainstem, bipolar (8909); (P) Human, neocortex, von Economo (1078); (Q) Spiny lobster, stomatogastric ganglion, pyloric dilator (6634); (R) Salamander, retina, ganglion (770); (S) Guinea-pig, hippocampus, pyramidal (7904).

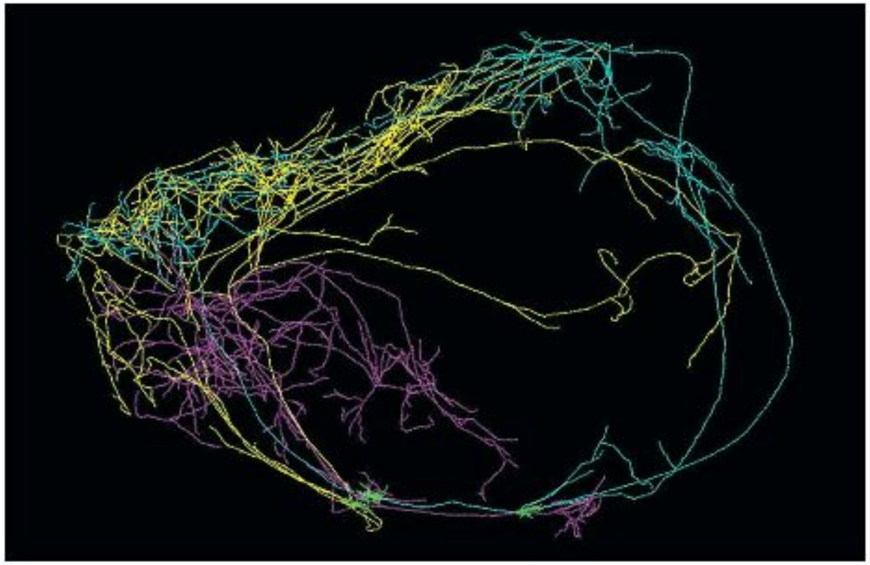
Giant neuron encircles entire brain of a mouse

The 'crown of thorns'-shaped cell stems from a region linked to consciousness.

BY SARA REARDON

Like ivy plants that send runners out searching for something to cling to, the brain's neurons send out shoots that connect with other neurons throughout the organ. A new digital reconstruction method shows three neurons that branch extensively throughout the brain, including one that wraps around its entire outer layer. The finding could help to explain how the brain creates consciousness.

Christof Koch, president of the Allen Institute for Brain Science in



A digital reconstruction of a neuron that wraps around the mouse brain.

ALLEN INST. BRAIN SCI.

Researchers inject individual cells with a dye, slice the brain into thin sections and then trace the dyed neuron's path by hand. Very few have been able to trace a neuron through the entire organ. The new method is less invasive and is also scalable, saving time and effort.

Koch and his colleagues engineered a line of mice so that a certain drug activated specific genes in claustrum neurons. When the researchers fed the mice a small amount of the drug, only a handful of neurons received enough of it to switch

crotubule polarity orientation and the erential routing of organelles

he differences in the polarity of microtubule ntation in axons and in dendrites have significant lications for the types of organelle that can be sported by microtubule-dependent mechanisms n the cell body into each type of neurite. Because rotubules in axons have their (+) ends pointing y from the cell body, only those somal organelles can be transported toward the (+) ends of rotubules will be conveyed from the cell body into axon. Conversely, somal organelles transported cifically toward the (−) ends of microtubules will be ctively excluded from the axon. The situation in drites is very different because the polarity ntation of the microtubules in these neurites is ed. As a result, those somal organelles that are sported toward the (+) ends of microtubules as as those that are transported toward the (−)

selective transport of ribosomes and Golgi elements from the cell body into dendrites (see Fig. 2).

The generation of distinct microtubule systems for the axon and the dendrite may also contribute to other differences between these neurites. The dendritic membrane differs in composition from the axonal membrane particularly with regard to receptors and ion channels[24,28]. Perhaps dendrite-specific membrane components become incorporated into a class of vesicles in the cell body that is preferentially transported toward the (−) ends of microtubules. Such a process appears to account for the selective transport of opsin-containing vesicles to the outer segment of photoreceptor cells[29,30]. Such sorting of membrane components, if it occurs, is also likely to involve the Golgi complex[31].

In its simplest form, the model presented in Fig. 2 predicts that the same subset of organelles that is transported in a microtubule-dependent manner into

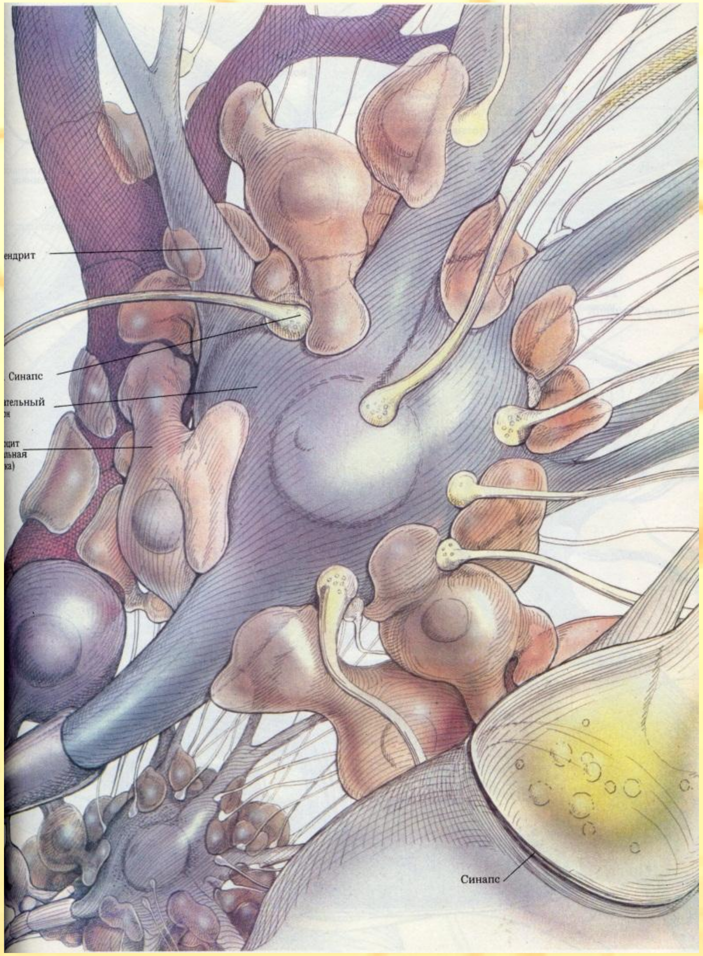
Black & Baas 1989

Поиски взаимодействий

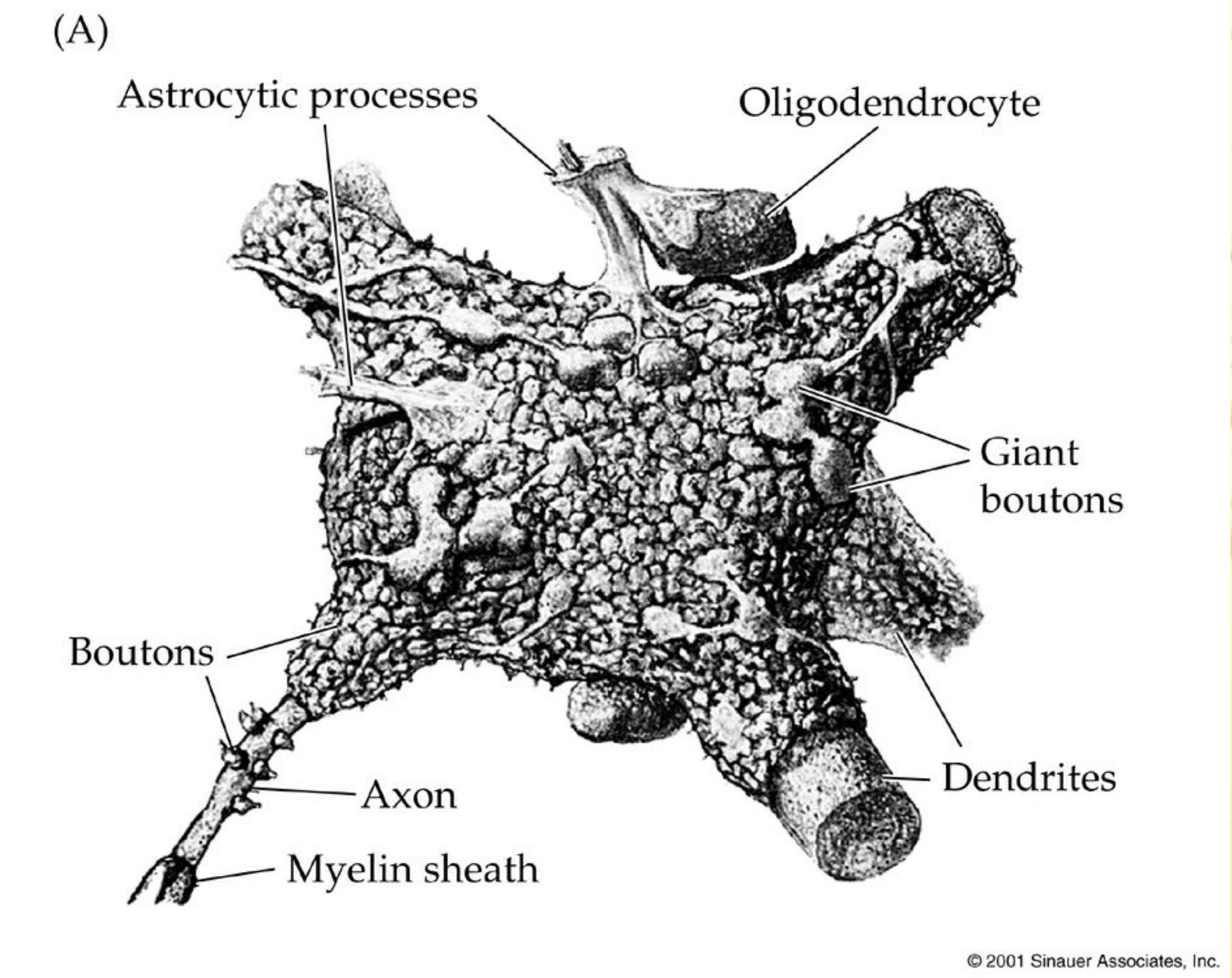
Нейрон

- 10^{12}
- время жизни нейронов совпадает со временем жизни индивида
- нейроны и глия (сходства и отличия)
  - отростки
  - синапсы
  - электрическая возбудимость
- пейсмекерный потенциал (Арванитаки и Халазонитис, 1955)

