Liqun Luo

PRINCIPLES OF NEUROBIOLOGY

Chapter 13

Ways of Exploring

CHAPTER OUTLINE

ANIMAL MODELS IN NEUROBIOLOGY RESEARCH
GENETIC AND MOLECULAR TECHNIQUES
ANATOMICAL TECHNIQUES
RECORDING AND MANIPULATING NEURONAL ACTIVITY
BEHAVIORAL ANALYSES

神经生物学研究的动物模型
遗传和分子学技术
解剖学技术
记录和操控神经活动
行为分析

ANIMAL MODELS IN NEUROBIOLOGY RESEARCH

13.1 Some invertebrates provide large, identifiable neurons for electrophysiological investigations

13.2 *Drosophila* and *C. elegans* allow sophisticated genetic manipulations

13.3 Diverse vertebrate animals offer technical ease or special faculties

13.1 一些无脊椎动物提供大量可识别的神经元用于电生理研究

13.2 果蝇和线虫允许复杂的遗传学操控

13.3 不同的脊椎动物在技术上提供了方便和特殊的用途

ANIMAL MODELS IN NEUROBIOLOGY RESEARCH

神经生物学研究的动物模型

13.4 Mice, rats, and nonhuman primates are important models for mammalian neurobiology research

13.5 Human studies are facilitated by a long history of medicine and experimental psychology and by the recent genomic revolution

13.4 小鼠，大鼠，非人类灵长类动物是哺乳动物神经生物学研究的重要模型

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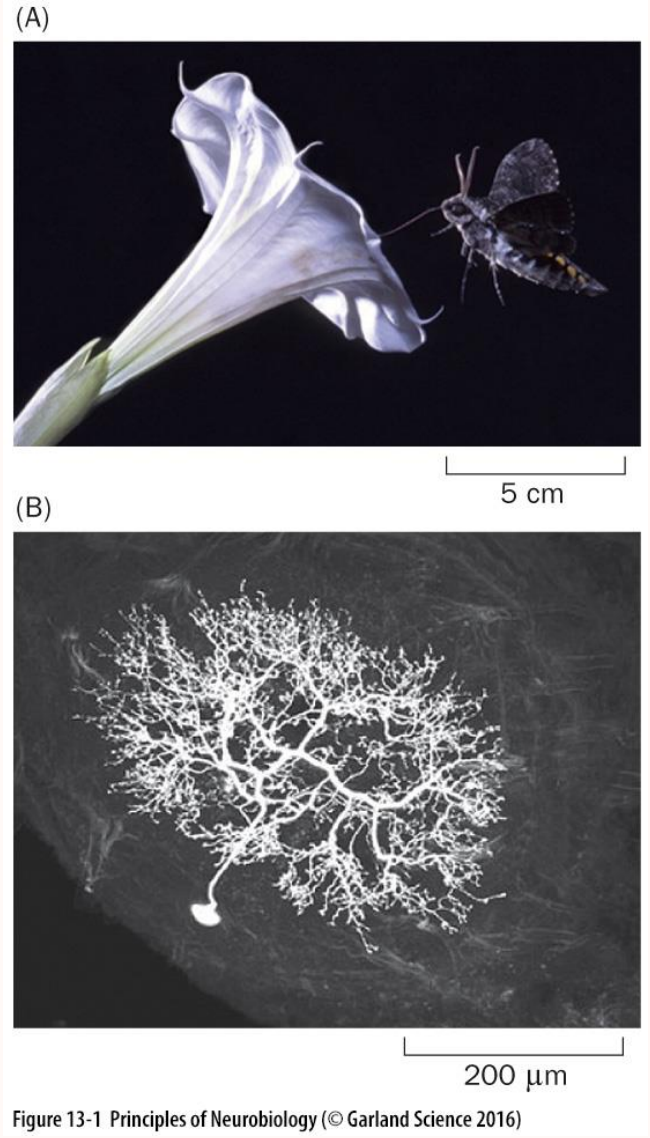

Figure 13-1 Principles of Neurobiology (© Garland Science 2016)

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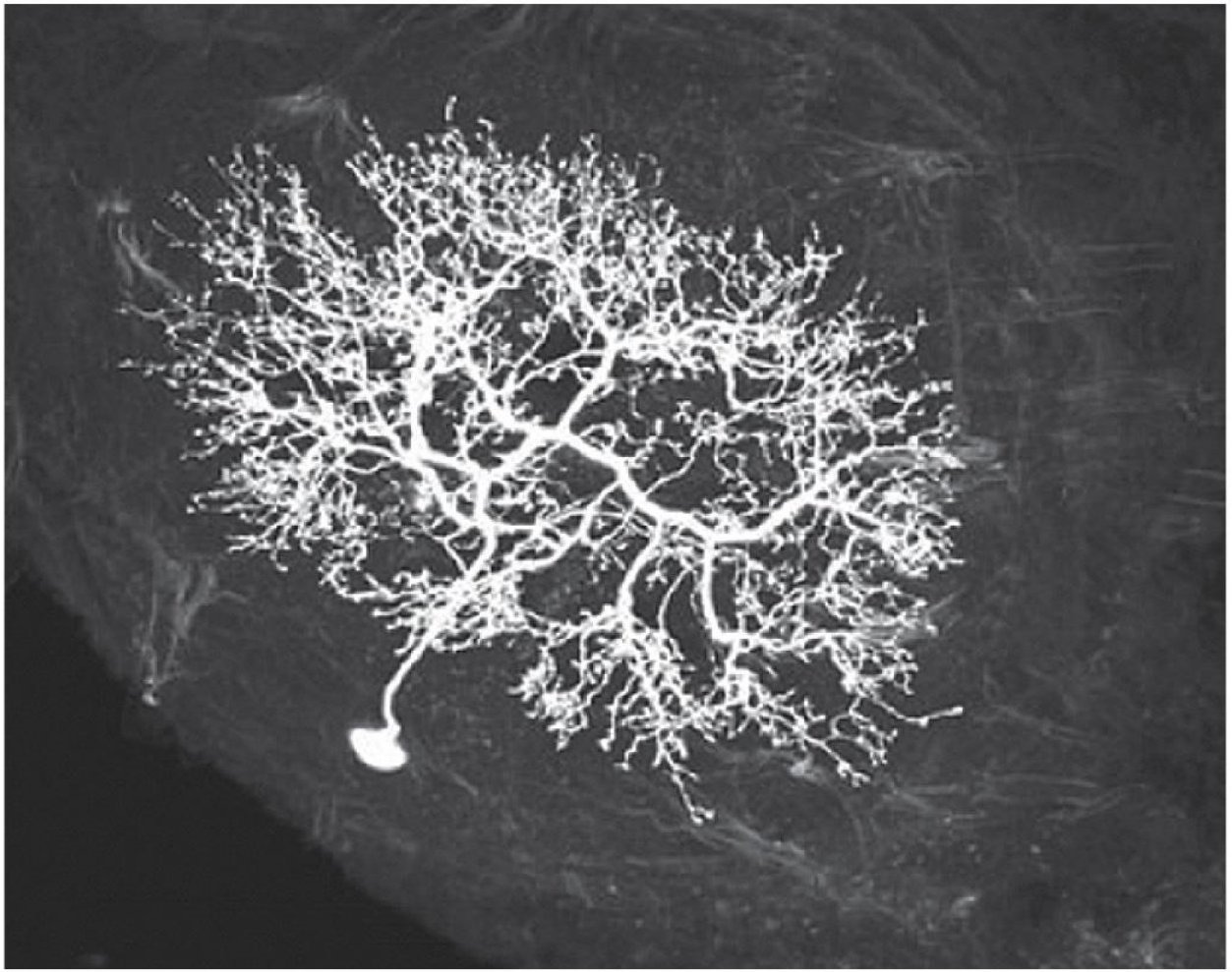

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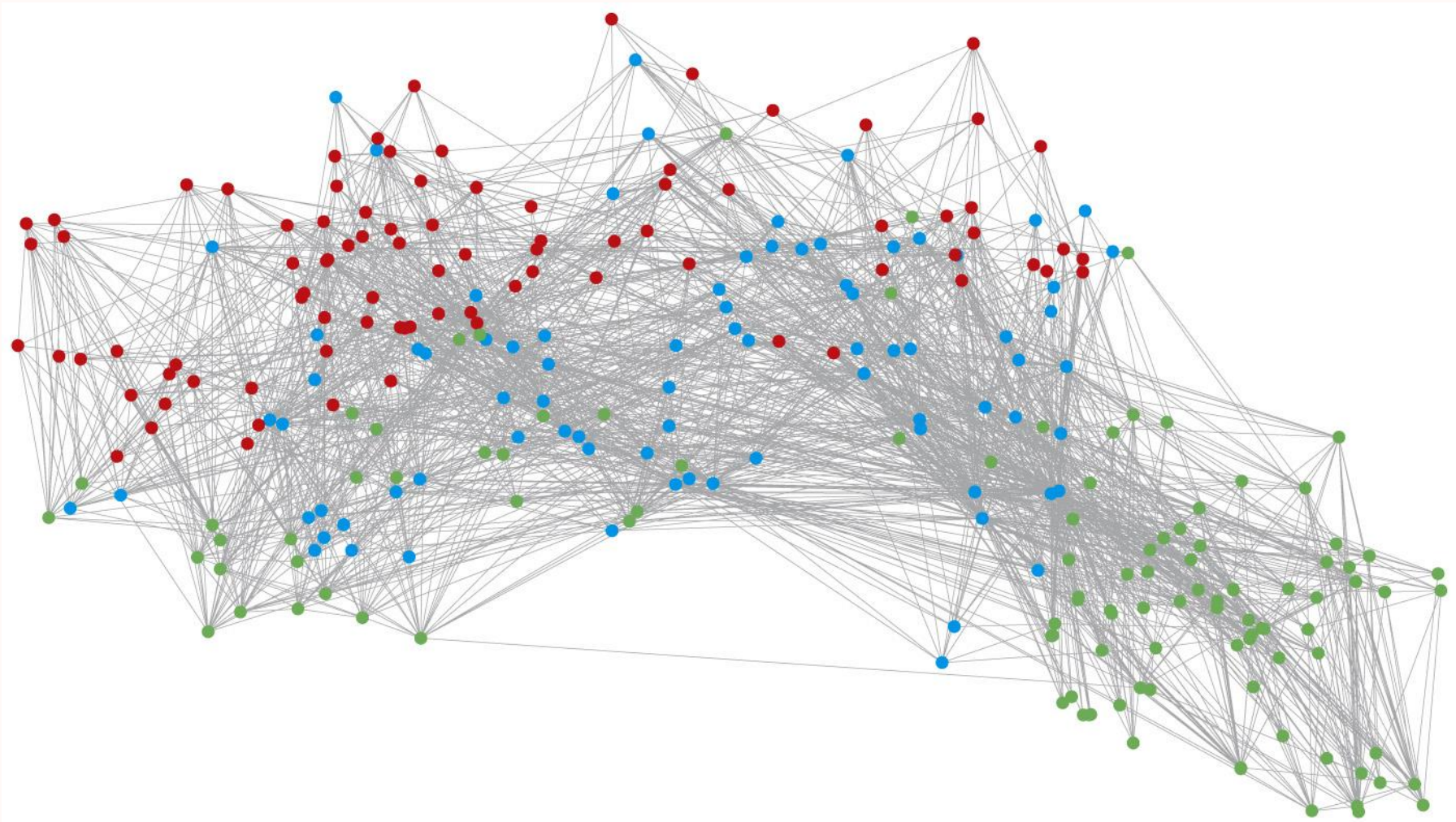