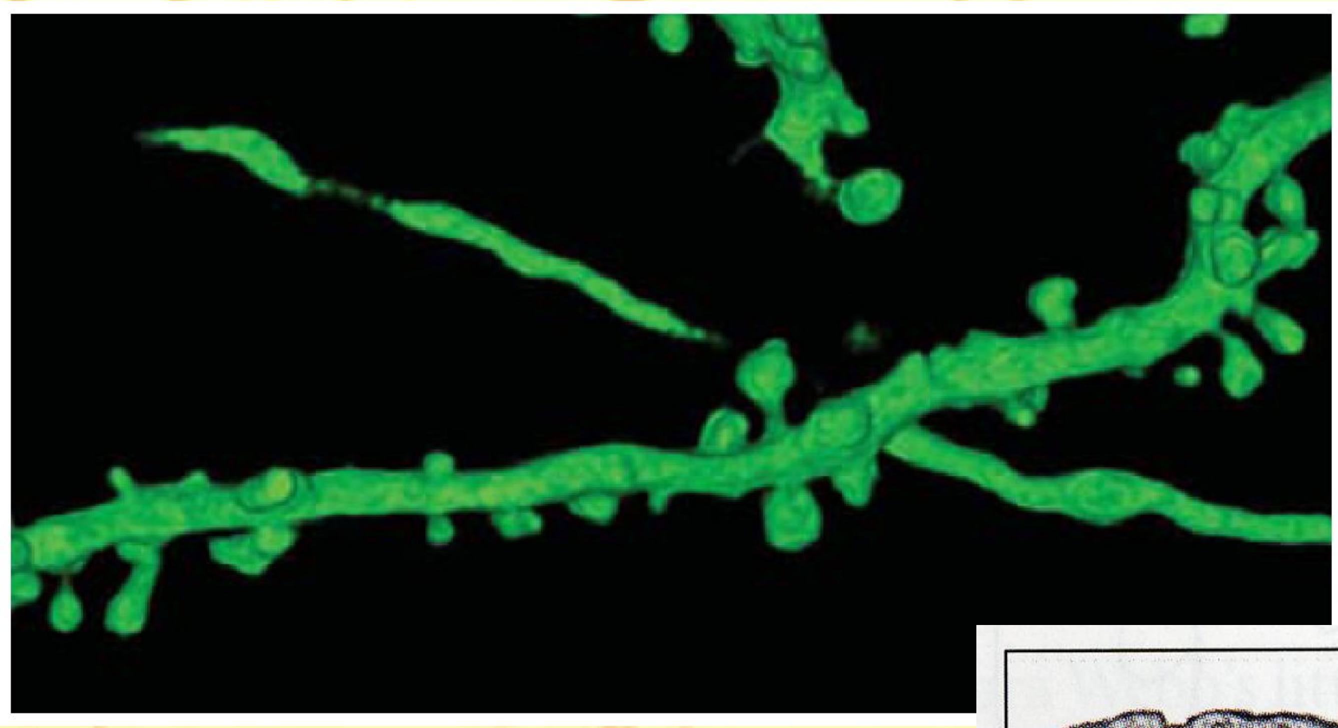
Синапсы

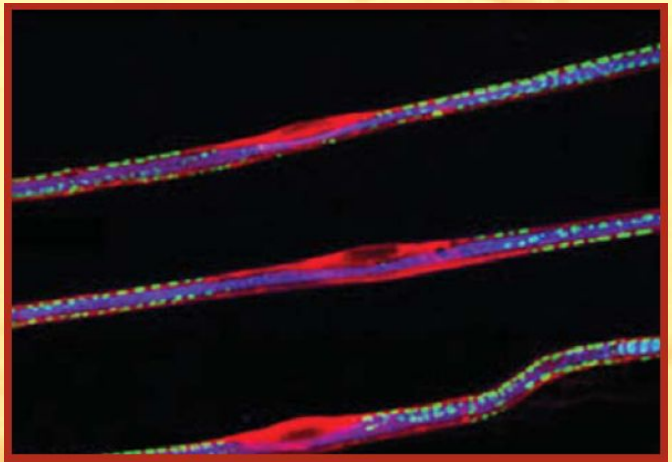


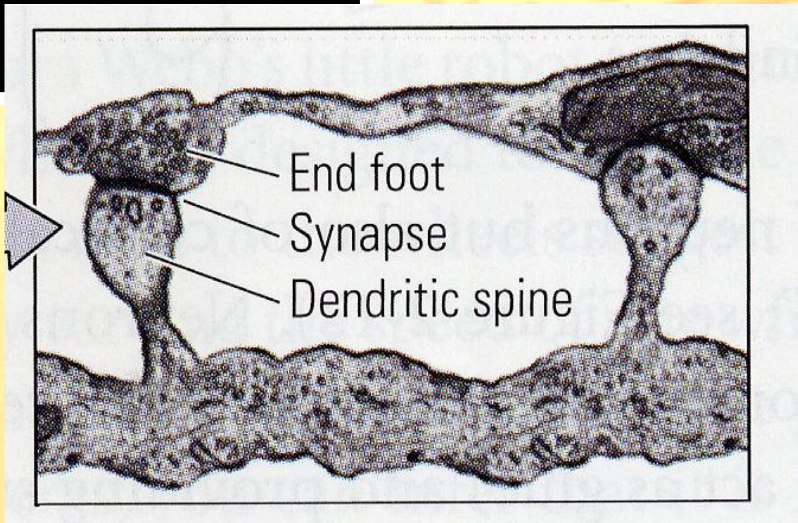
В реальности



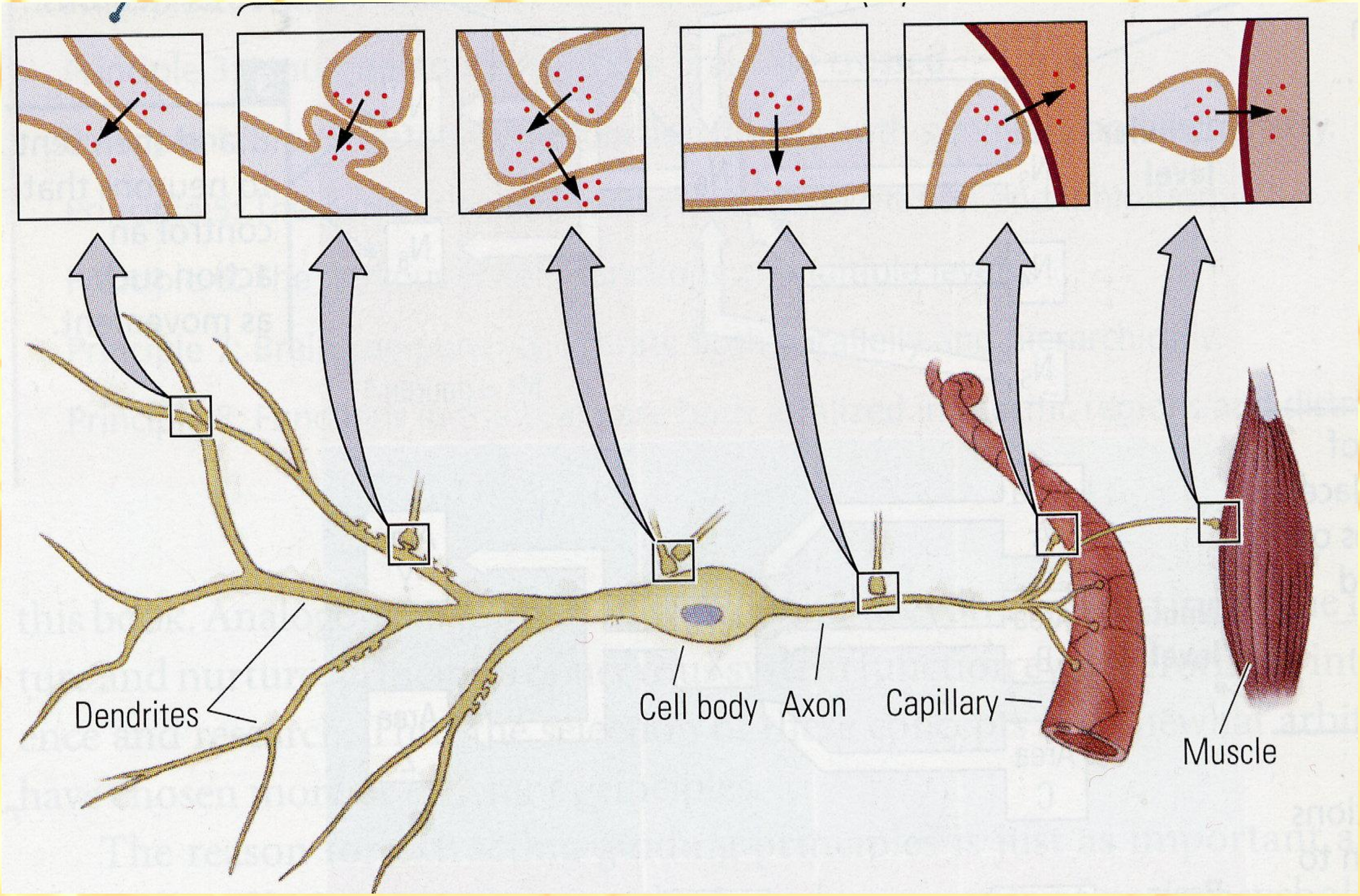
Синапсы - места контактов







Контакты



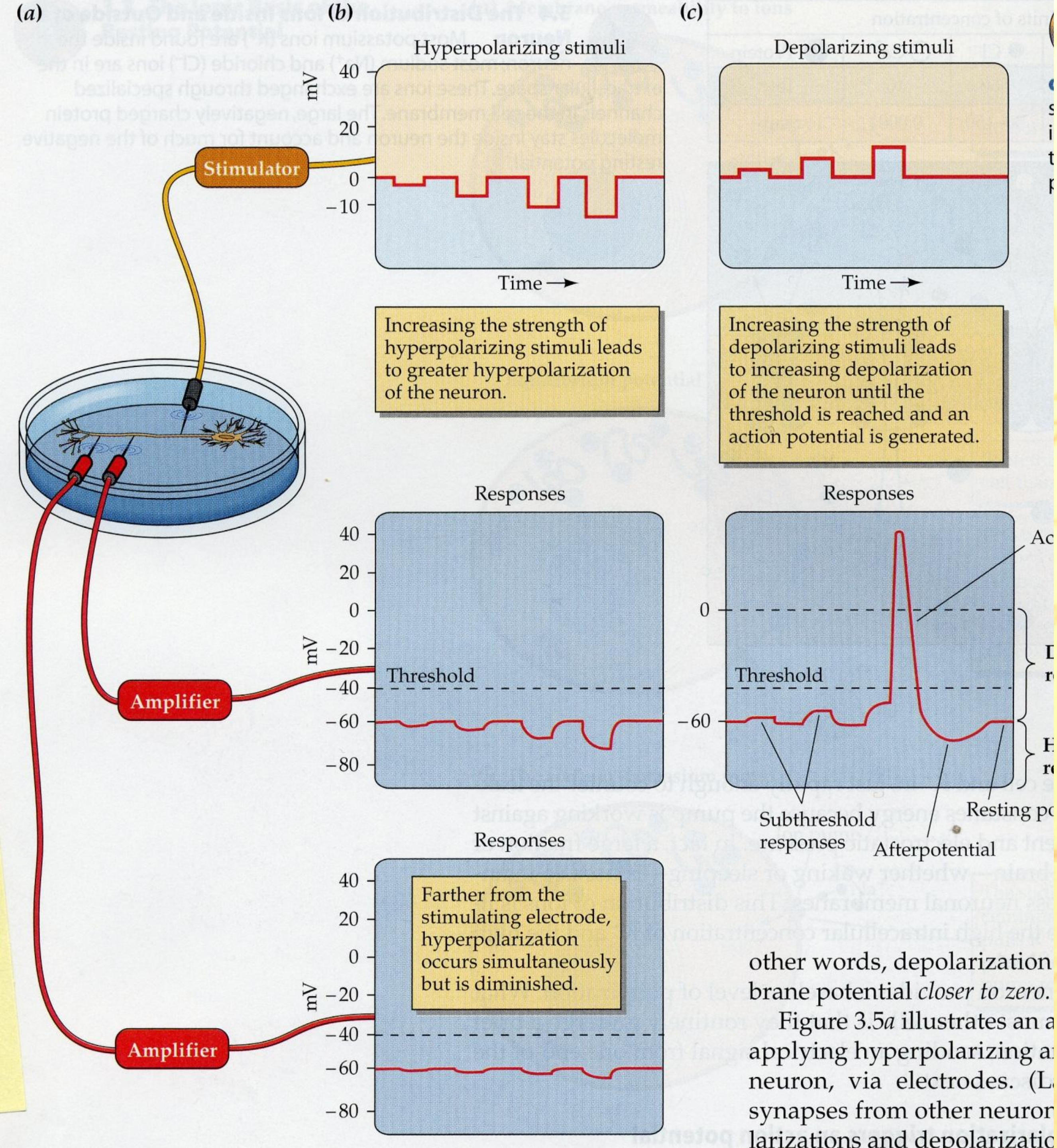
Нейрон

- ~~«микросхема, которая перерабатывает поступающую информацию и пересылает ее дальше, чтобы повлиять на другие микросхемы, с которыми она соединена.»~~

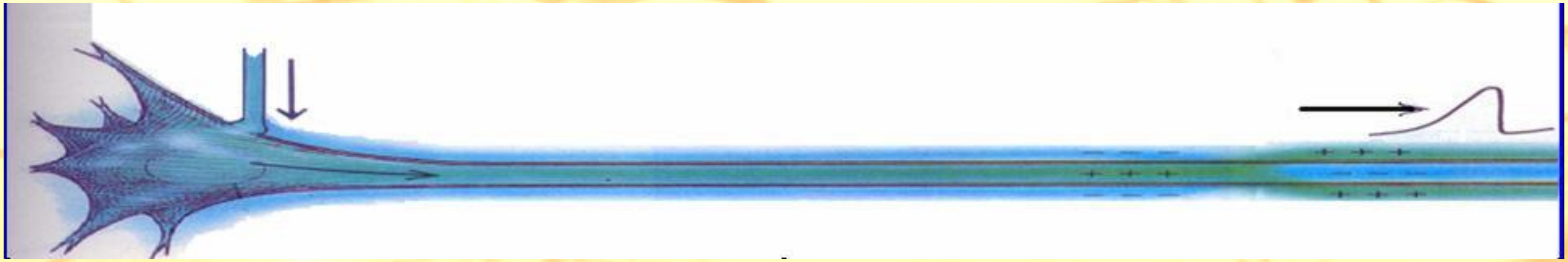
- самая сложная клетка, также как и другие клетки, выживает за счет взаимодействий с другими клетками (с химическим супом), НО ЧИСЛО ВЗАИМОДЕЙСТВИЙ ОГРОМНО (координирует всех)

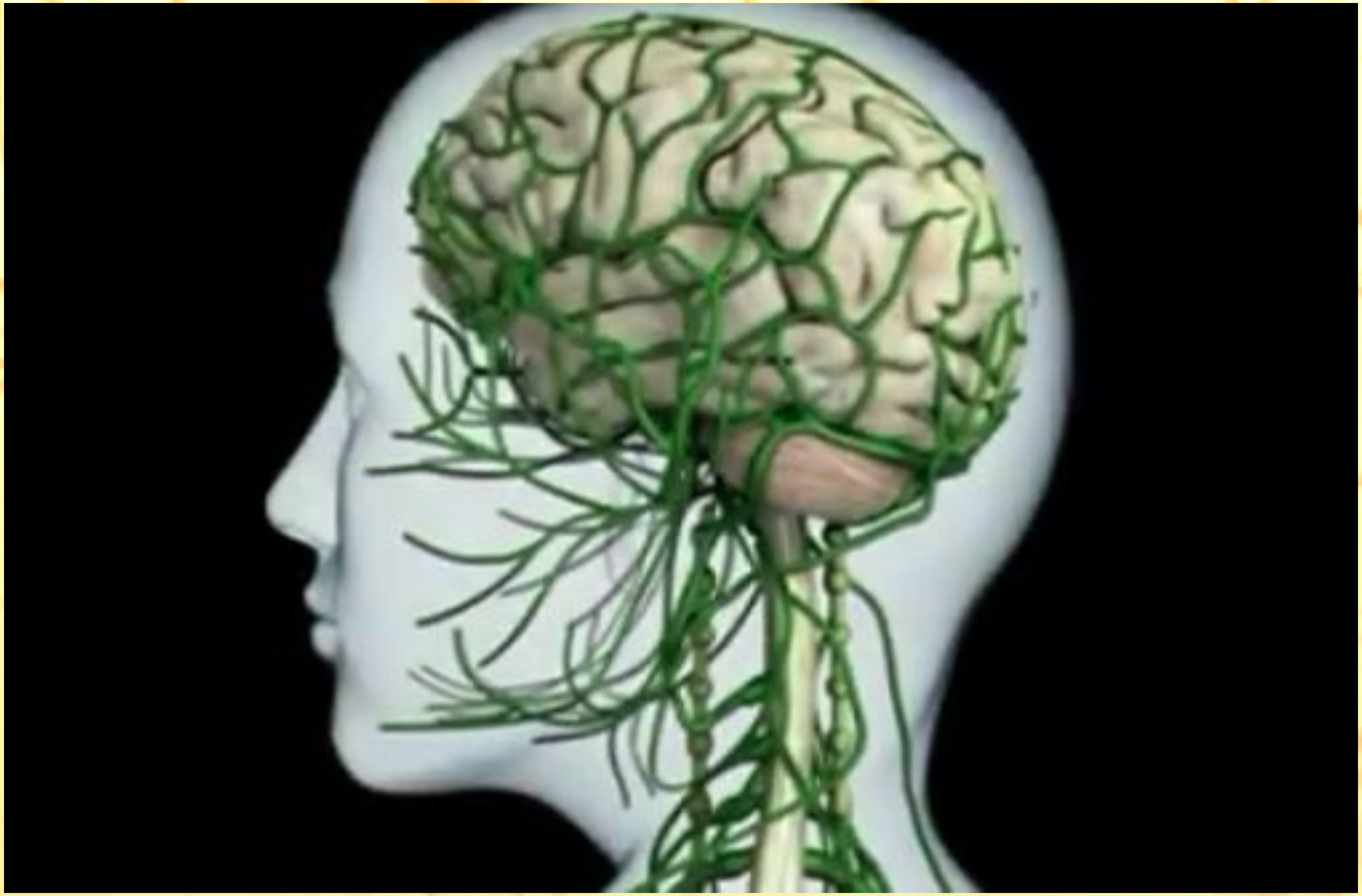
Нейрон

- 10^{12}
- время жизни нейронов совпадает со временем жизни индивида
- нейроны и глия (сходства и отличия)
  - отростки
  - синапсы
  - электрическая возбудимость
- пейсмекерный потенциал (Арванитаки и Халазонитис, 1955)

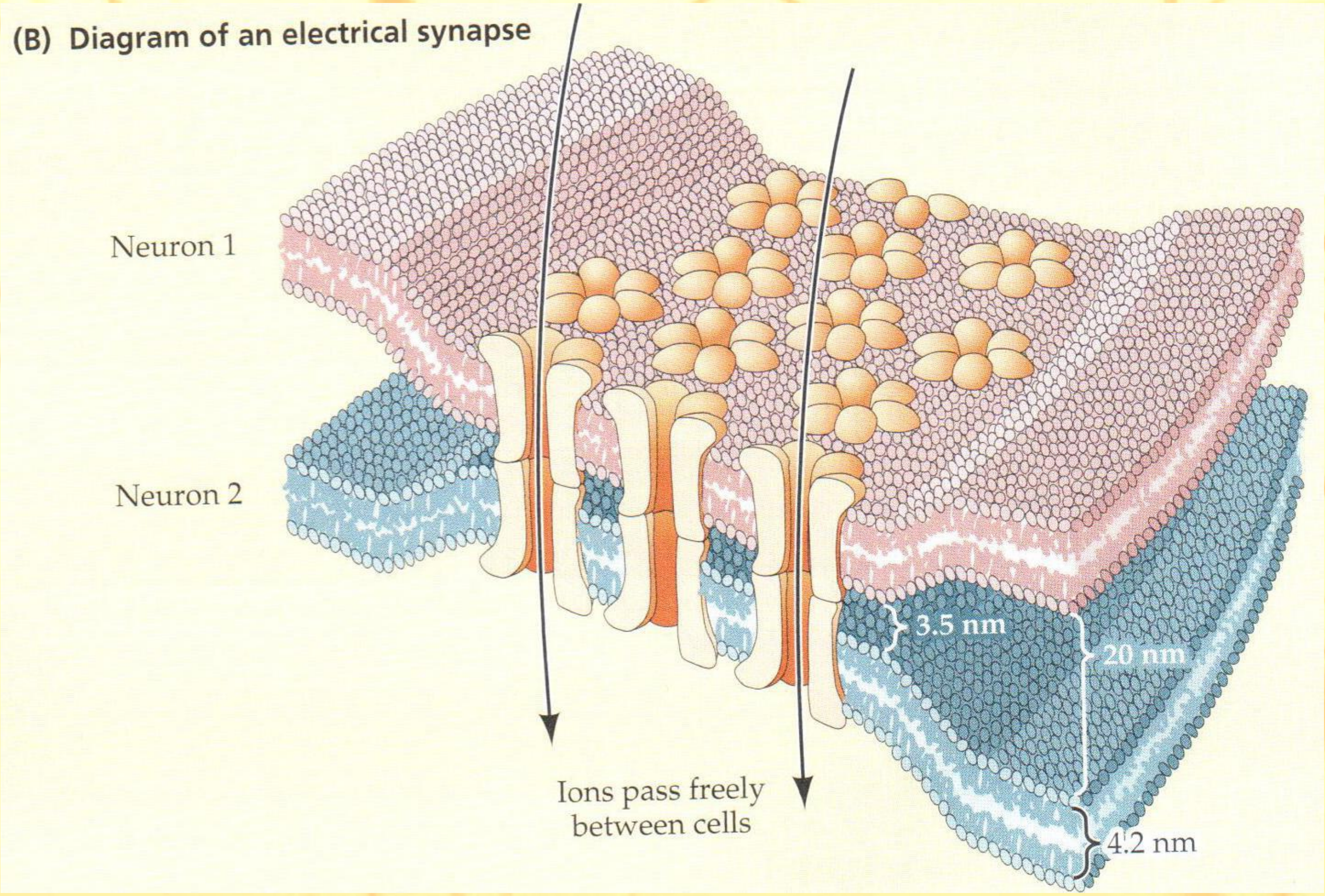


Элек-трические свойства нейронов





Электрические синапсы



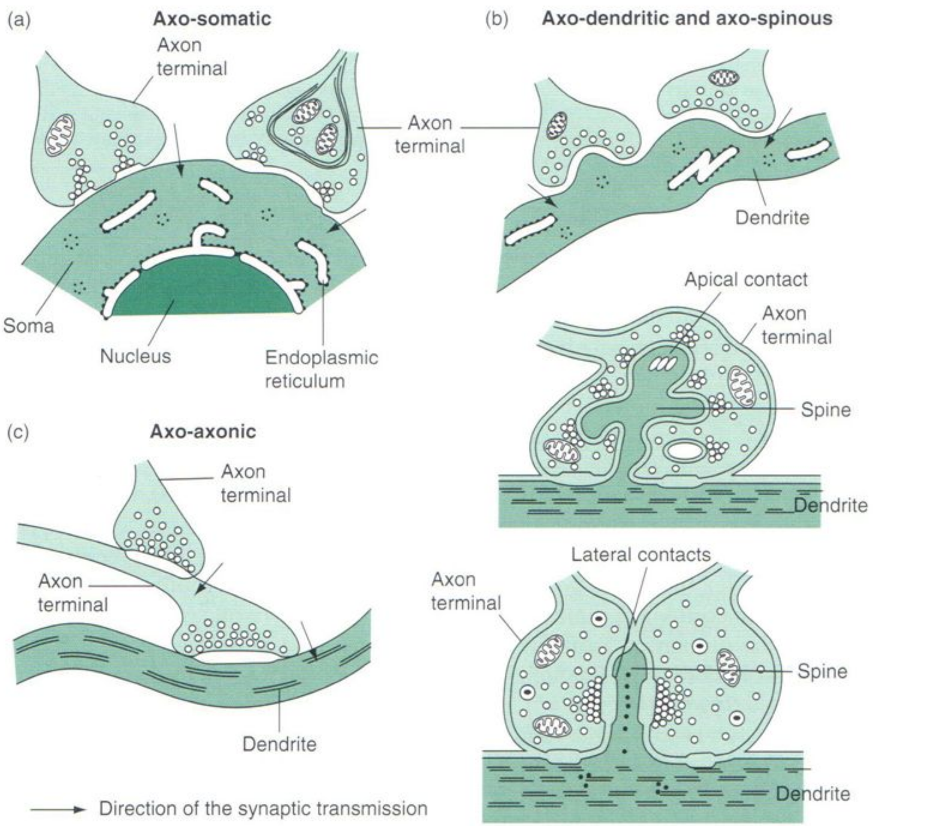
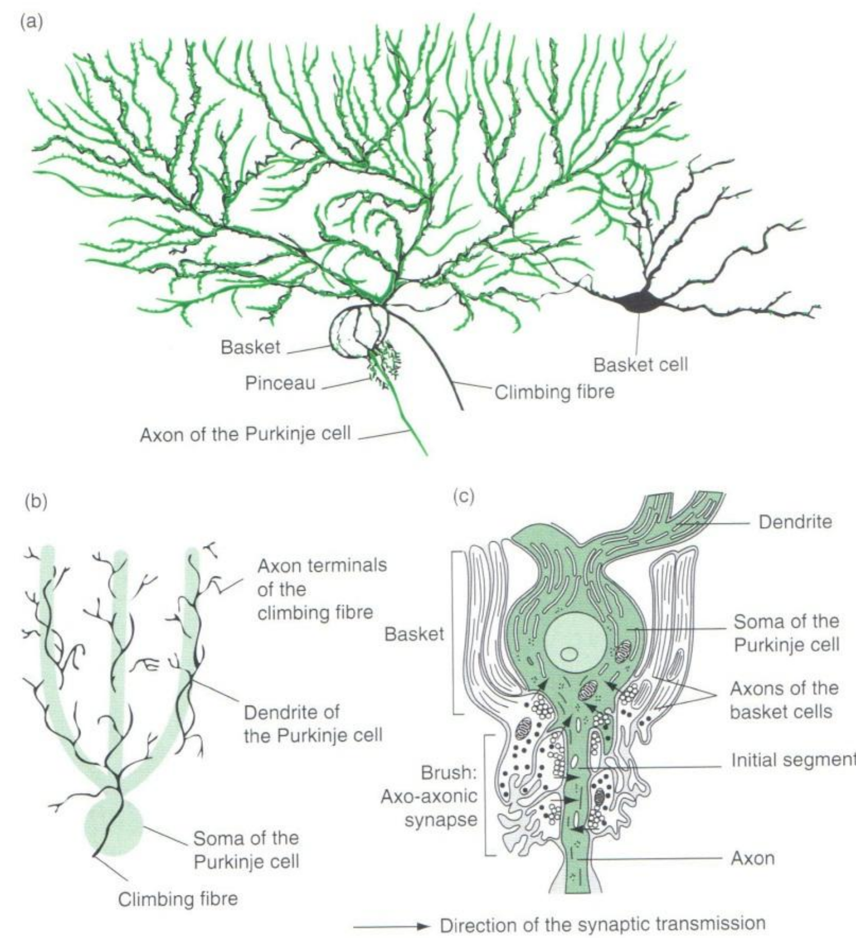


FIGURE 6.7 Types of interneuronal synapses.
(a) Terminal boutons forming axo-somatic synapses. **(b)** Top to bottom: Synapses between terminal boutons and a smooth dendritic branch (axo-dendritic synapse) and two examples of indented synapses between terminal boutons and a dendritic spine (axo-spinous synapses). **(c)** Synapse between an axon terminal and a terminal axon collateral (axo-axonic synapse). The 'postsynaptic' axon terminal is itself 'presynaptic' to a dendrite. From Hamlyn LH (1972) The fine structure of the mossy fiber endings in the hippocampus of the rabbit. *J. Anat.* **96**, 112–120, with permission.



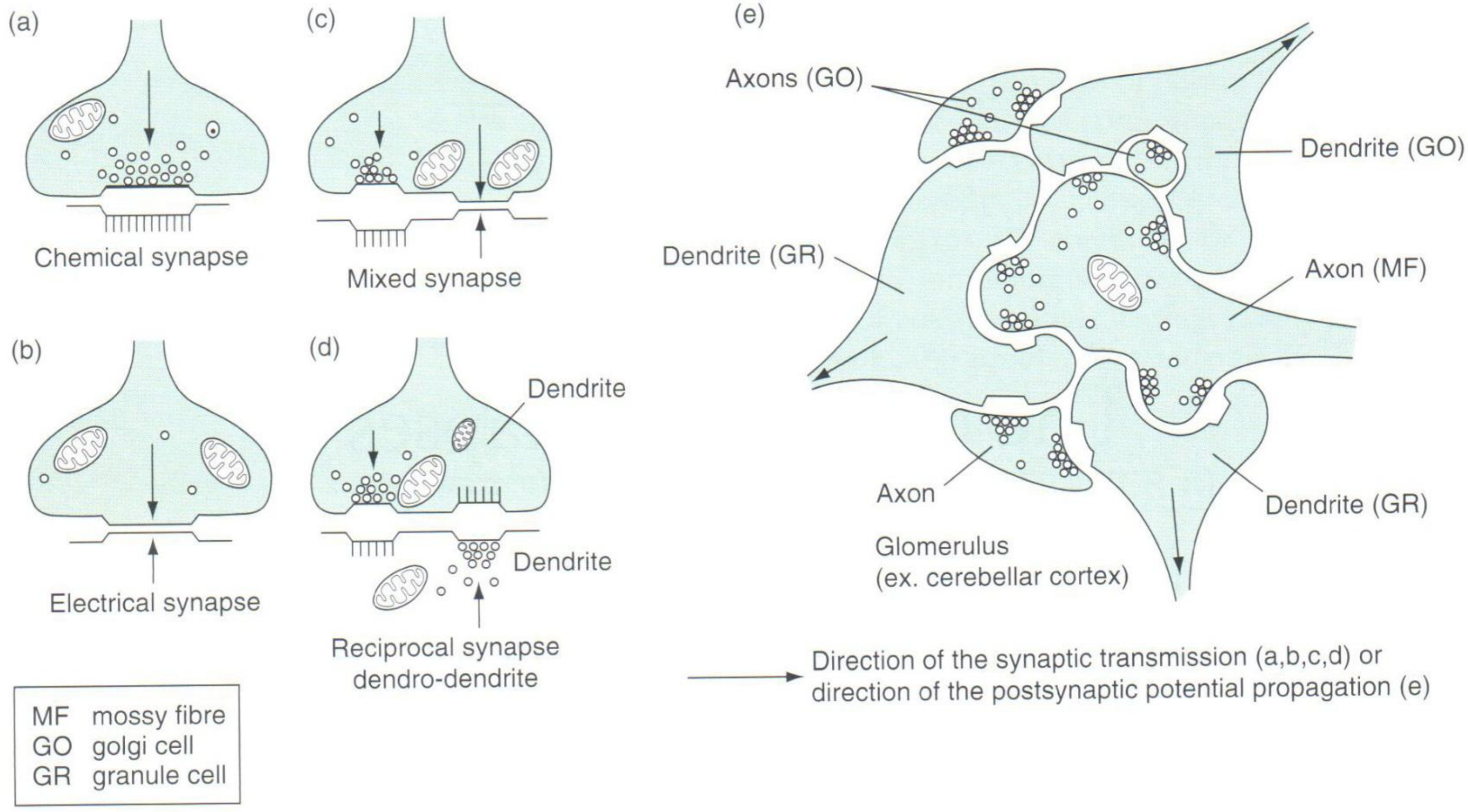


FIGURE 6.2 Types of synapses.
See text for explanations. MF, mossy fibre; GO, Golgi cell; GR, granule cell. Parts **(a)–(d)** from Bodian D (1972) Neuronal junctions: a revolutionary decade. *Anat. Rec.*, **174**, 73–82, with permission. Drawing **(e)** from Steiger U (1967) Uber den Feinbau des Neuropils im Corpus pedunculatum des Waldaneise. Z. *Zelforsch*. **81**, 511–536, with permission.

Нейрон

- 10^{12}
- время жизни нейронов совпадает со временем жизни индивида
- нейроны и глия (сходства и отличия)
    - отростки
    - синапсы
    - электрическая возбудимость
- пейсмекерный потенциал (Арванитаки и Халазонитис, 1955)

Потенциал покоя

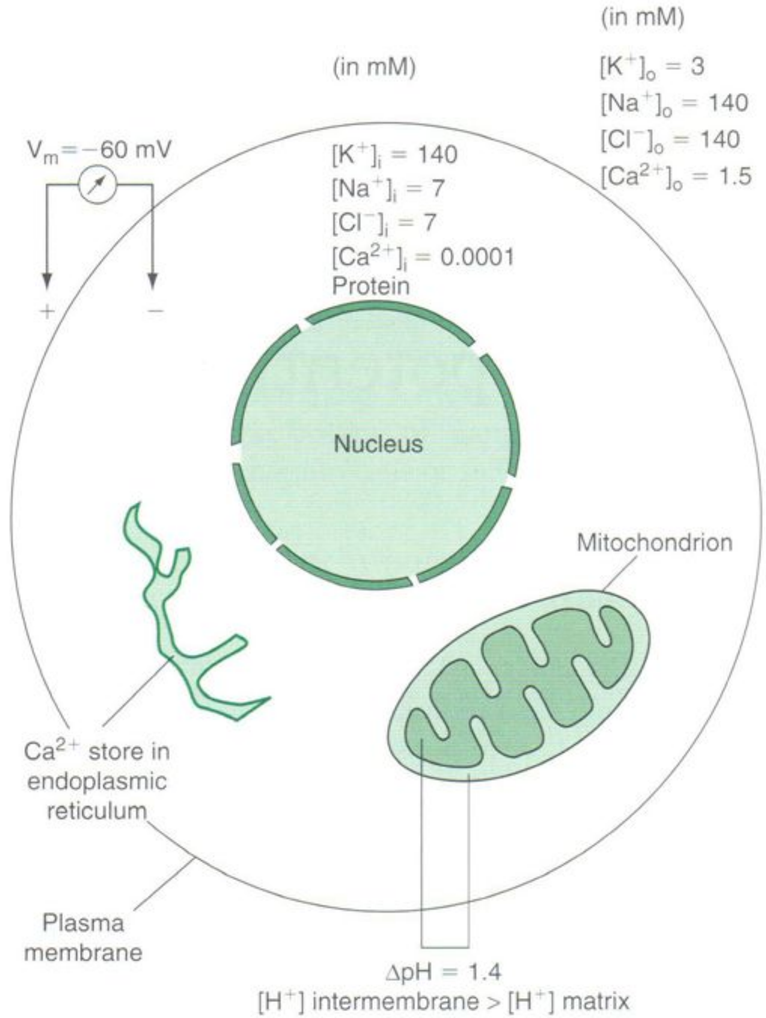
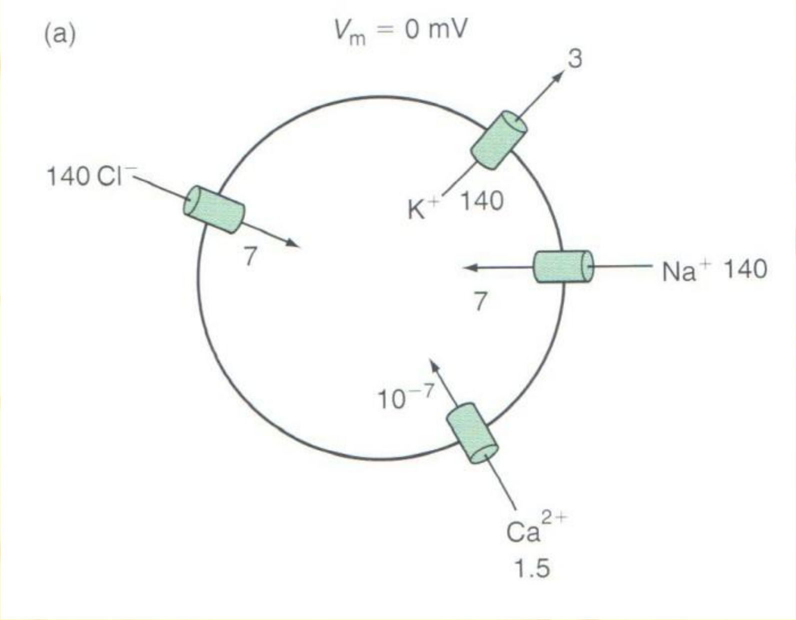
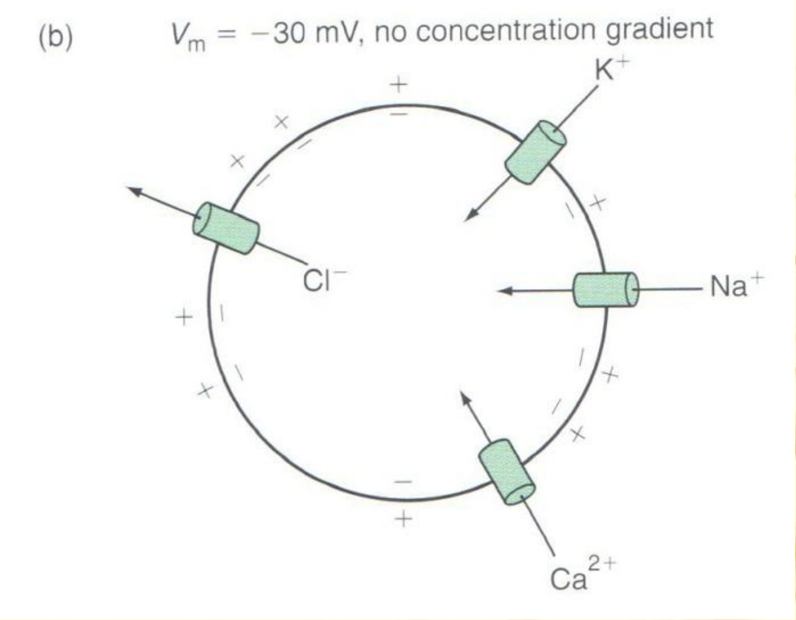


FIGURE 3.2 There is an unequal distribution of ions across neuronal plasma membranes. Membrane potential.
Idealized nerve cell (depicted as a sphere) with relative concentra-

Пассивное движение ионов

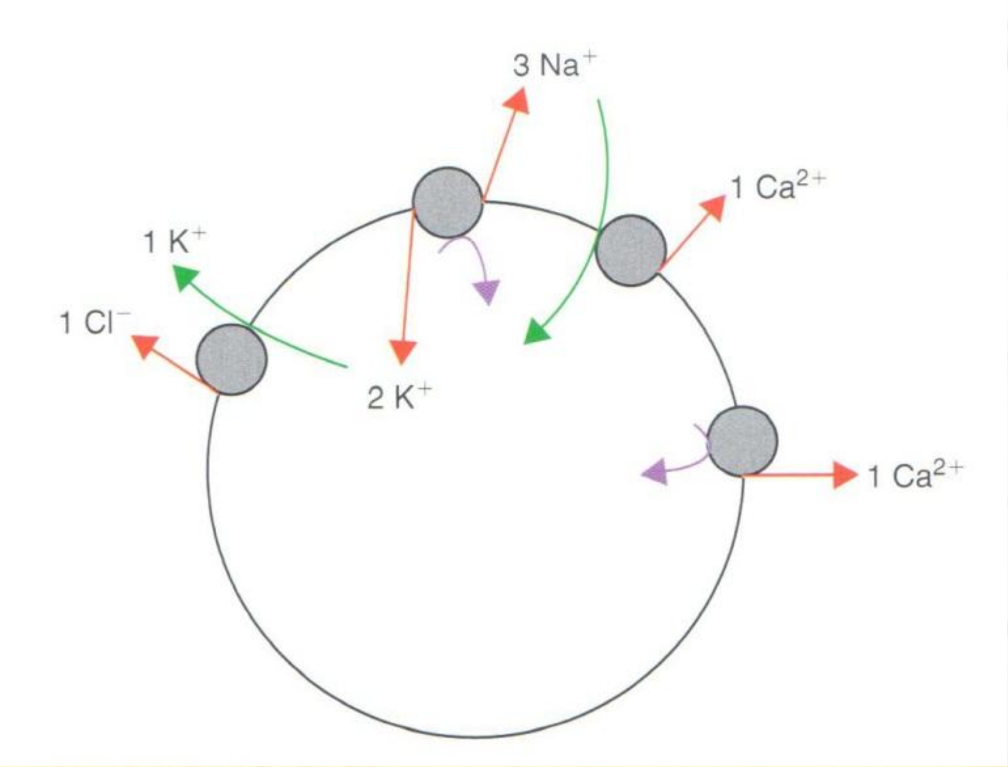


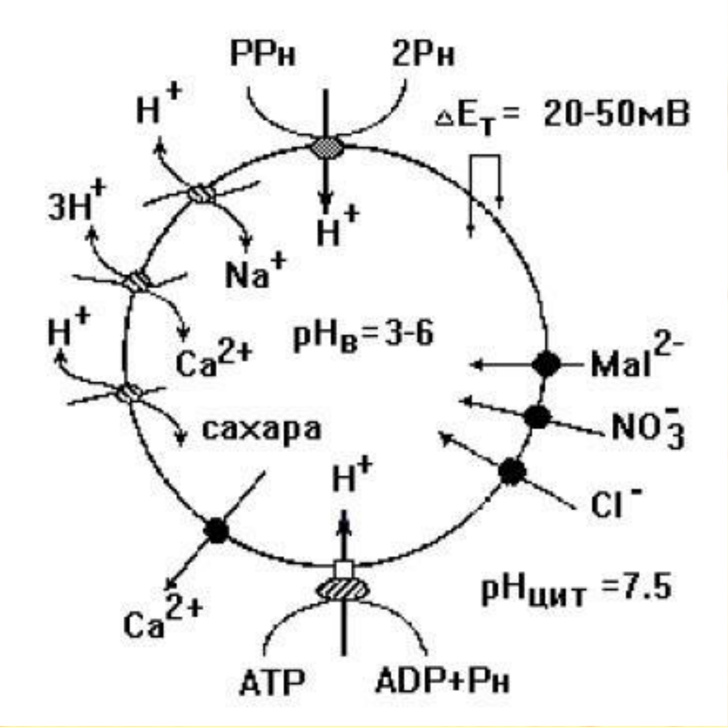


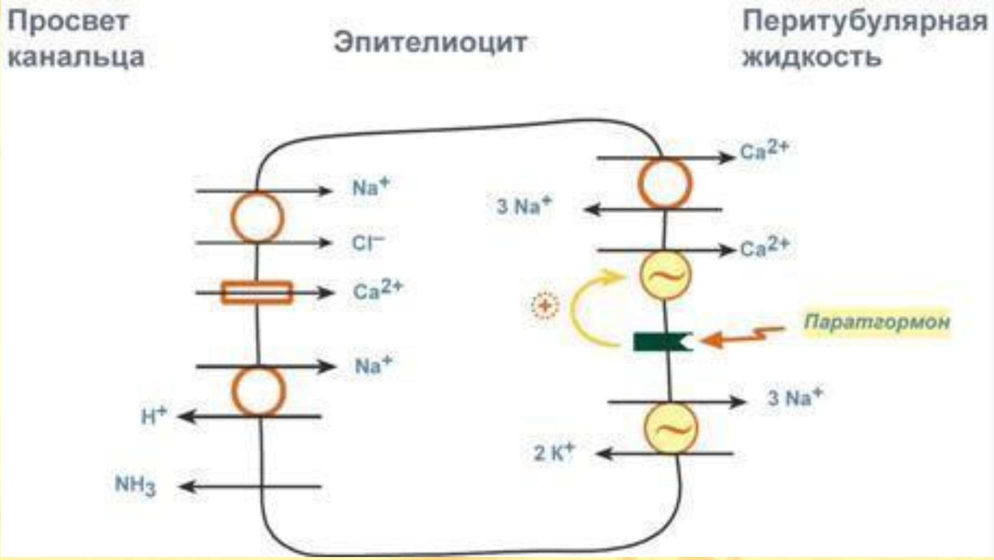
Движение по градиентам концентрации

Движение по электрическому градиенту

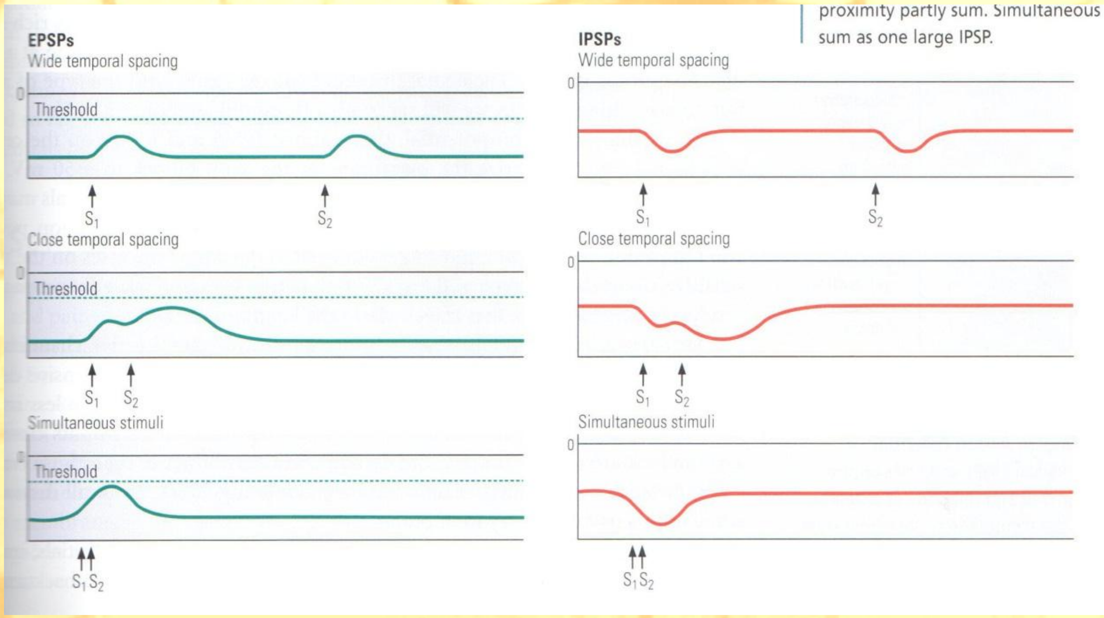
Активный транспорт ионов

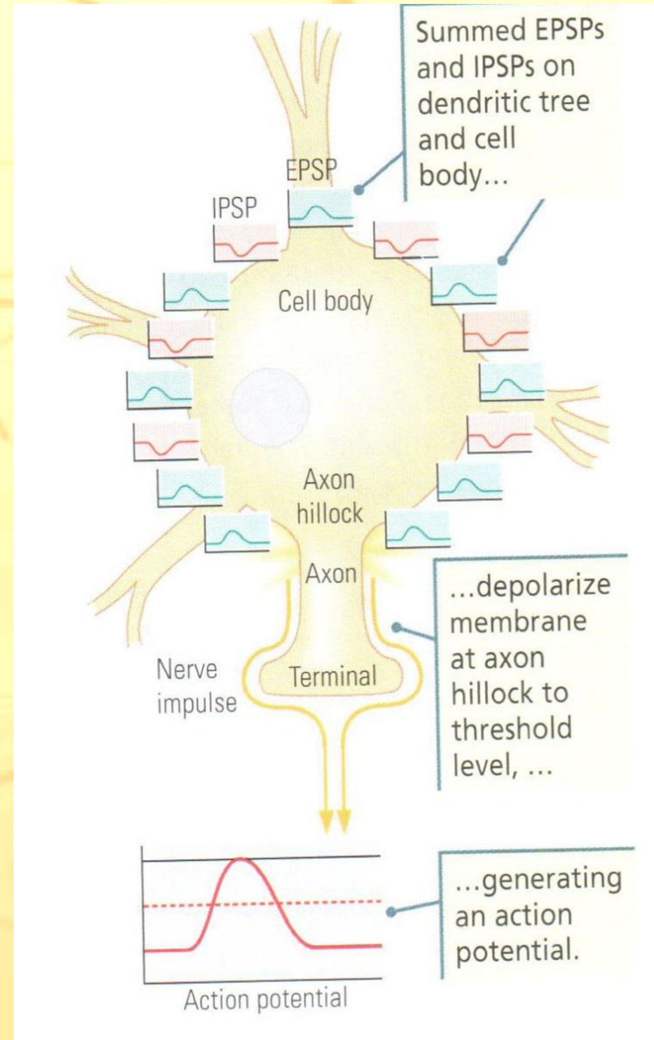



PPн
2Pн
H+
ΔEт = 20-50мВ
3H+
H+
Na+
H+
Ca2+
pHв=3-6
Mal2-
NO3-
сахара
H+
Cl-
Ca2+
pHцит =7.5
ATP
ADP+Pн


Просвет канальца
Эпителиоцит
Перитубулярная жидкость
Na+
Cl−
Ca2+
Na+
H+
NH3
Ca2+
3 Na+
Ca2+
Паратгормон
3 Na+
2 K+