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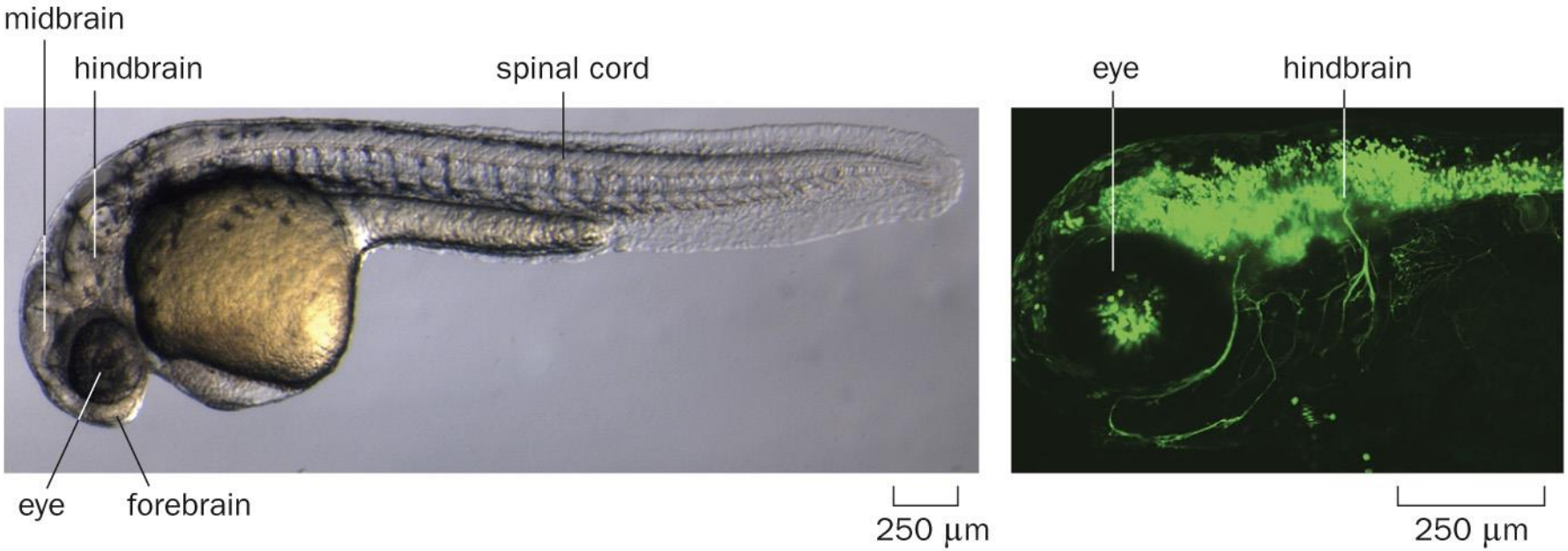