Множественность событий на мембране





Вероятность генерации ПД

Распространение ПД

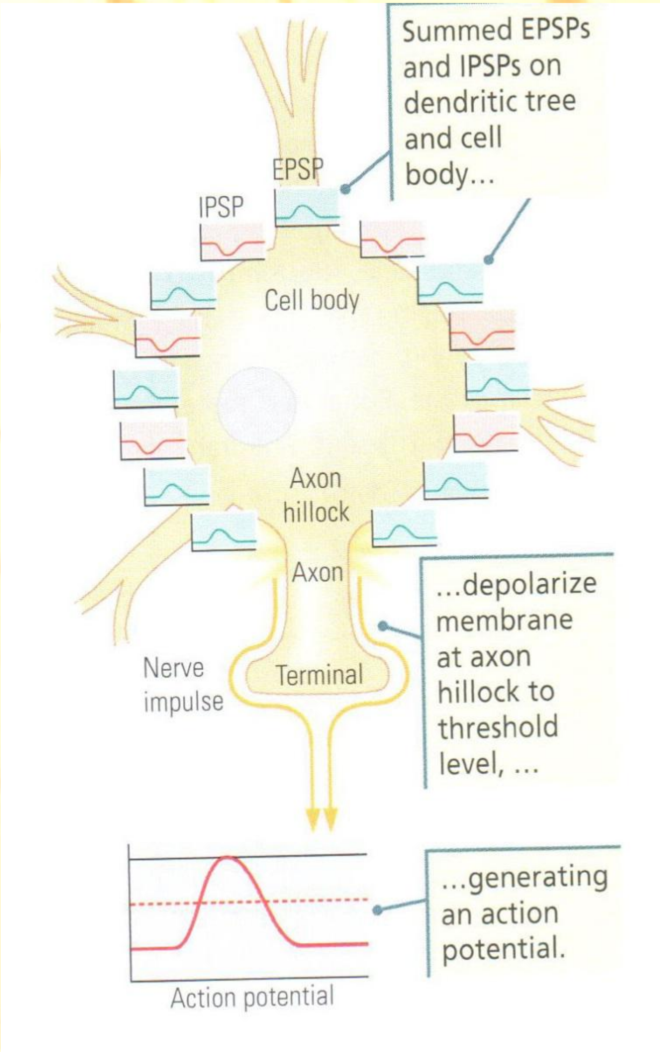
Action potential initiation and backpropagation in neurons of the mammalian CNS

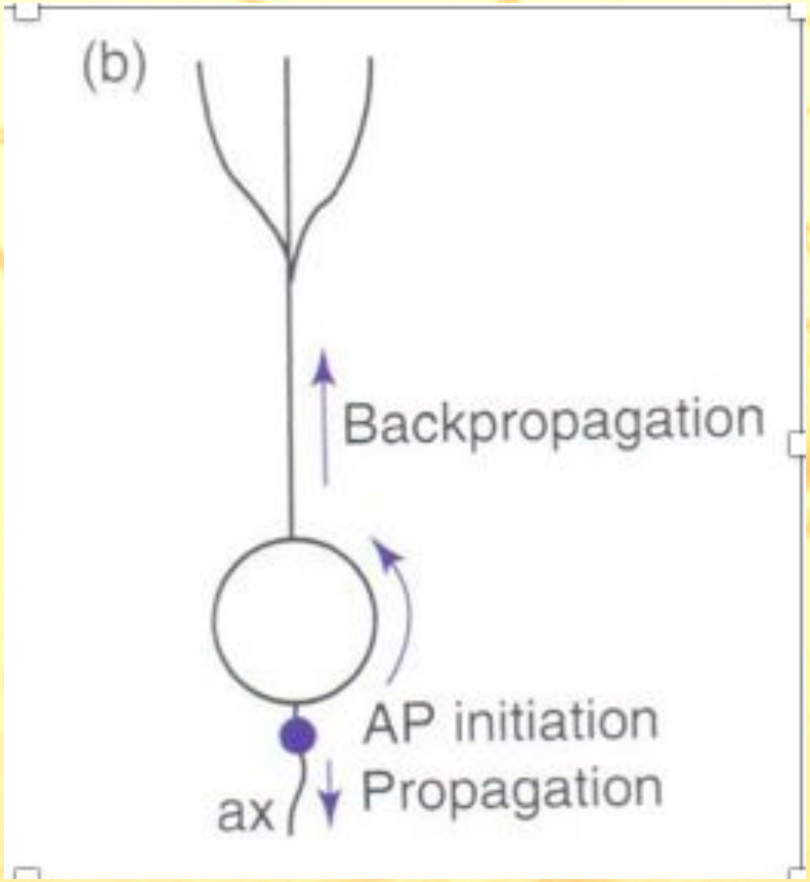
Greg Stuart, Nelson Spruston, Bert Sakmann and Michael Häusser

Most neurons in the mammalian CNS encode and transmit information via action potentials. Knowledge of where these electrical events are initiated and how they propagate within neurons is therefore fundamental to an understanding of neuronal function. While work from the 1950s suggested that action potentials are initiated in the axon, many subsequent investigations have suggested that action potentials can also be initiated in the dendrites. Recently, experiments using simultaneous patch-pipette recordings from different locations on the same neuron have been used to address this issue directly. These studies show that the site of action potential initiation is in the axon, even when synaptic activation is powerful enough to elicit dendritic electrogenesis. Furthermore, these and other studies also show that following initiation, action potentials actively backpropagate into the dendrites of many neuronal types, providing a retrograde signal of neuronal output to the dendritic tree.

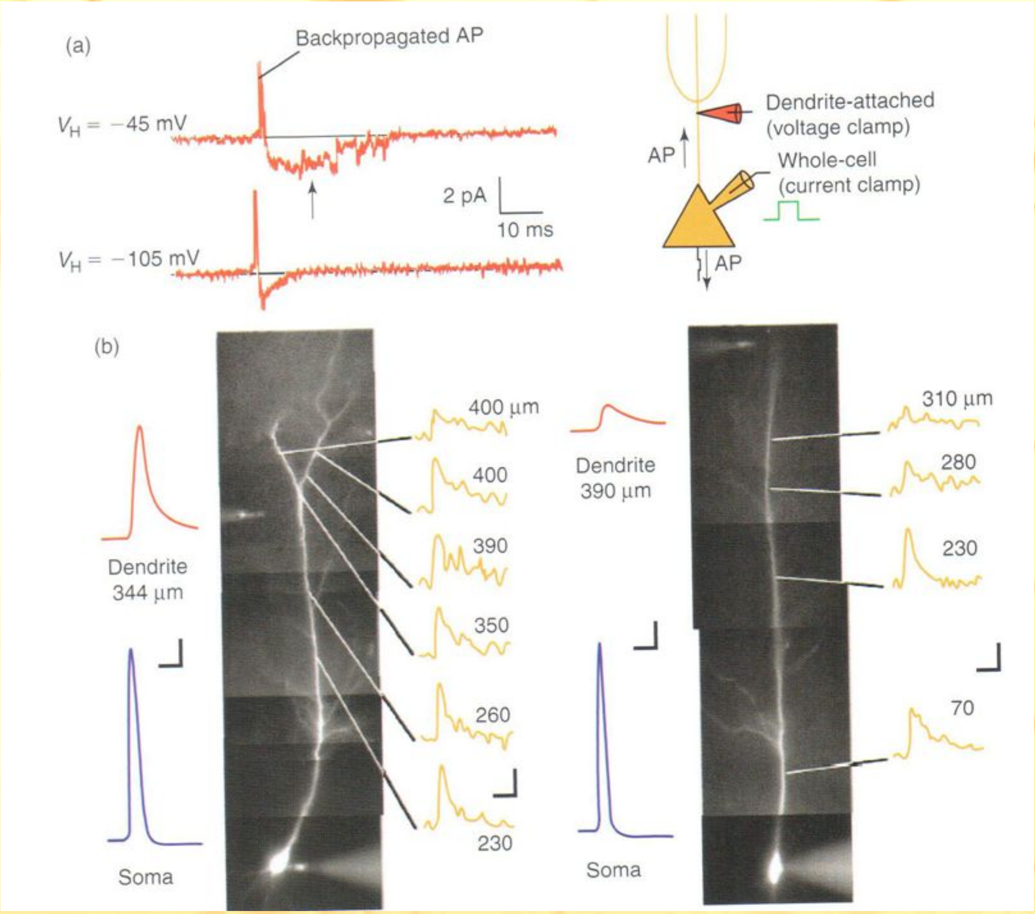
Trends Neurosci. (1997) 20, 125–131

Активное обратное распространение ПД





Распространение ПД



Генераторы центральных паттернов

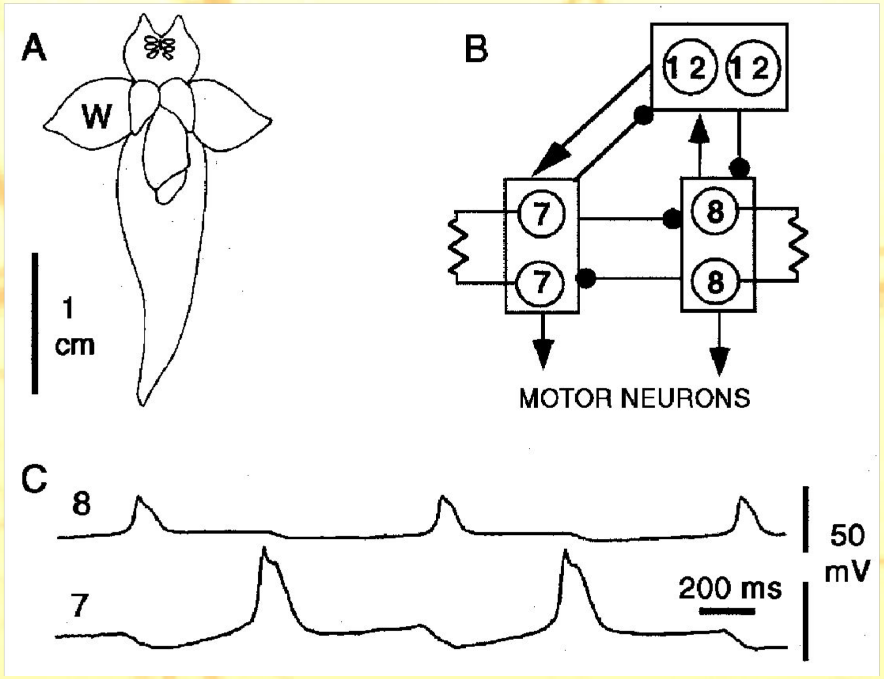
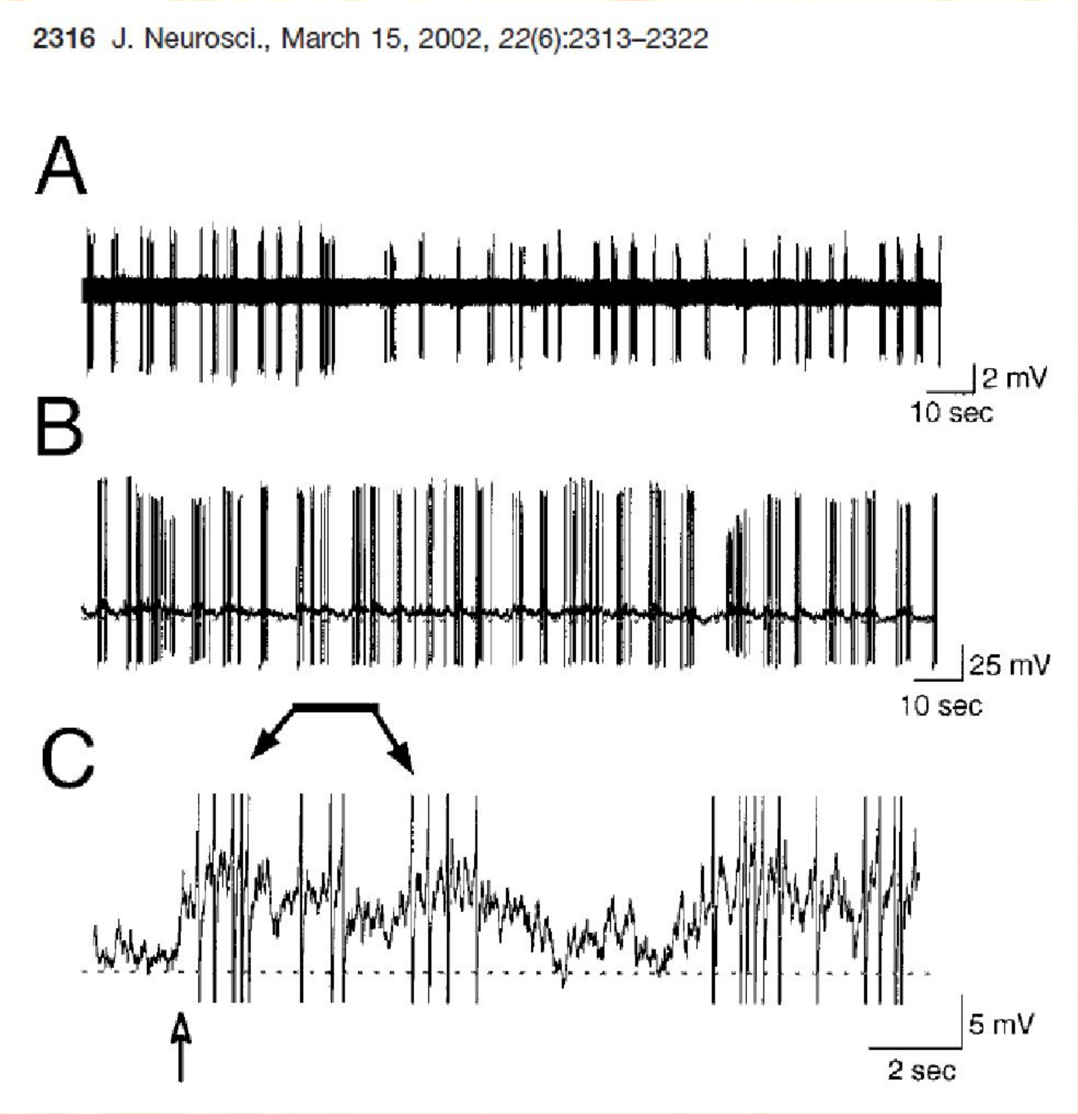


Fig. 1. Characterization of the central pattern generator for swimming in the marine mollusk *Clione limacina* (class Gastropoda, subclass Opistho-

Спонтанная активность

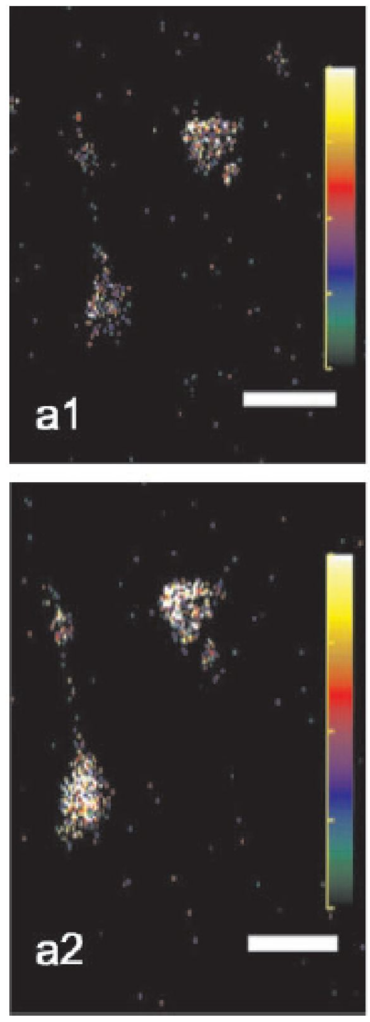


Спонтанная активность

American Journal of Pathology, Vol. 161, No. 5, November 2002

Technical Advance

Isolation of Living Neurons from Human Elderly Brains Using the Immunomagnetic Sorting DNA-Linker System



Spontaneous cortical activity in awake monkeys composed of neuronal avalanches

Thomas Petermann[a], Tara C. Thiagarajan[a], Mikhail A. Lebedev[b], Miguel A. L. Nicolelis[b], Dante R. Chialvo[c], and Dietmar Plenz[a,1]

[a]Section on Critical Brain Dynamics, National Institute of Mental Health, Bethesda, MD 20892; [b]Department of Neurobiology, Center for Neuroengineering, Duke University, Durham, NC 27710; and [c]Department of Physiology, Northwestern University, Chicago, IL 60611

Edited by Eve Marder, Brandeis University, Waltham, MA, and approved July 16, 2009 (received for review April 16, 2009)

The cerebral cortex displays spontaneous activity, also known as 'ongoing' or 'resting state' activity, which persists in the absence of sensory stimuli or motor outputs. The ongoing activity is a robust feature of cortical dynamics as it is only modulated to a small extent by stimulus presentation (1), but contributes significantly to the large variability observed in stimulus responses (2–5). In fact,

Spontaneous neuronal activity is an important property of the cerebral cortex but its spatiotemporal organization and dynamical framework remain poorly understood. Studies in reduced systems—tissue cultures, acute slices, and anesthetized rats—show that spontaneous activity forms characteristic clusters in space and time, called neuronal avalanches. Modeling studies

Проблемы

- зачем медиаторы?
  - «Почему имеются разные нейротрансмиттеры, если лишь одного достаточно для того, чтобы опосредовать передачу всех электрических сигналов?»

    Э. Кендел

- зачем сложнейший внутриклеточный аппарат?

Клетка

«Утверждение, что из клеток, составляющих нас каждая является индивидуальной эгоцентричной жизнью – не просто фраза. Это не просто удачный способ описания. Клетка как компонент тела – не только визуально ограниченный модуль, это отдельная жизнь, сосредоточенная на себе. Она живет собственной жизнью ... Клетка – это отдельная жизнь, и наша жизнь, которая в свою очередь, является отдельной жизнью, всецело состоит из жизней-клеток.»

Sherrington, 1951

«Единство» нейрона

- Анатомическое (сначала без связей, затем отростки формируют контакты)
- Регенеративное (отражение соматических процессов в самых отдаленных частях аксона)
- Функциональное (нейрон обладает «физиологической» индивидуальностью)
- Генетическое (онтогенетическое развитие)

Где граница: отдельный организм – неотдельный организм

- Аналоги в эволюции

Клетка

«Нервные клетки, как и все другие клетки, ведут индивидуальное существование, они дышат, они ассимилируют, они расходуют свои собственные запасы энергии, они воссоздают утраченные части собственного тела; короче говоря, каждая клетка является самостоятельной живой единицей, осуществляющей более или менее совершенно регуляцию трофических процессов протекающих в ней.»

Sherrington, 1969

Метаболизм клетки

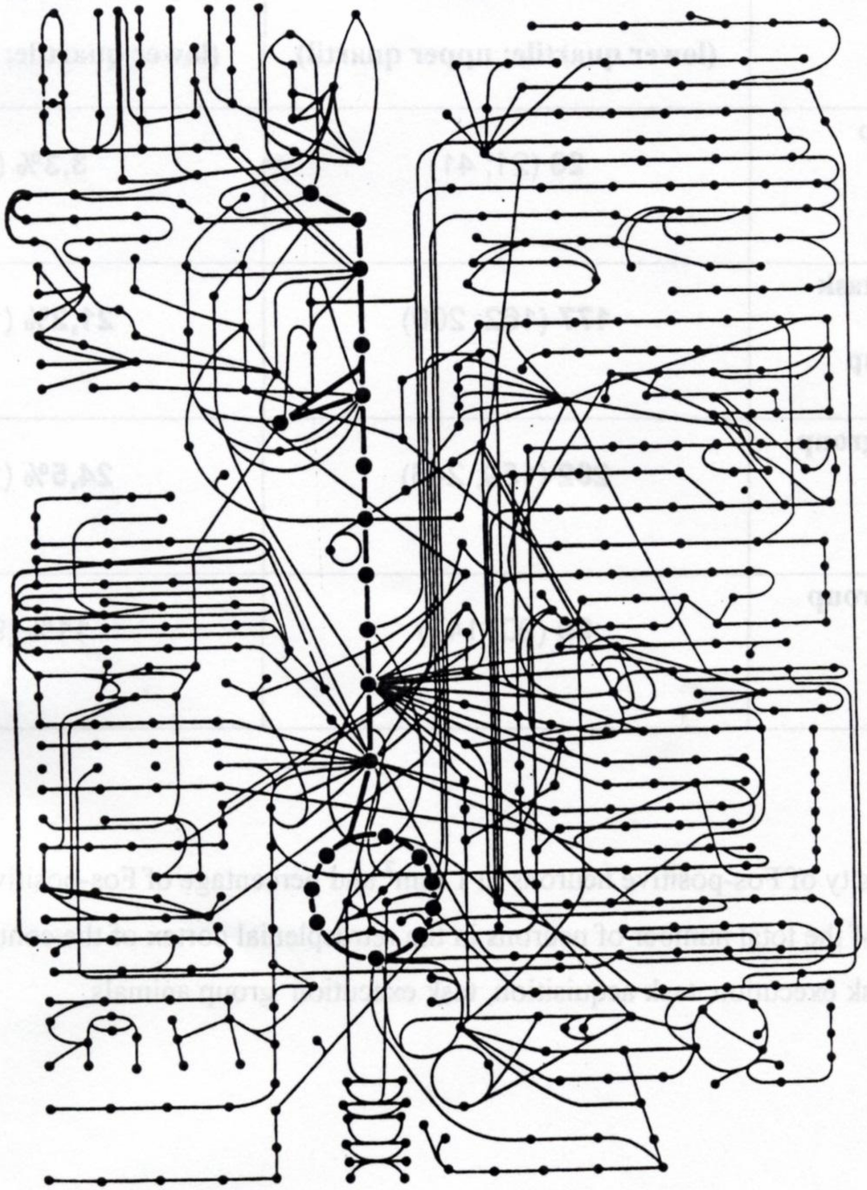
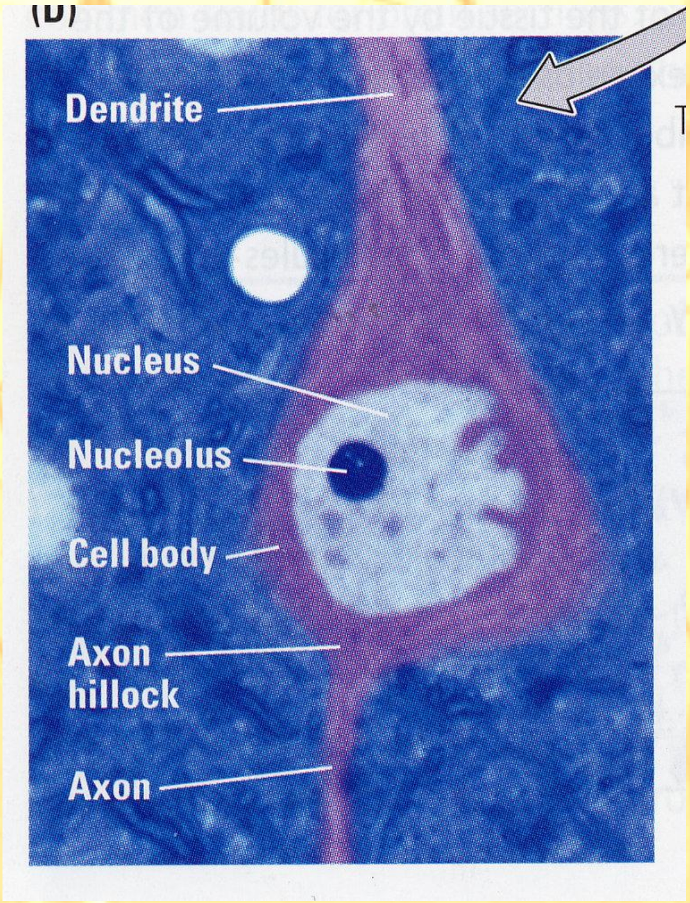
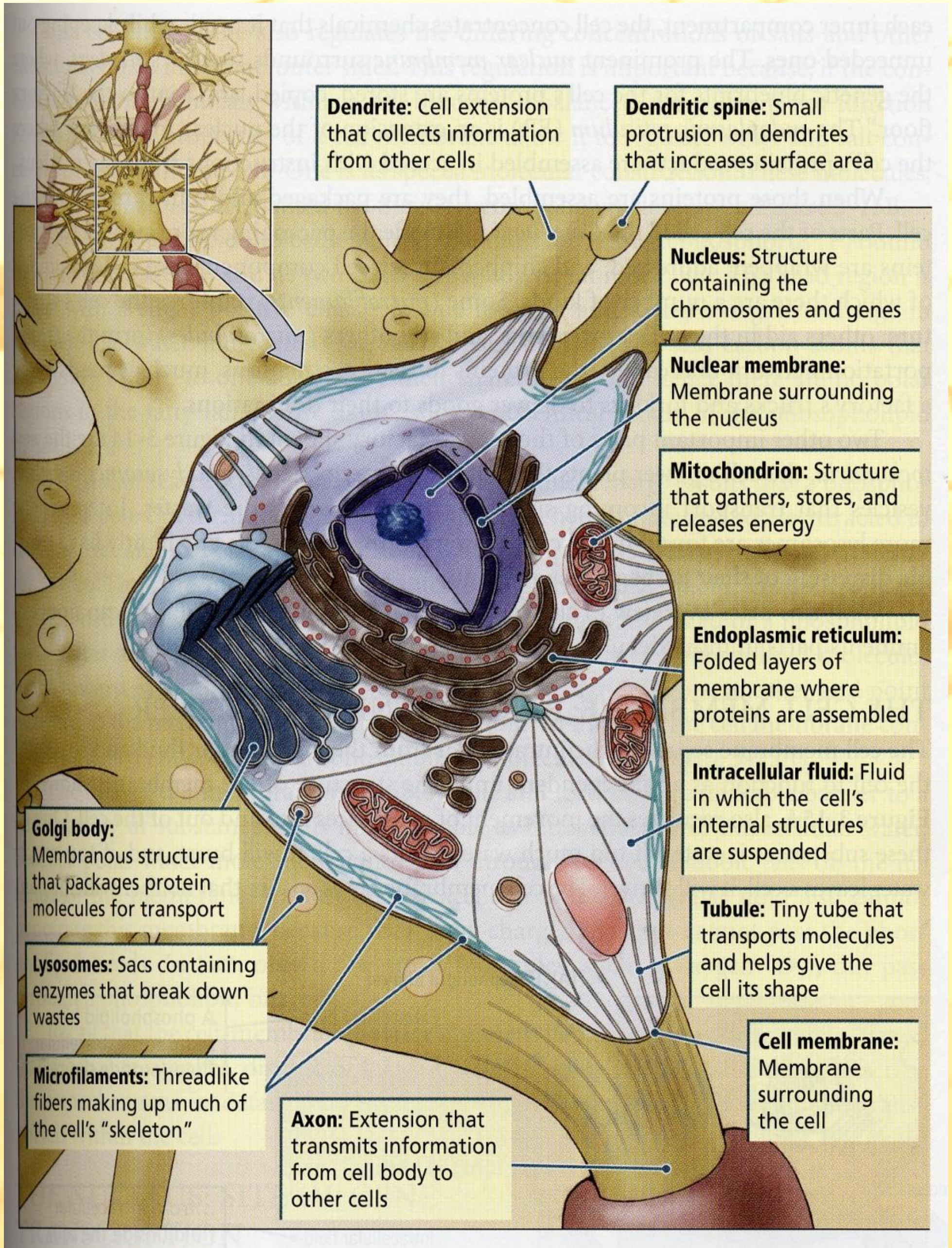


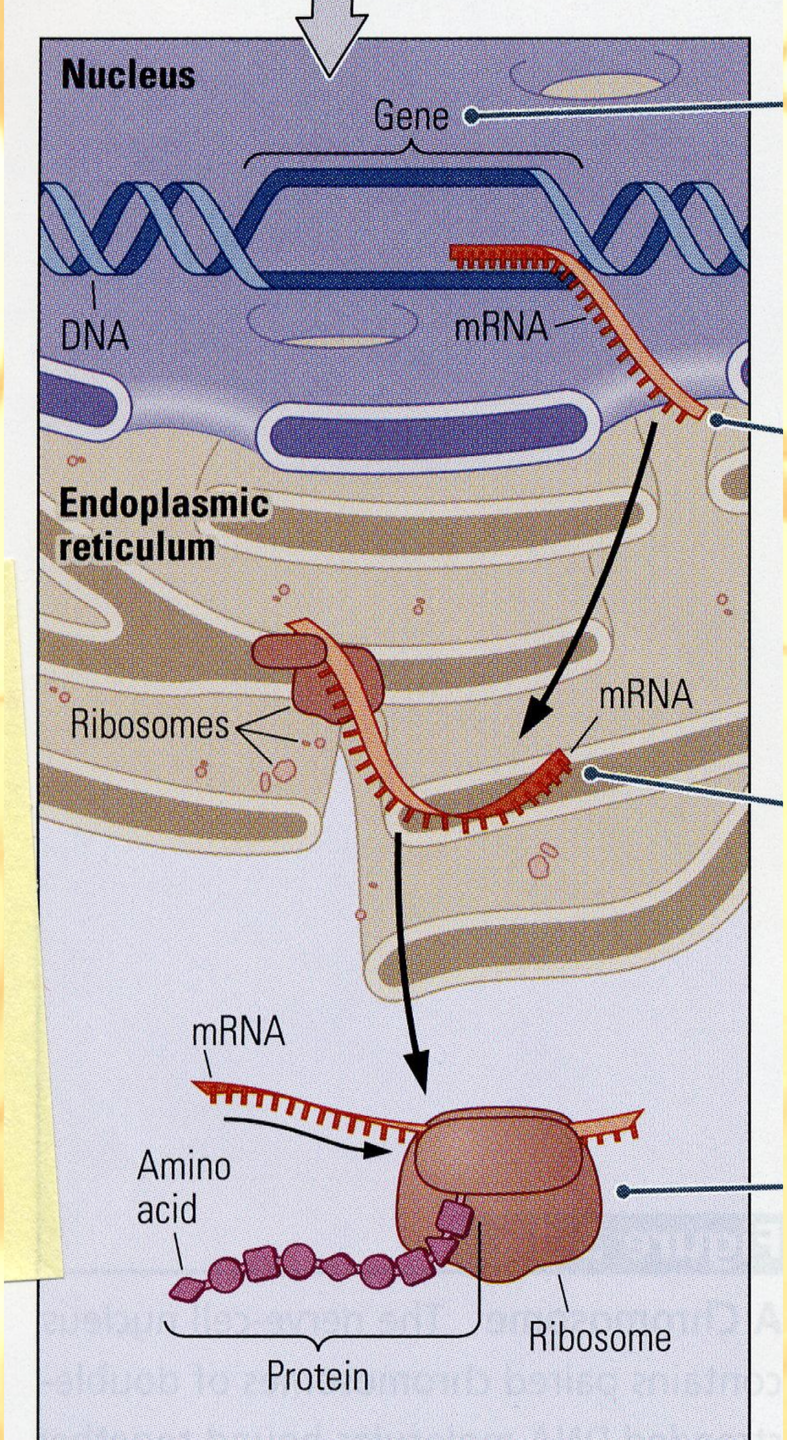
Figure 6.8 The network of intermediary metabolism. The chart shows about 700 small molecules interacting; each dot is a metabolite, each line a reaction pathway.

Внутриклеточная жизнь

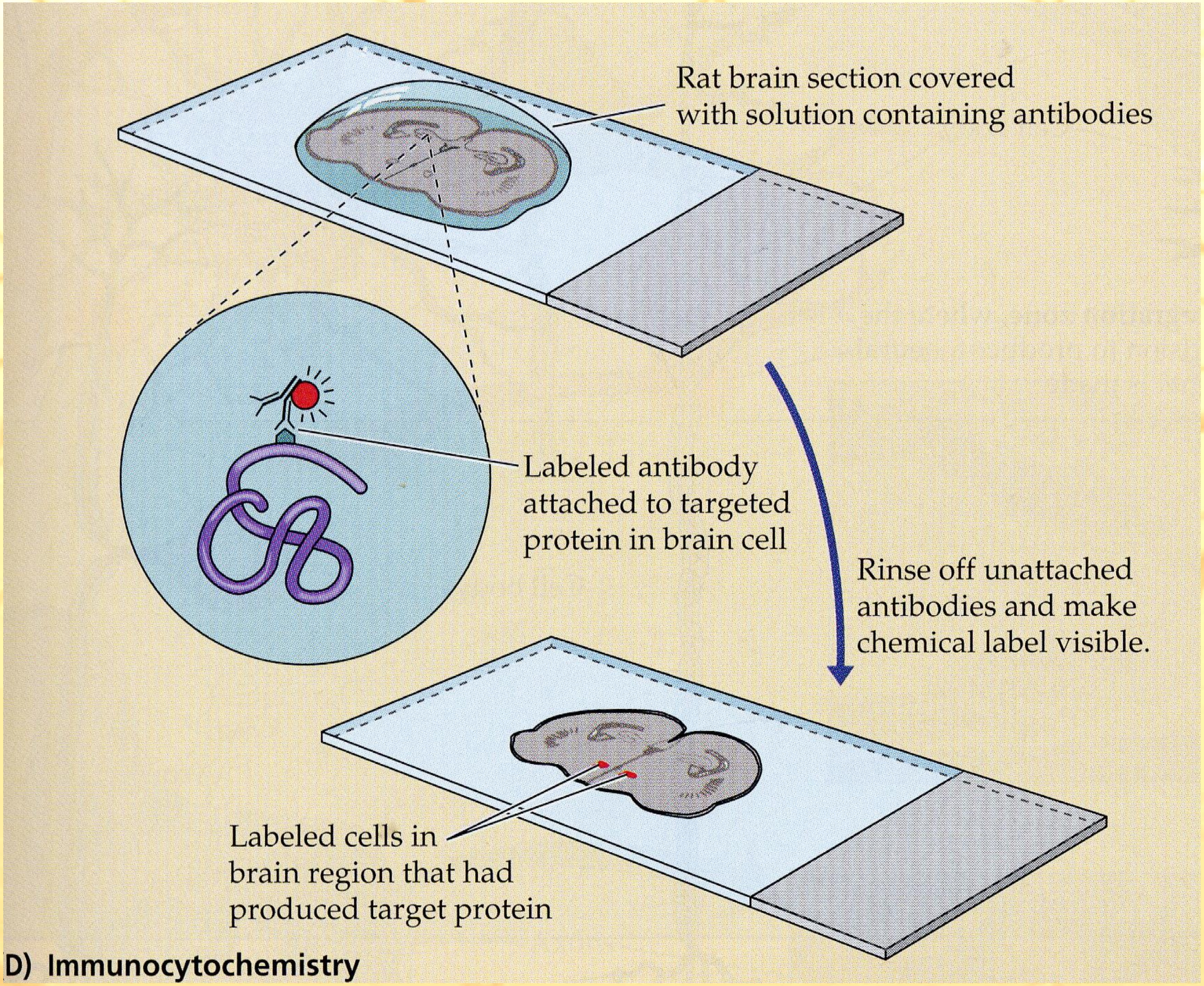




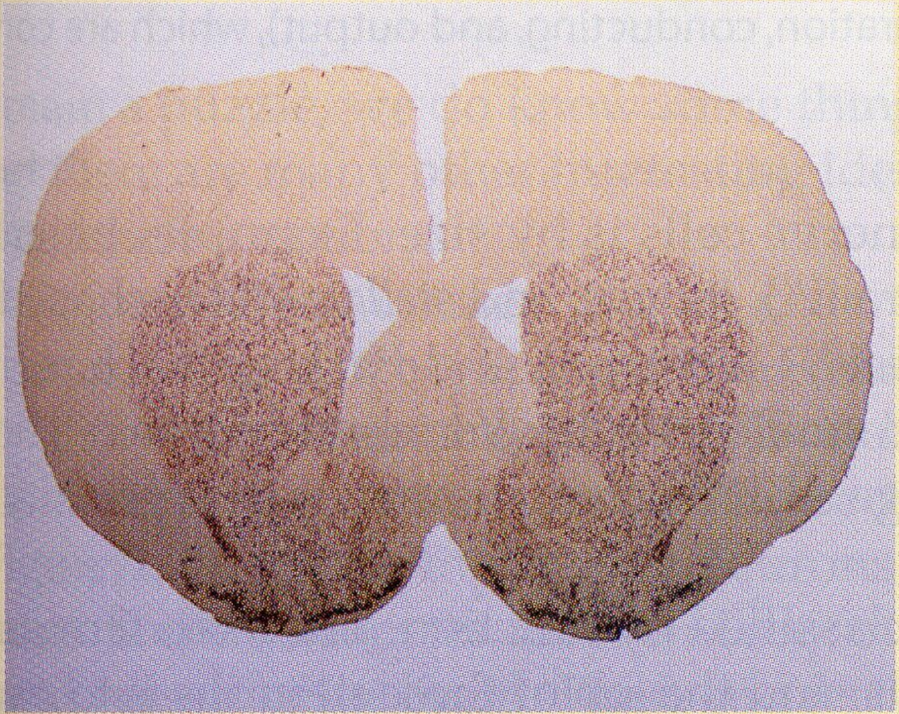
Активность генома



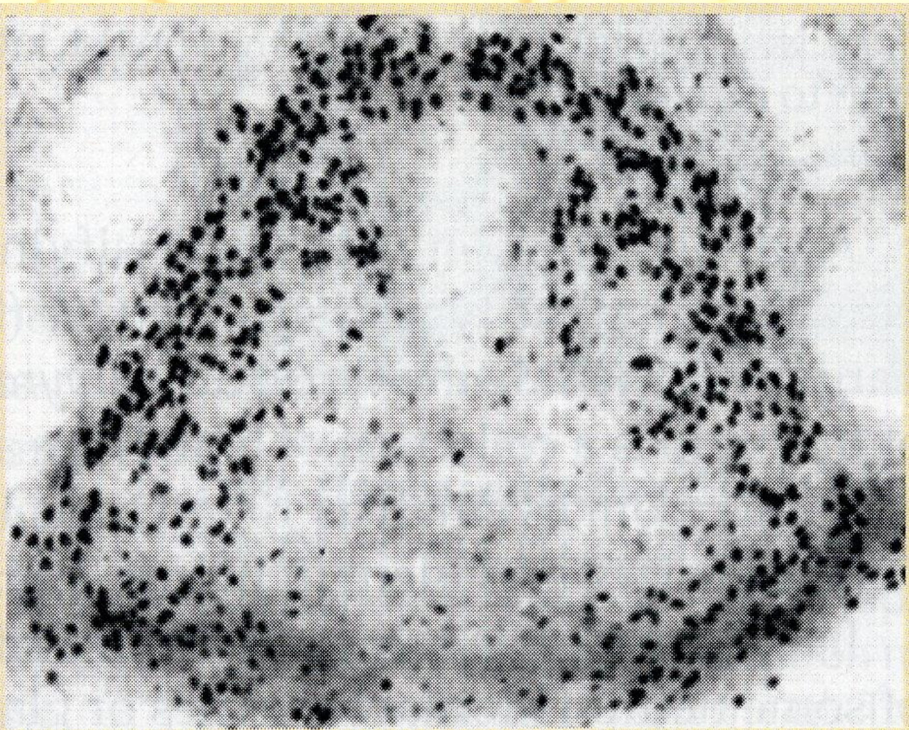
Экспрессия генов



Экспрессия генов



(E) In situ hybridization: enkephalin gene expression



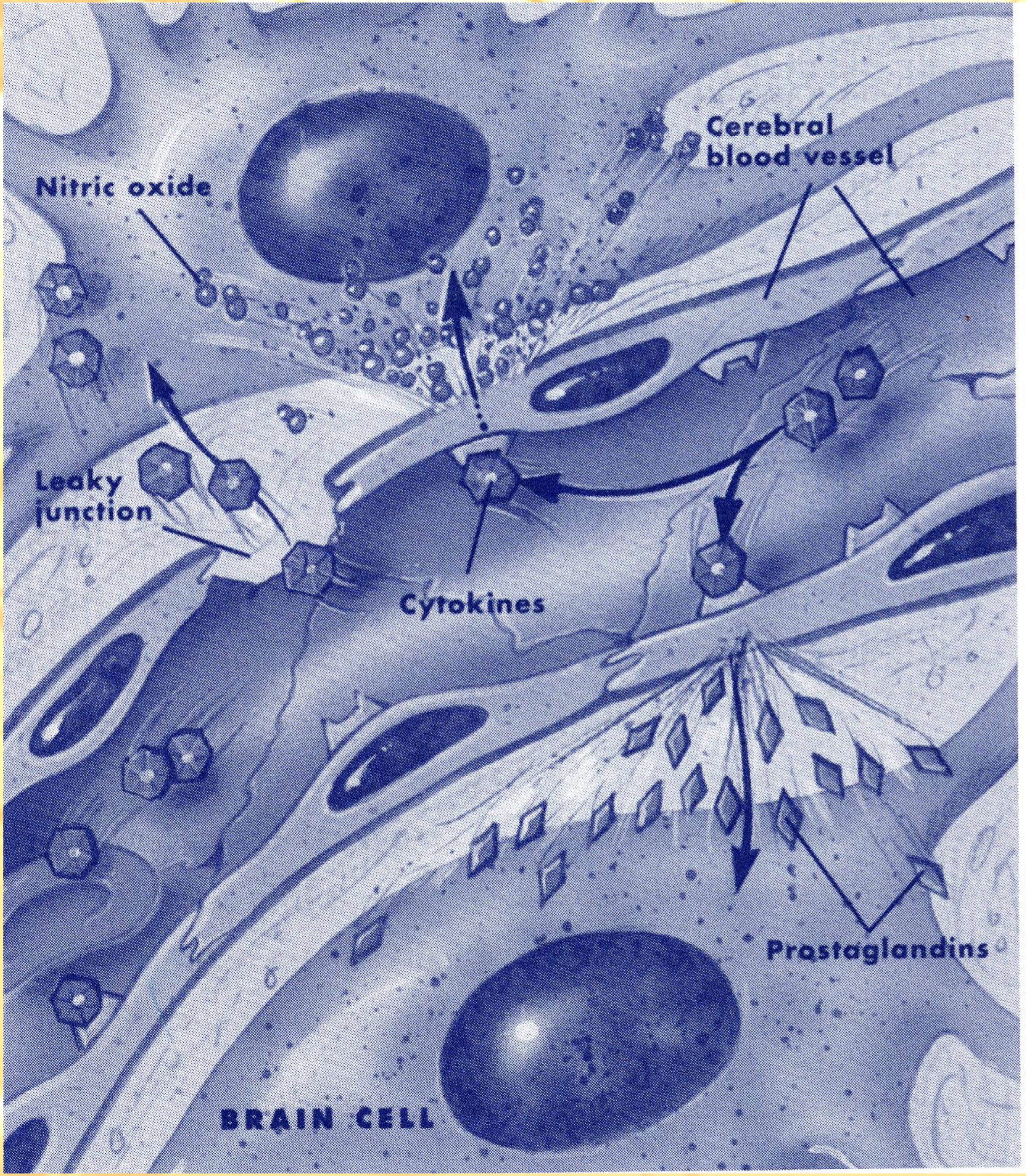
(F) Expression of c-fos in activated cells

Метаболизм

«Как любая живая клетка, нервная клетка в своем метаболизме реализует генетическую программу жизненного цикла, нуждаясь в метаболитах, поступающих от других клеток. «Потребности» нейронов индивидуальны, т.к. в них экспрессируются индивидуальные наборы генов.»