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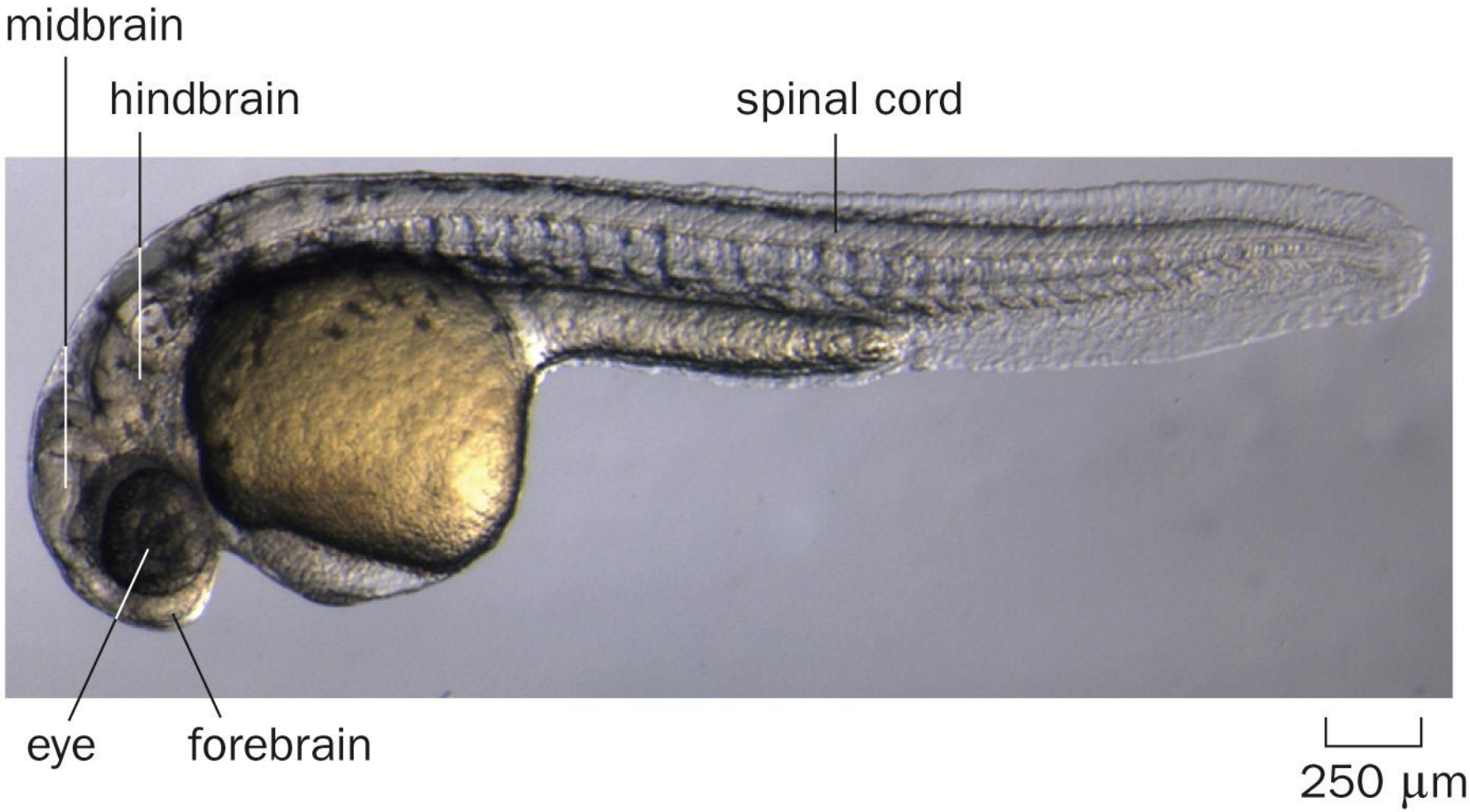

Figure 13-3 (part 1 of 2) Principles of Neurobiology (© Garland Science 2016)

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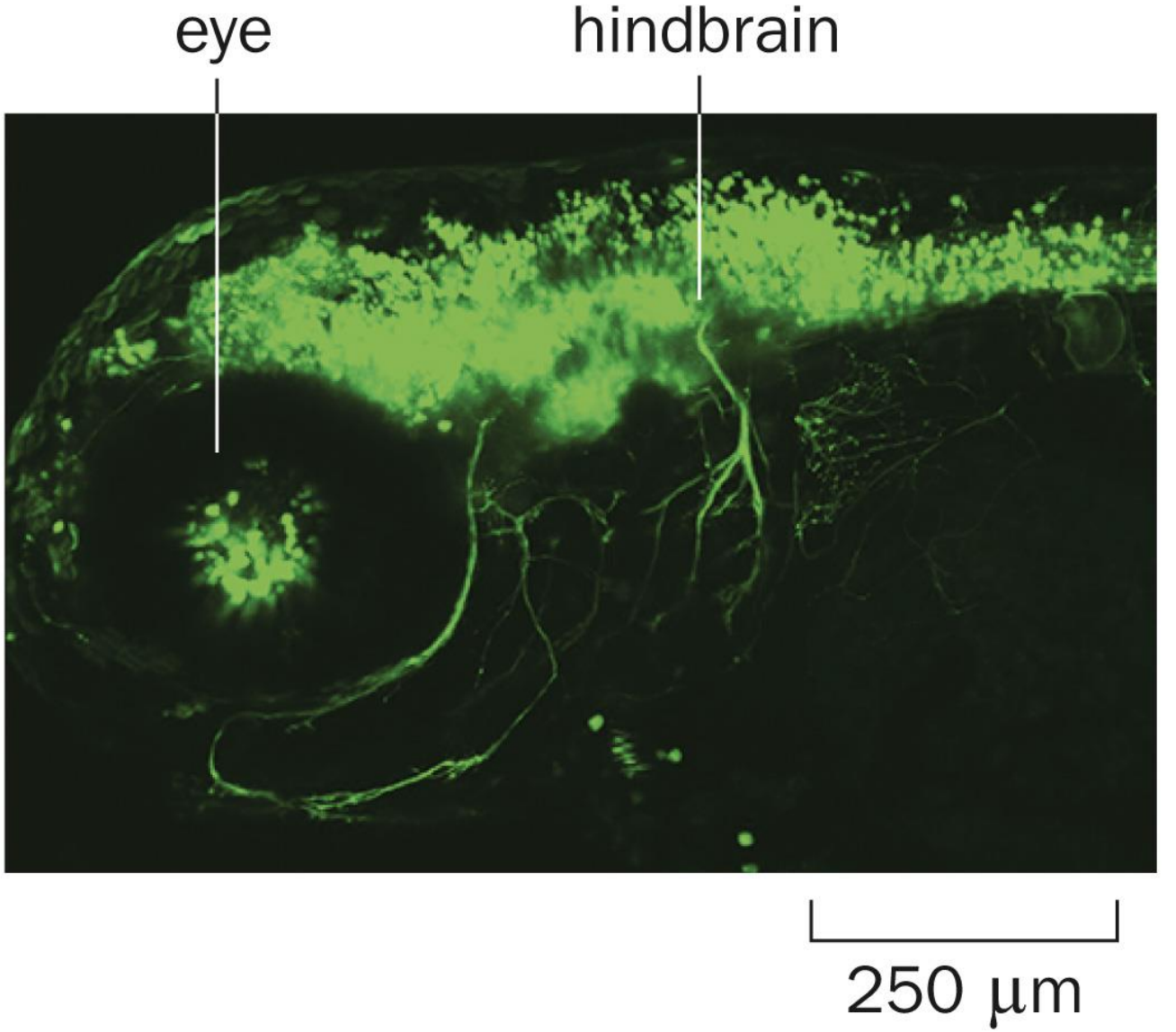