В.Б. Швырков

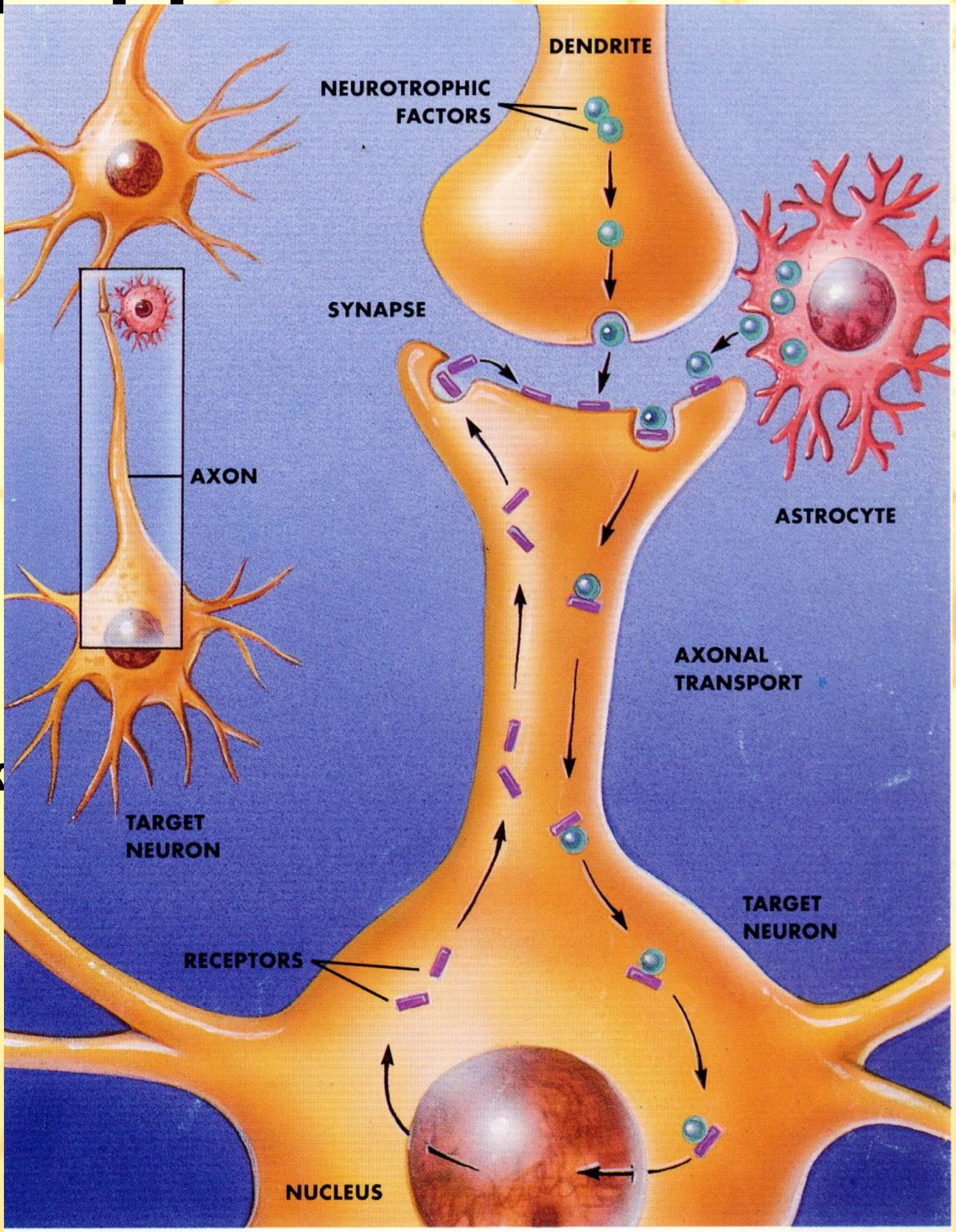
Влияние кровотока



- зачем?

3 вида ретроградных влияний

- производство факторов (**окись азота, арахидоновая кислота**), диффундирующих через мембраны к пресинаптическому нейрону
- выделение растворимых факторов (**нейротрофины**), связывающихся с пресинаптическими рецепторами **(последние могут транспортироваться к ядру)**
- модуляция постсинаптич. мембранных белков, активирующих пресинаптические рецепторы



Кризис теоретической нейробиологии

- «... множество деталей работы клеток ... невозможно интегрировать в когерентное представление об организации функций мозга.»

  О.С. Виноградова

«Потребности» нейрона

- «типичная» белковая молекула разрушается в среднем через 2 дня после того, как она была синтезирована
- структурные перестройки при научении

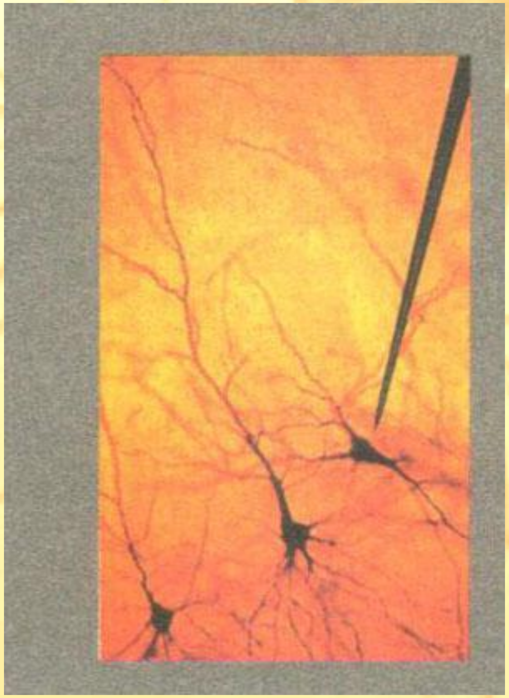
Рецепторы

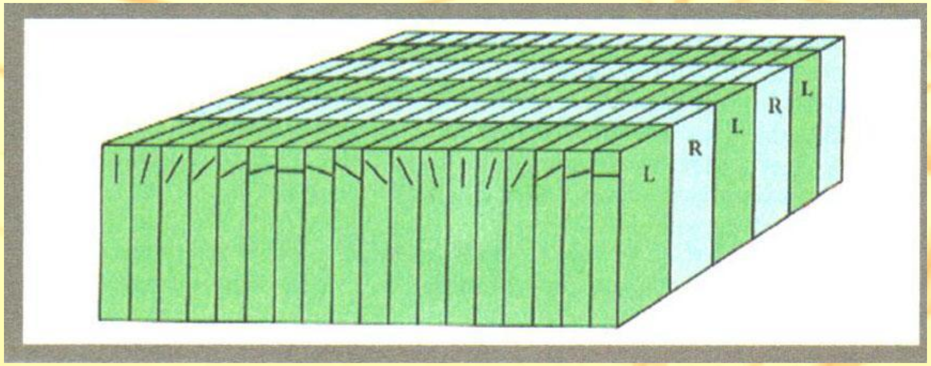
- белковые структуры, роль которых состоит в «узнавании» соответствующих молекул и обеспечении последующего развертывания тех или иных метаболических процессов

Происхождение активности нейрона

- активность детерминирована метаболическими «потребностями» нейрона и возникает при несоответствии состояния микросреды нейрона и «потребностями»
  - ✔ экзогенная активность (внешним стимулом)
  - ✔ эндогенная активность (пейсмейкер) (многие, если не все)

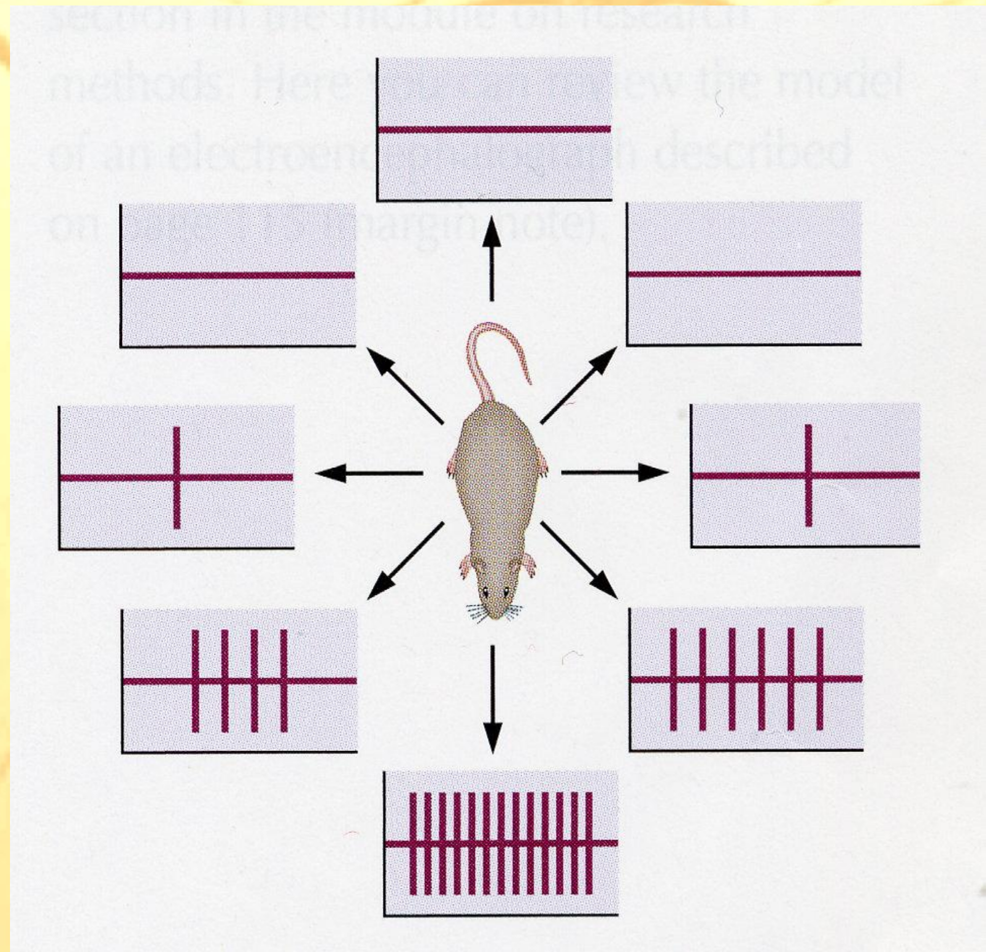
Активность нейрона



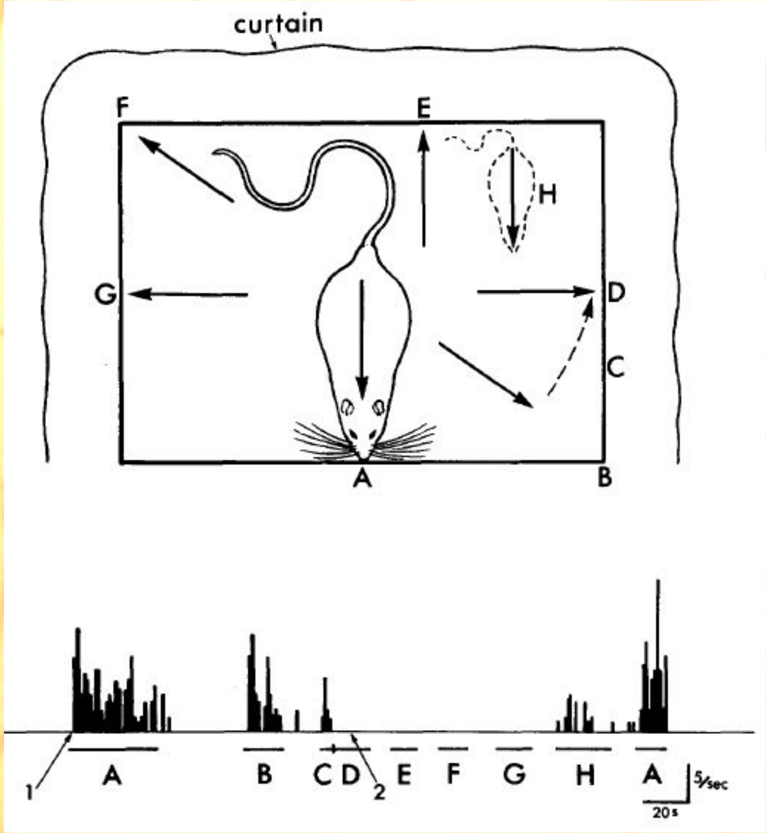


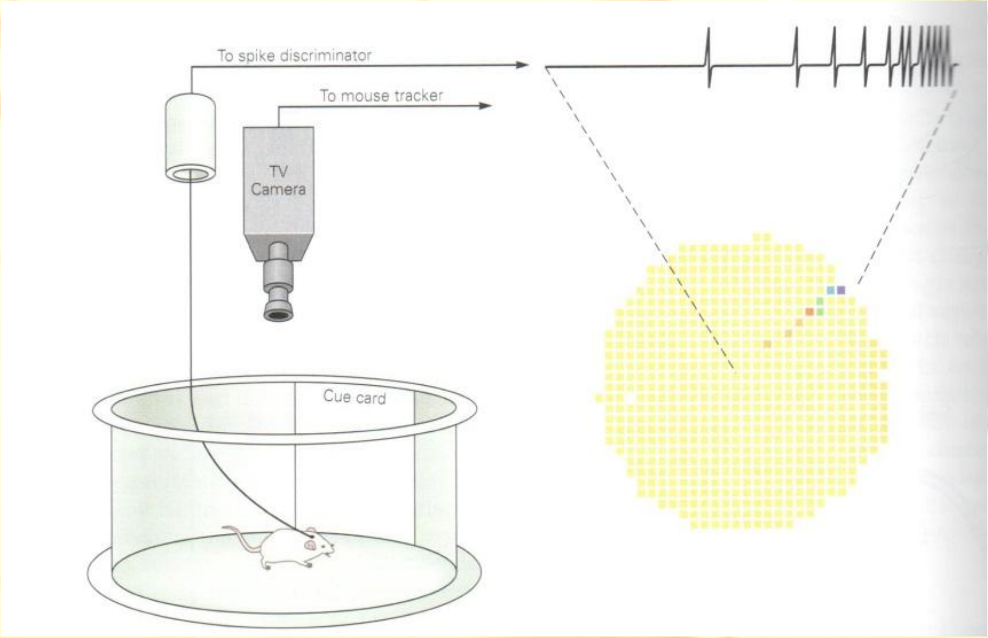
Поведенческая специализация нейрона

- связь с демонстрируемым поведением



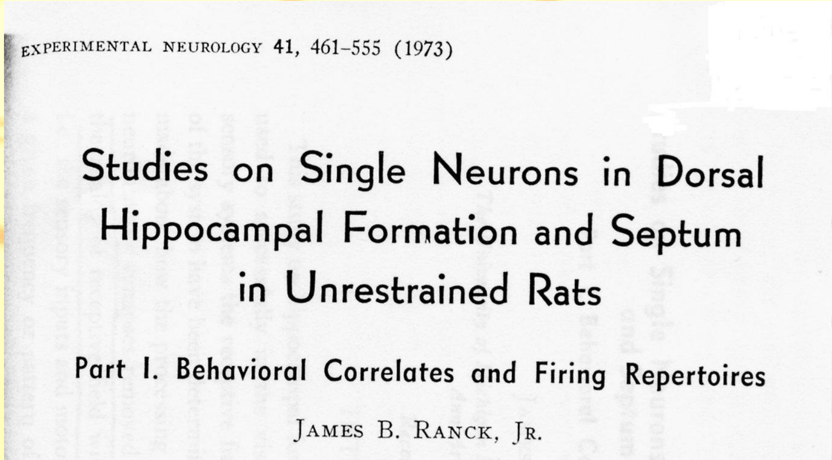
АКТИВНОСТЬ ОТДЕЛЬНЫХ НЕЙРОНОВ СВЯЗАНА С ТЕМ, ЧТО ДЕЛАЕТ ОРГАНИЗМ





O'Keefe & Dostrovsky, 1971

Специализация нейрона



EXPERIMENTAL NEUROLOGY 41, 461–555 (1973)

Studies on Single Neurons in Dorsal Hippocampal Formation and Septum in Unrestrained Rats

Part I. Behavioral Correlates and Firing Repertoires

JAMES B. RANCK, JR.

Ranck, 1973

13:44, 6 октября 2014

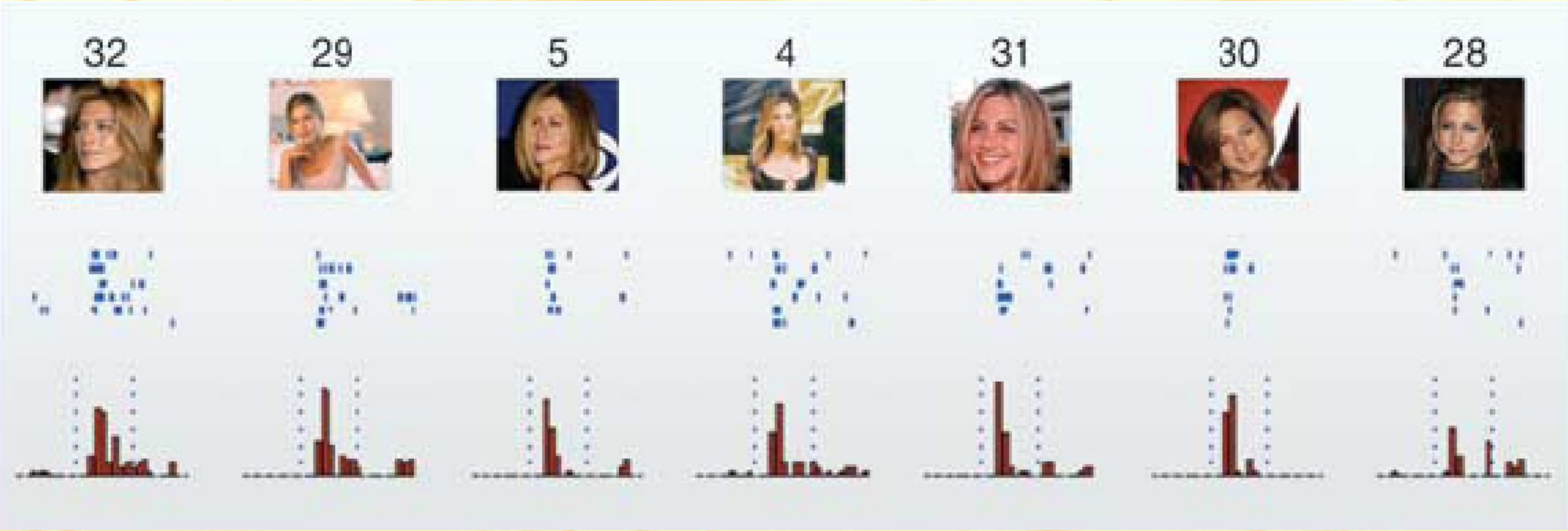
Присуждена Нобелевская премия по физиологии и медицине

Мэй-Бритт Мозер и Эдвард Мозер
Фото: The Kavli Institute at the NTNU / Wikipedia

Джон О`Киф
Фото: University College London

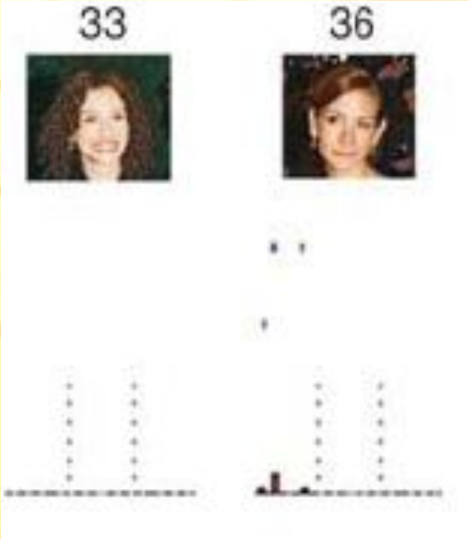
Нейроны «места»

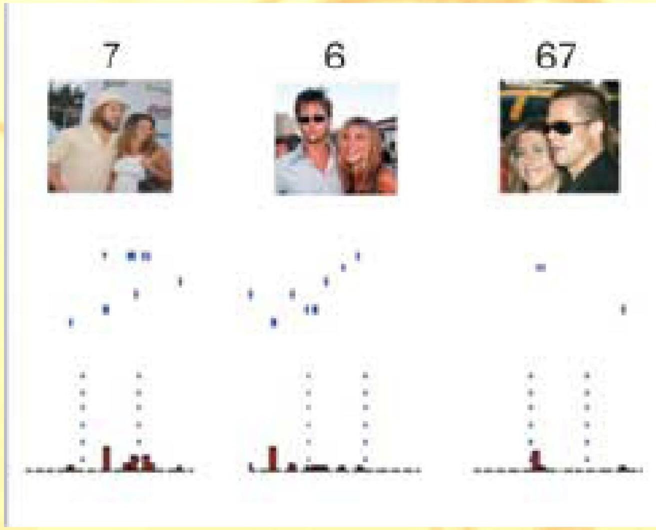
Связь активности с поведением



Nature, 2005

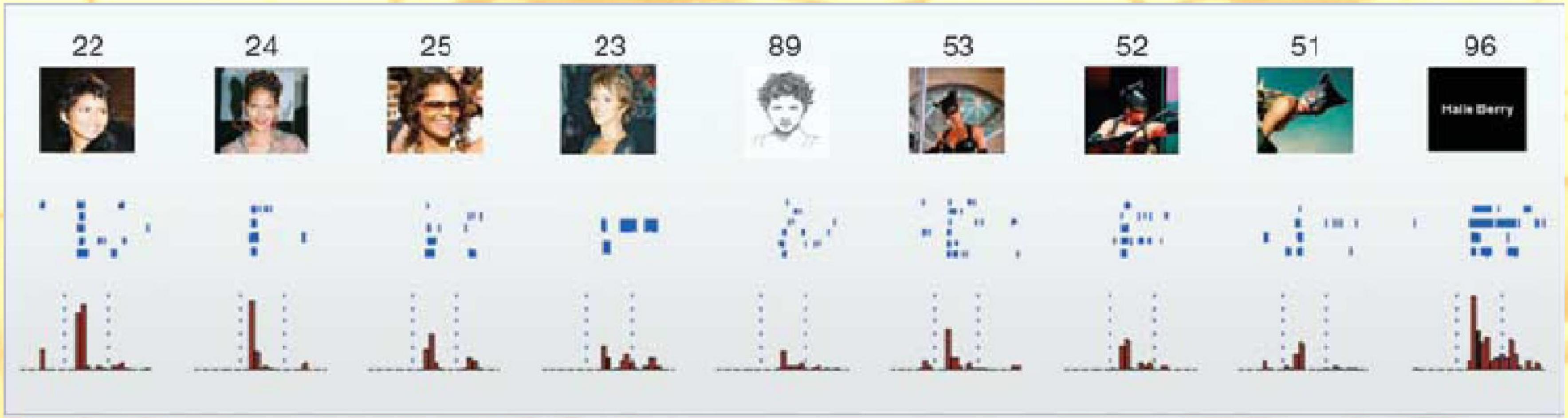
Связь активности с поведением



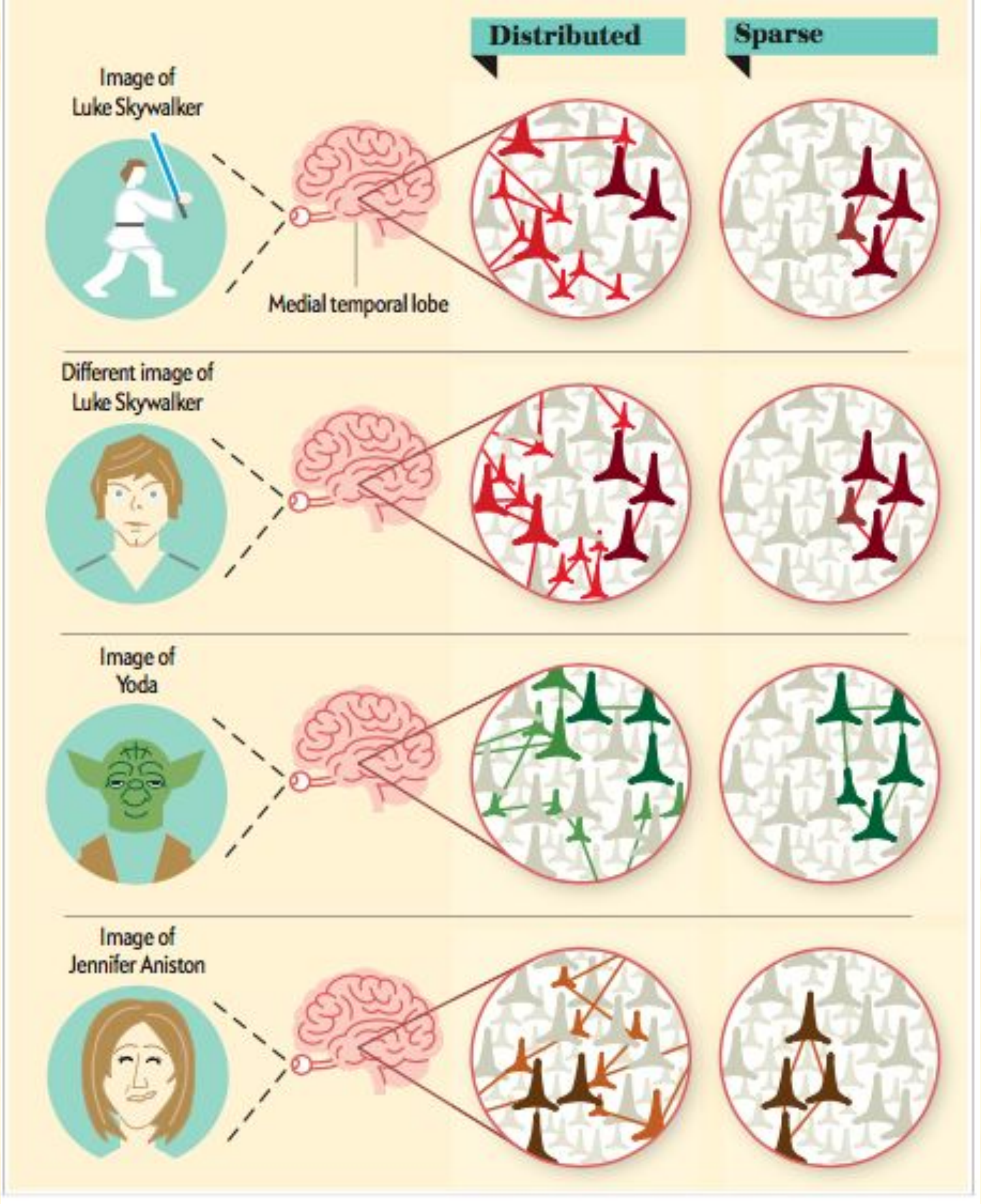


Nature, 2005

Связь активности с поведением



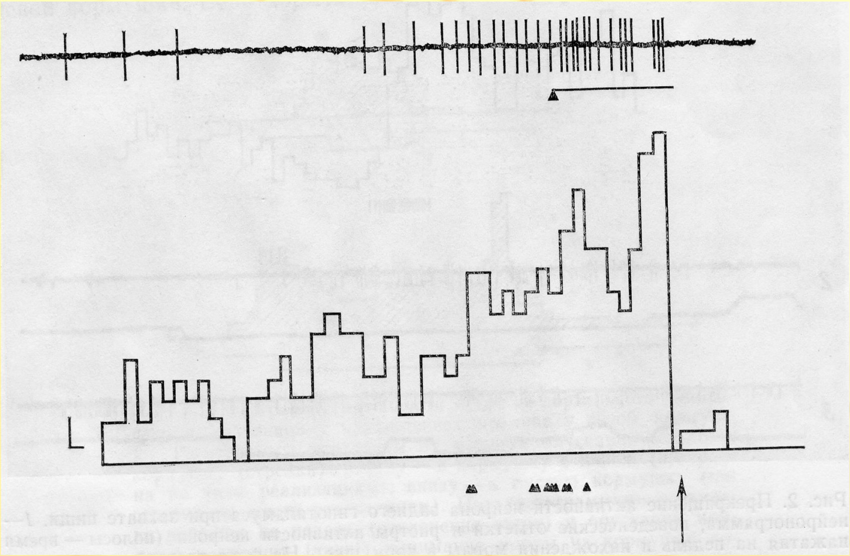
Nature, 2005



Distributed
Sparse
Image of
Luke Skywalker
Medial temporal lobe
Different image of
Luke Skywalker
Image of
Yoda
Image of
Jennifer Aniston

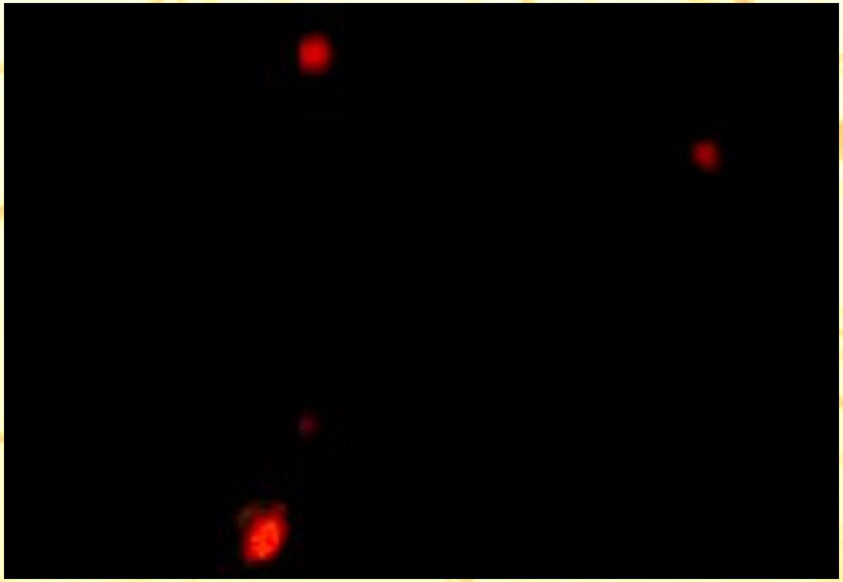
Анализ активности нейрона

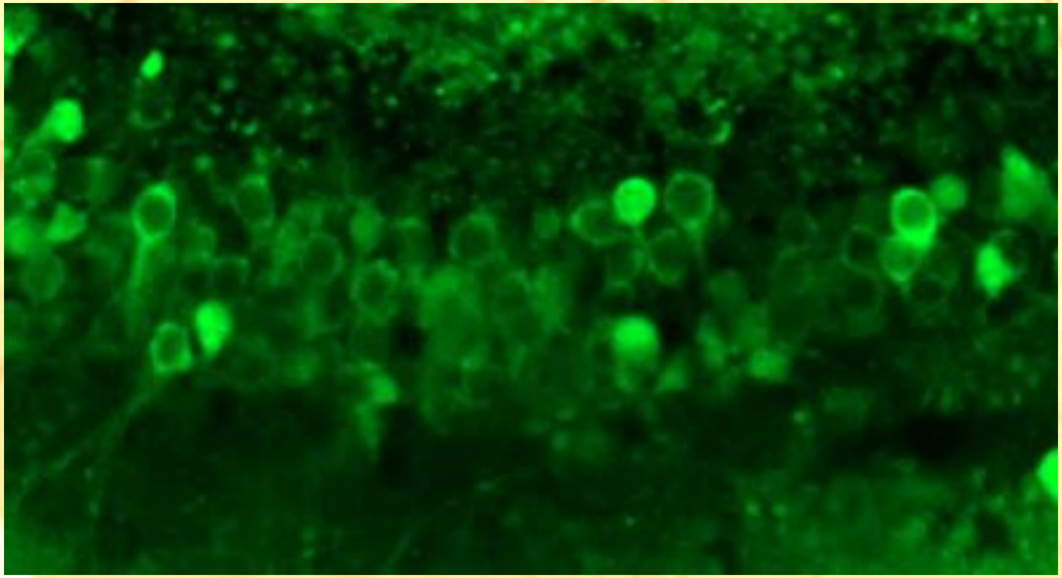
- объединение с другими нейронами
- «предрезультатная» гистограмма (Д.Г. Шевченко, 1987: нейрон заднего гипоталамуса при захвате пищи)

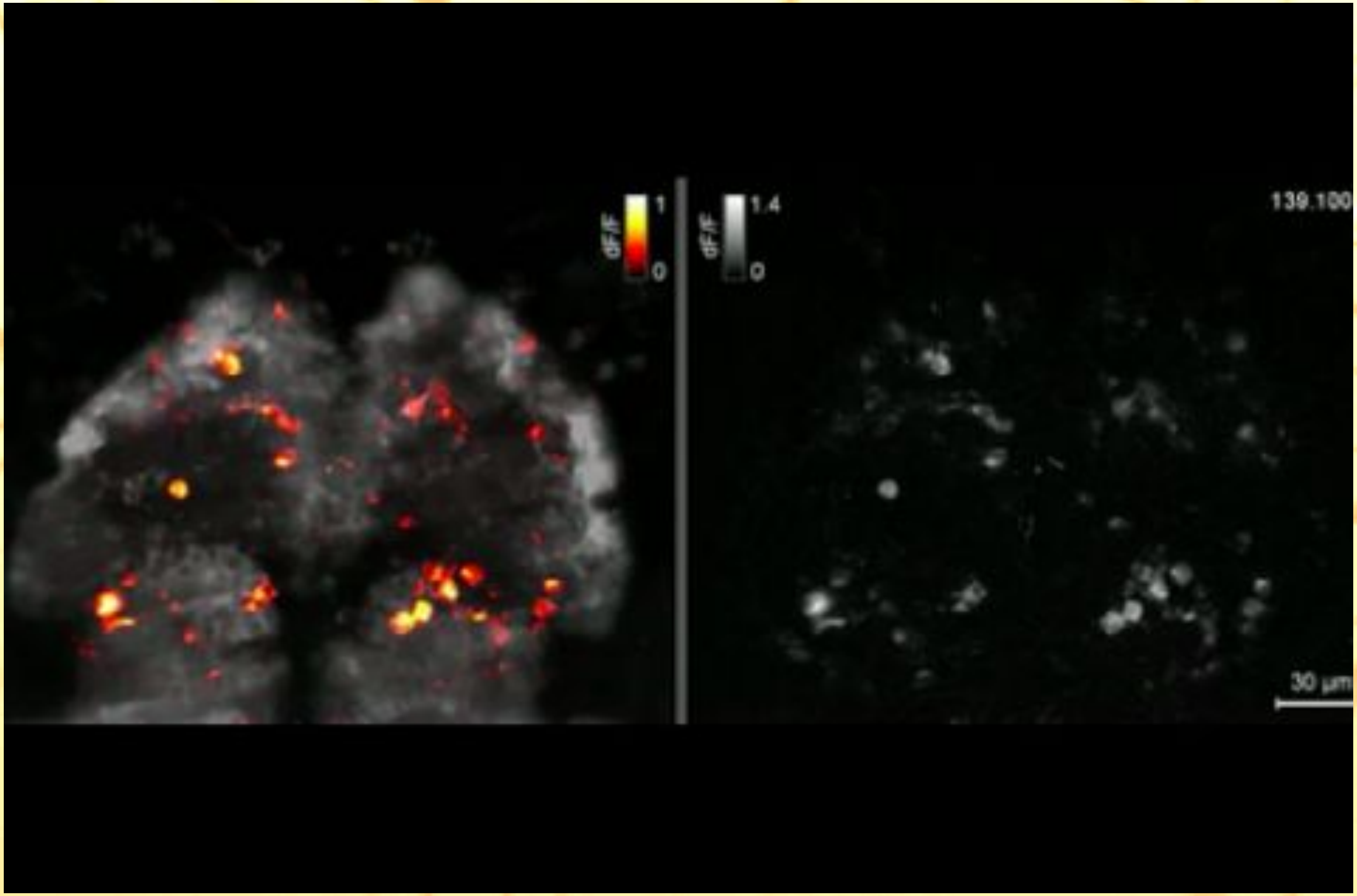


(Д.Г.Шевченко)