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ANIMAL MODELS IN NEUROBIOLOGY RESEARCH

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GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

Introduction

介绍

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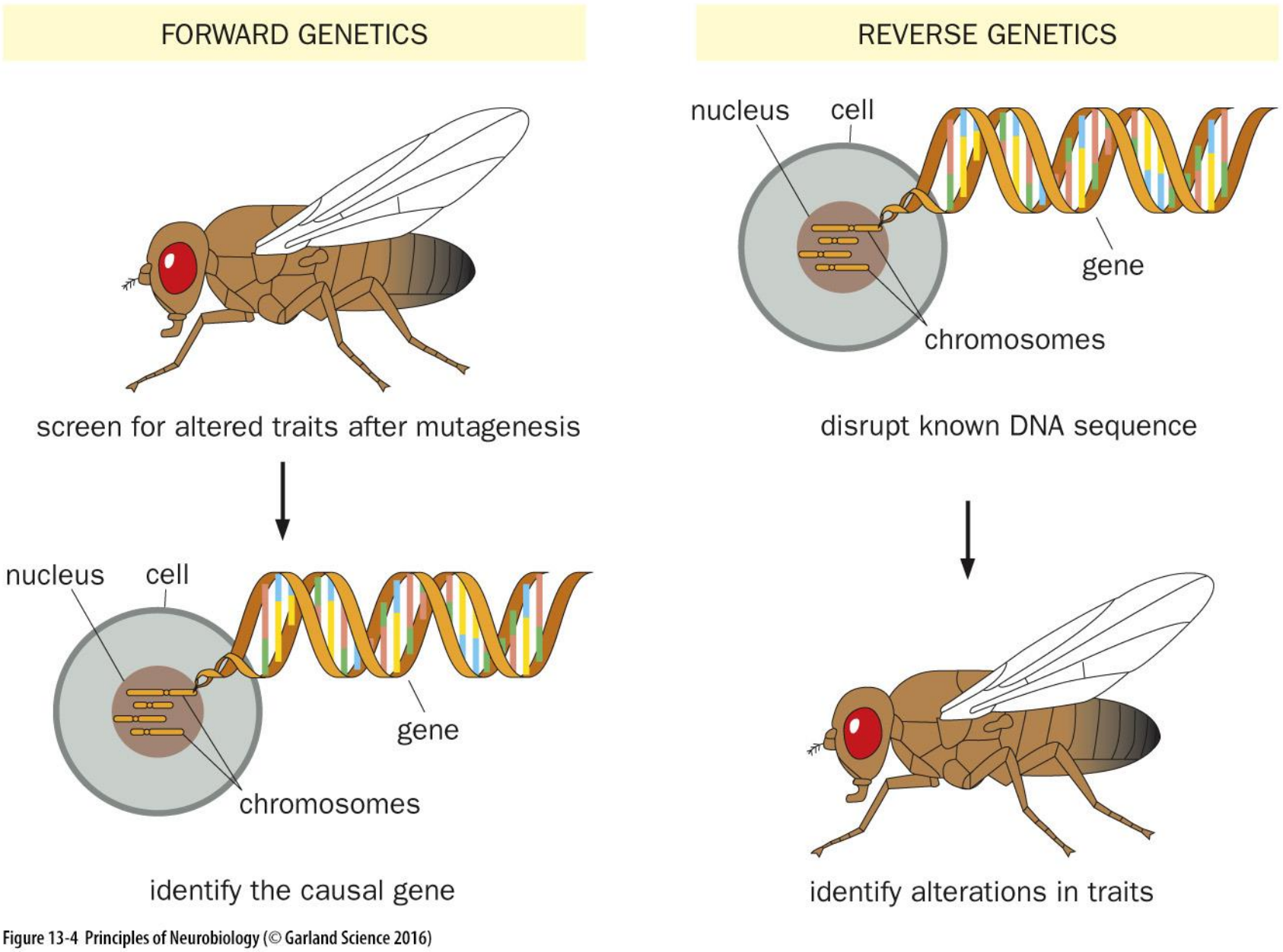

Figure 13-4 Principles of Neurobiology (© Garland Science 2016)

GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

13.6 Forward genetic screens use random mutagenesis to identify genes that control complex biological processes

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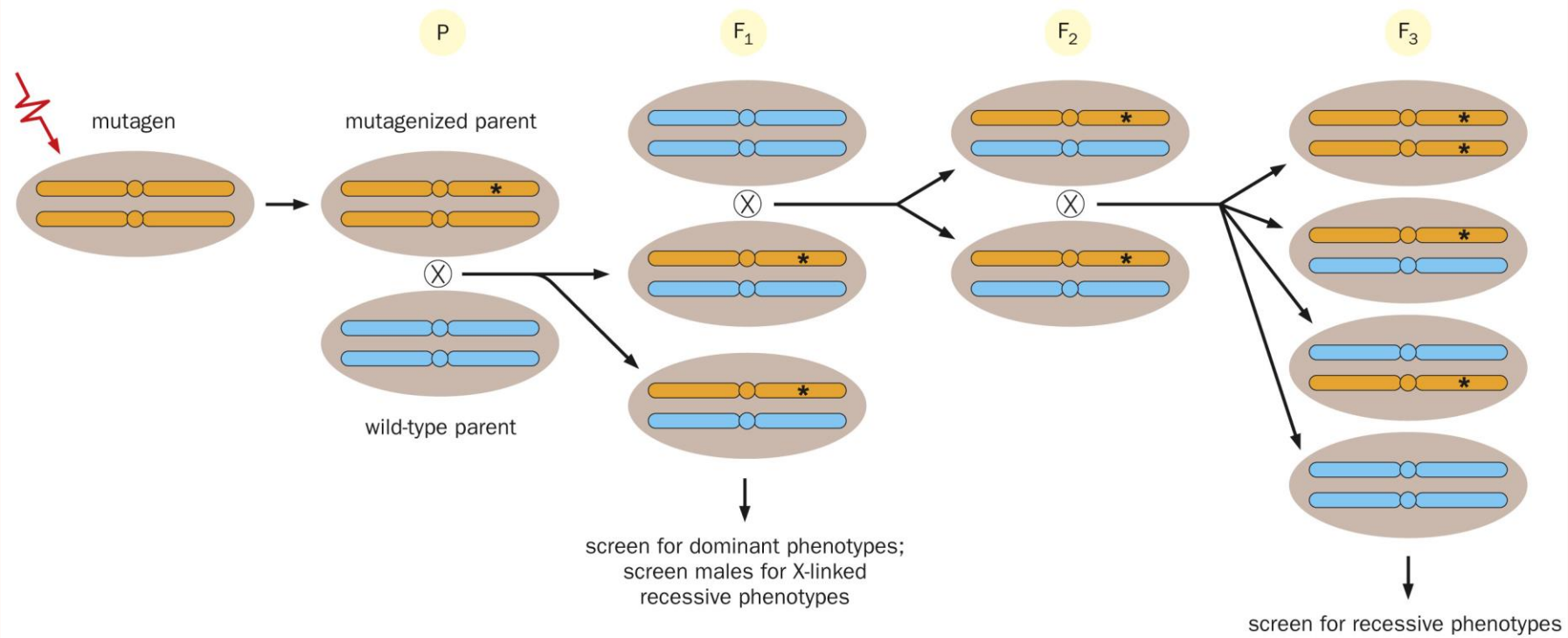

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GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