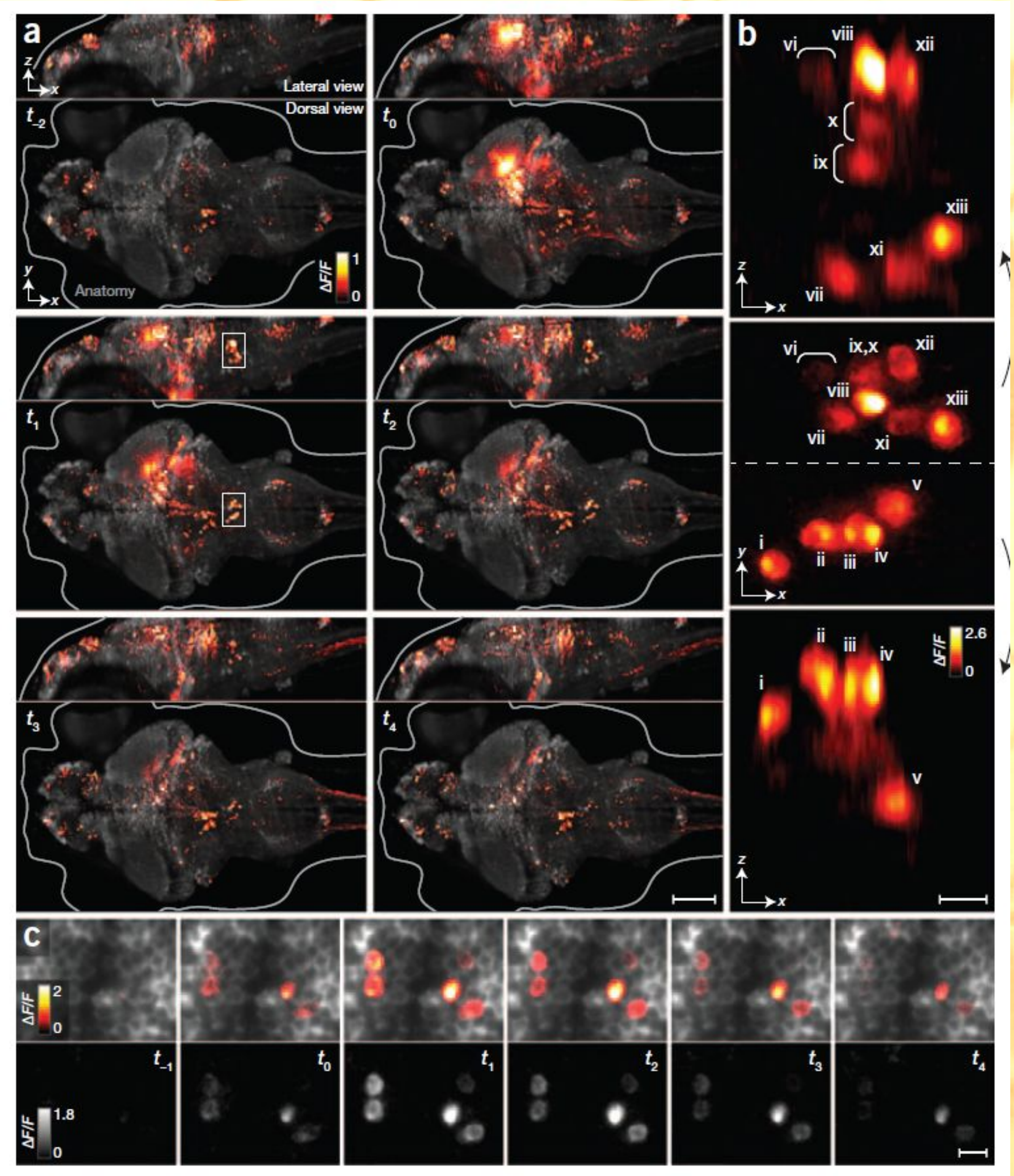
Связь активности с поведением





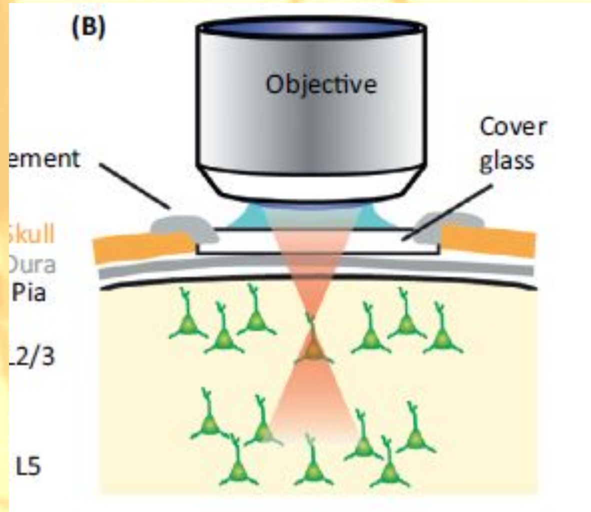


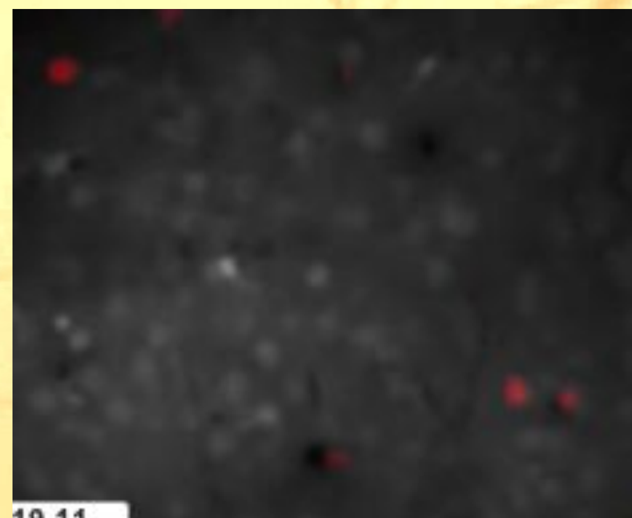
Ahrens & Keller, 2013



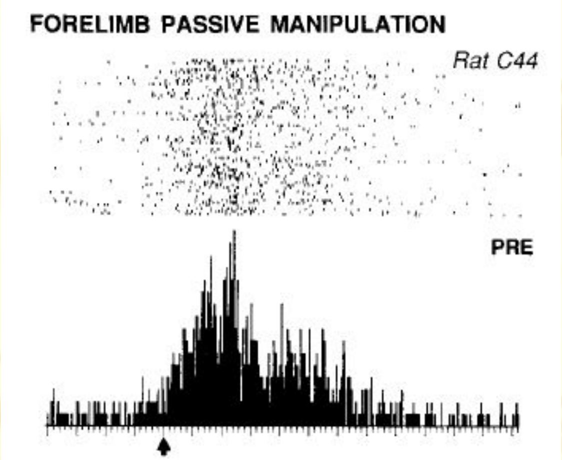
Ahrens & Keller, 2013

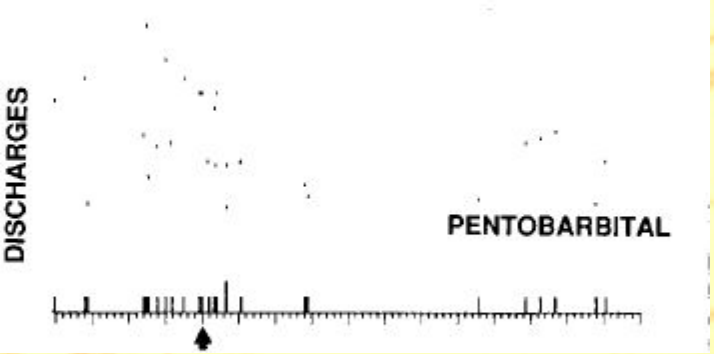
«РАБОТА» МОЗГА СКЛАДЫВАЕТСЯ ИЗ АКТИВАЦИЙ ОТДЕЛЬНЫХ НЕЙРОНОВ

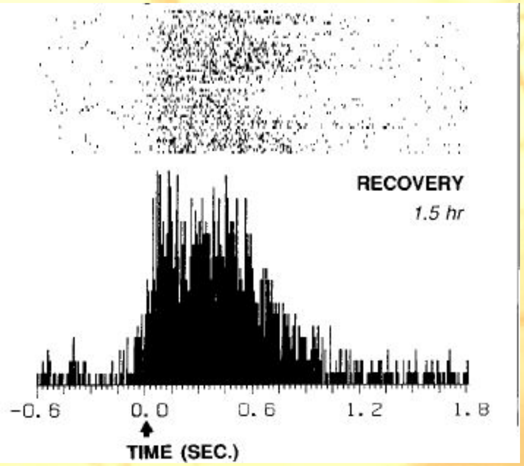




Нейроны в поведении



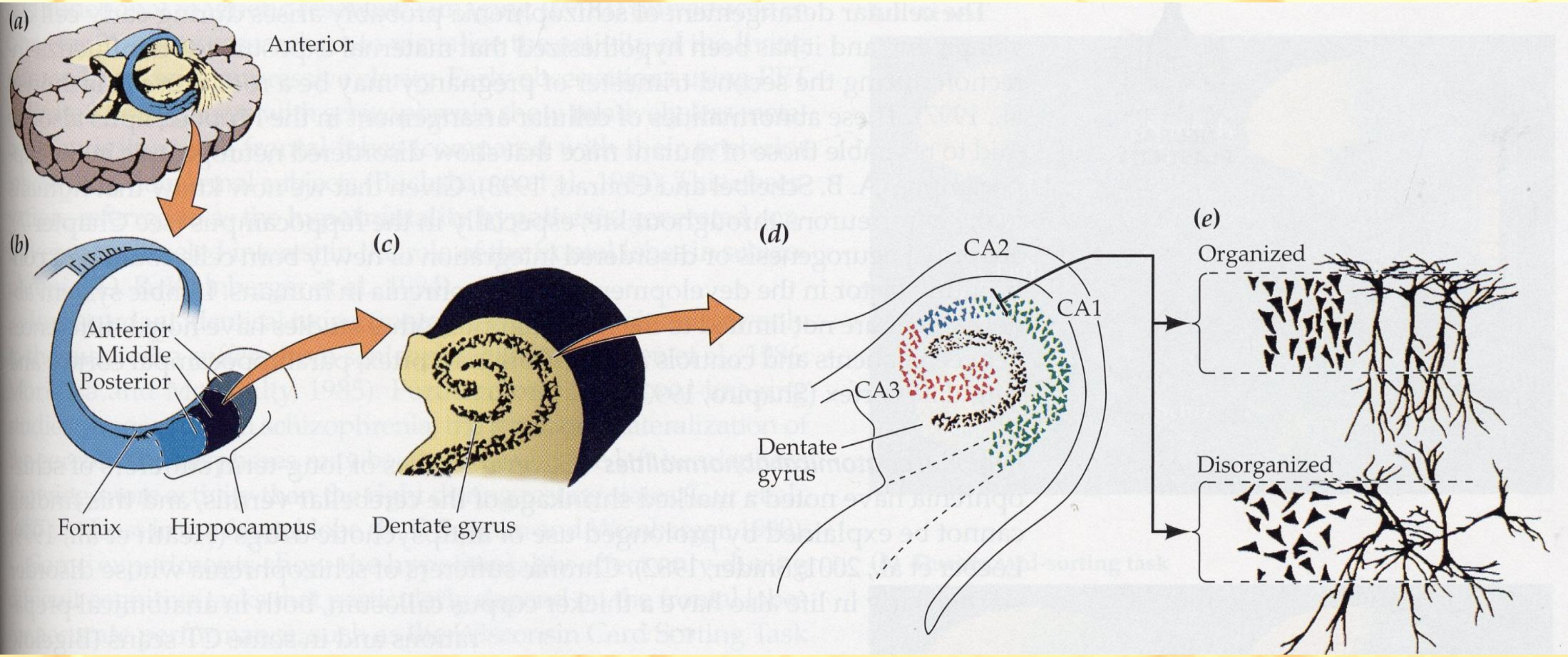




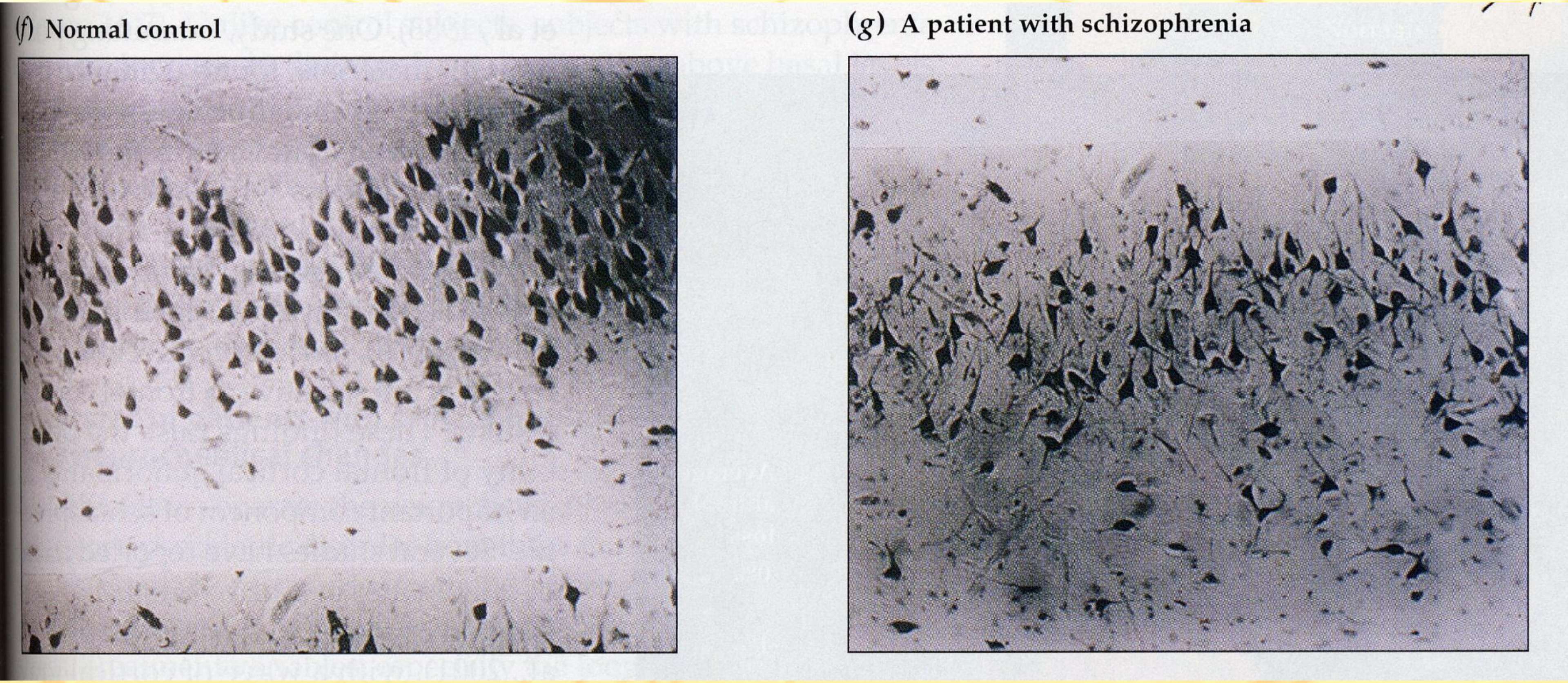
«результаты полученные при анестезии **не** могут быть экстраполированы на закономерности поведения»

M.O. West, 1998

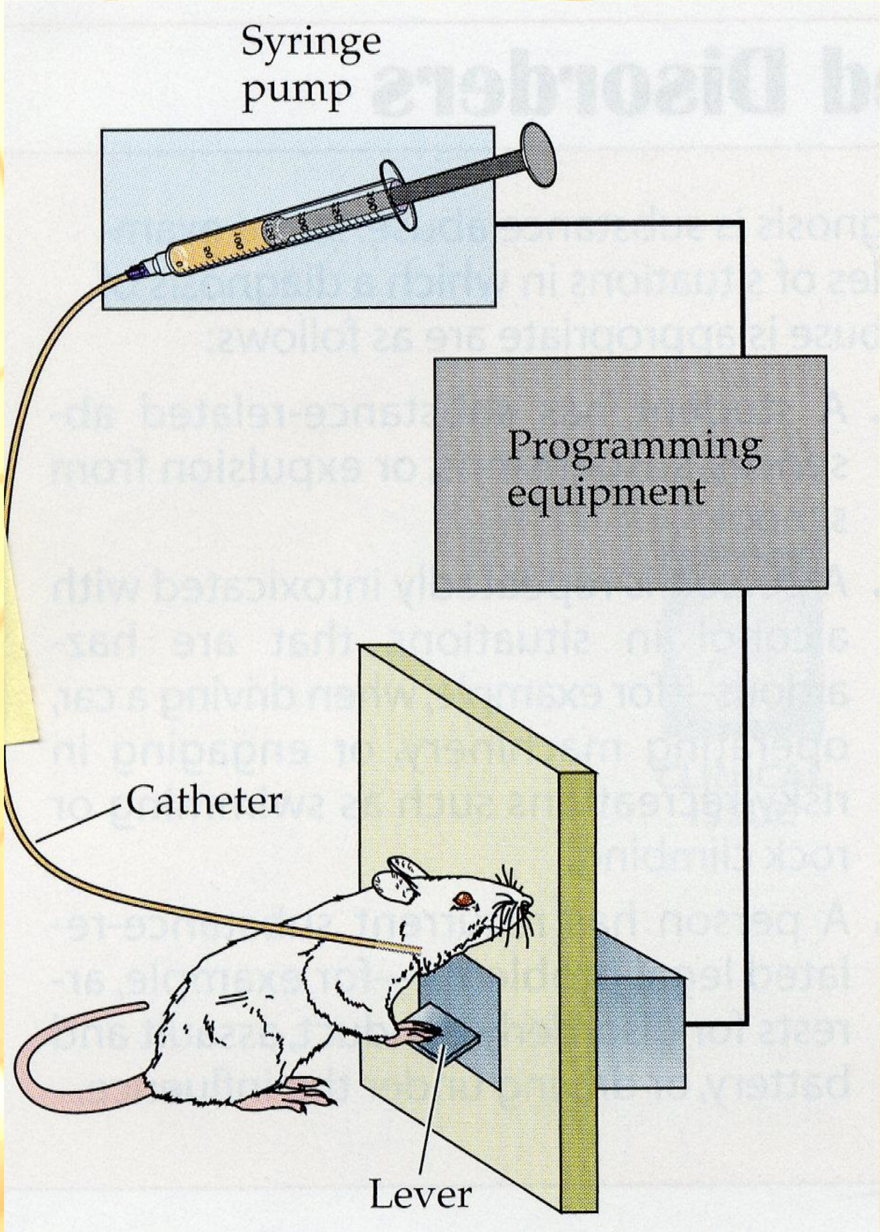
Шизофрения: разные уровни анализа



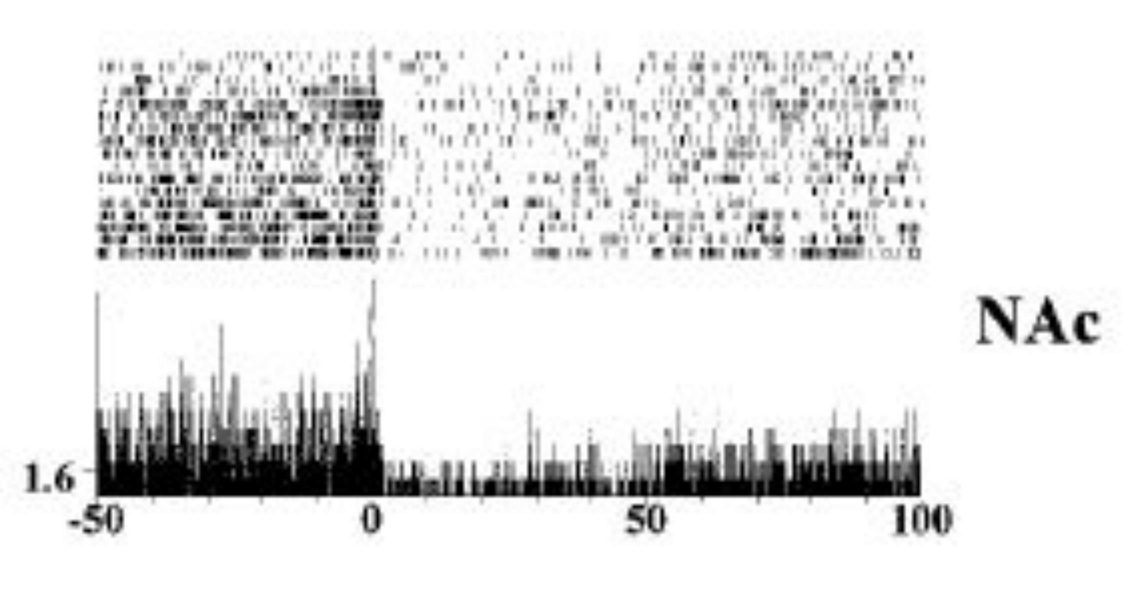
Шизофрения



Происхождение активности



Почему нейрон активен



(Chang et al., 1998)

- активность детерминирована метаболическими «потребностями» нейрона и возникает при несоответствии состояния микросреды нейрона и «потребностями»

- 50 первых поцелуев
- Помни (Memento)