13.7 Reverse genetics disrupts pre-designated genes to assess their functions

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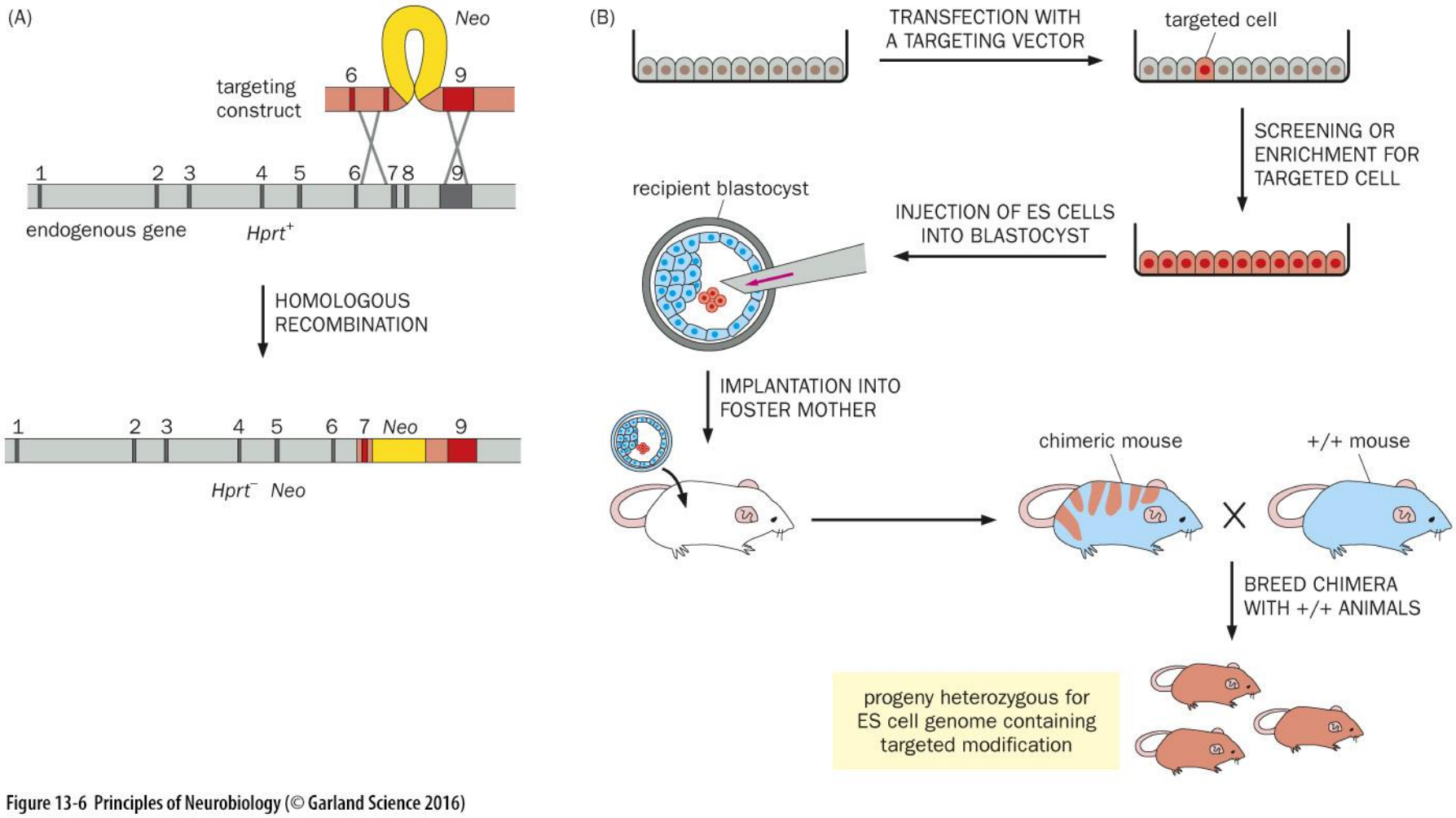

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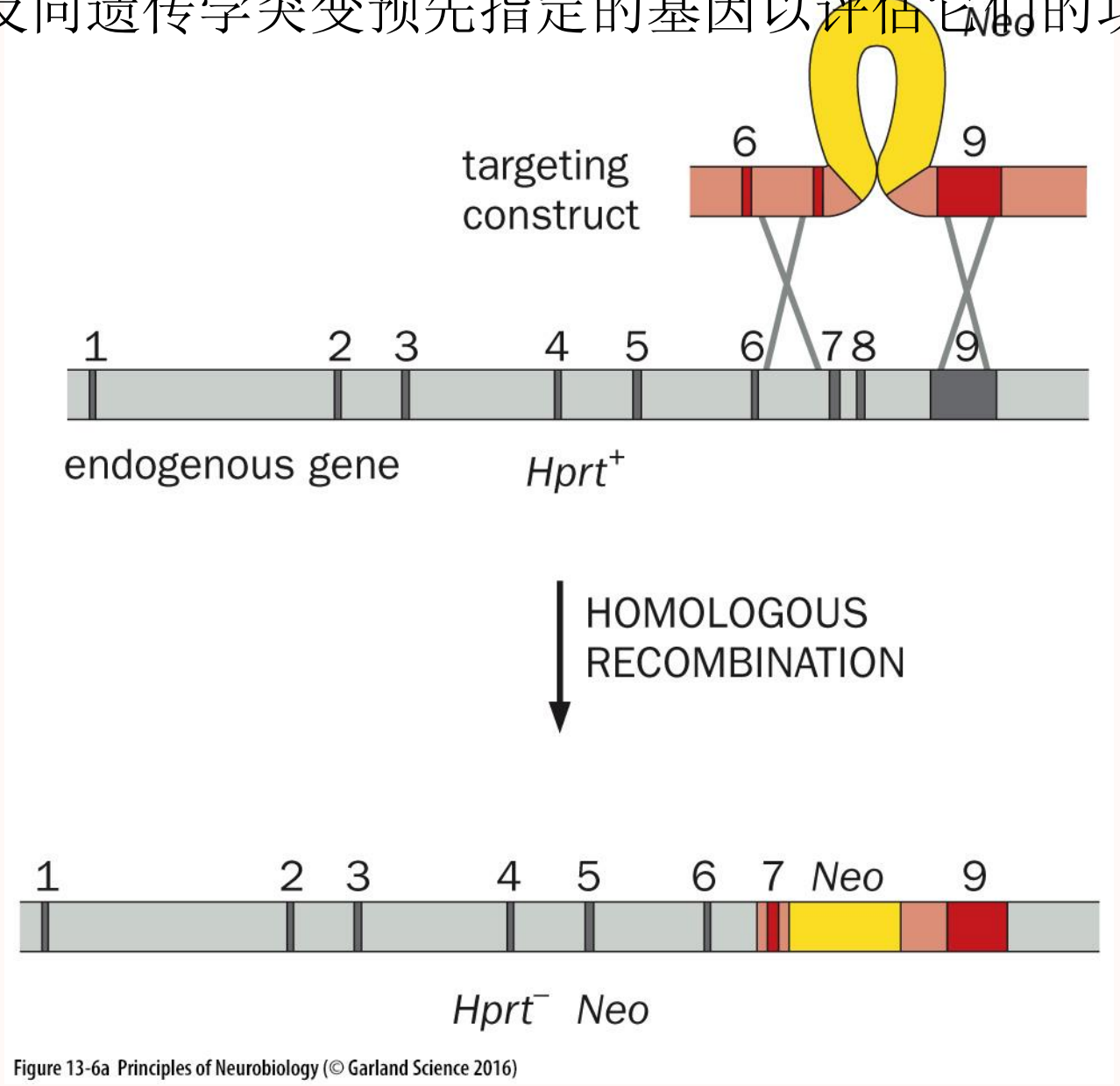

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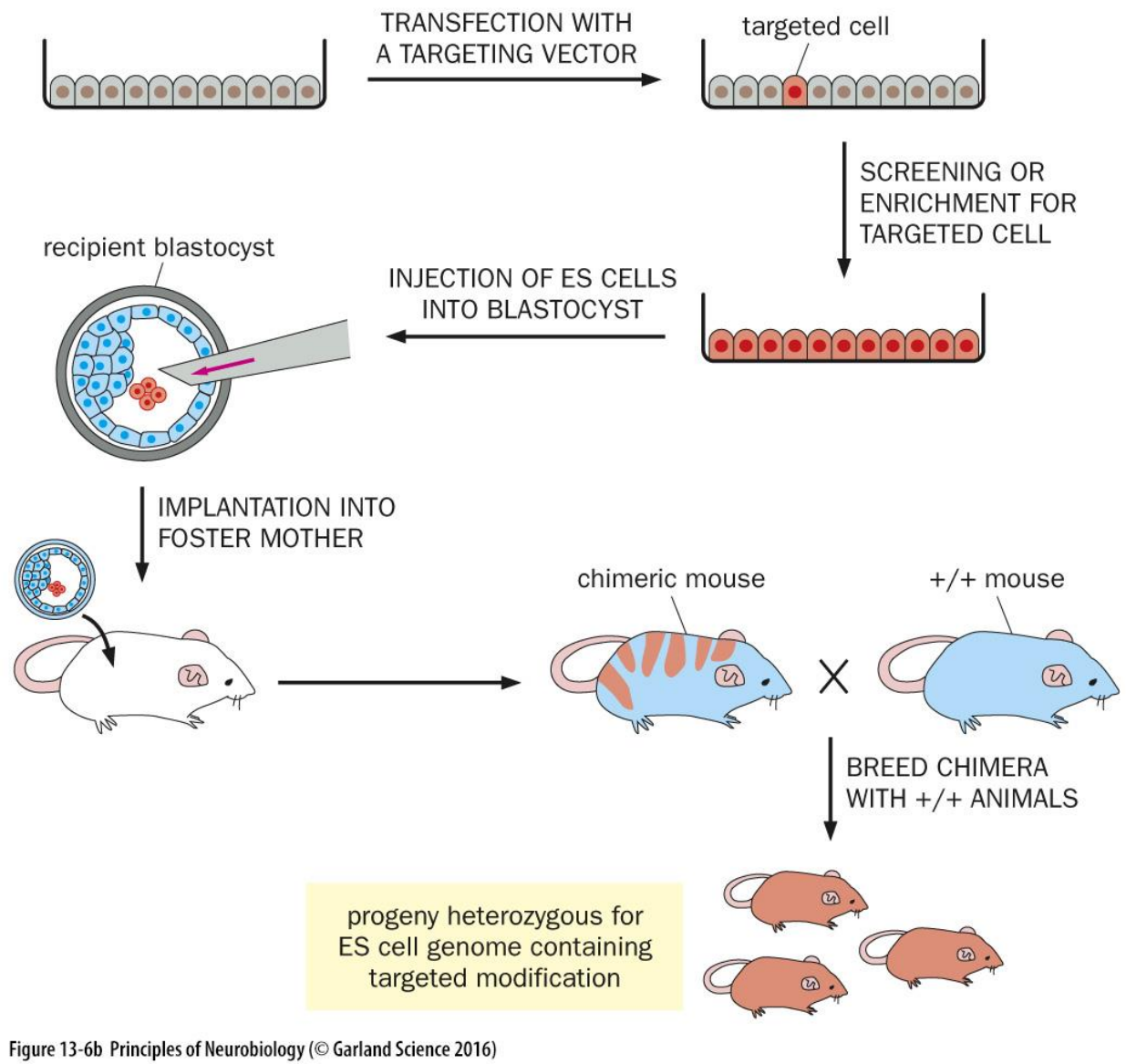

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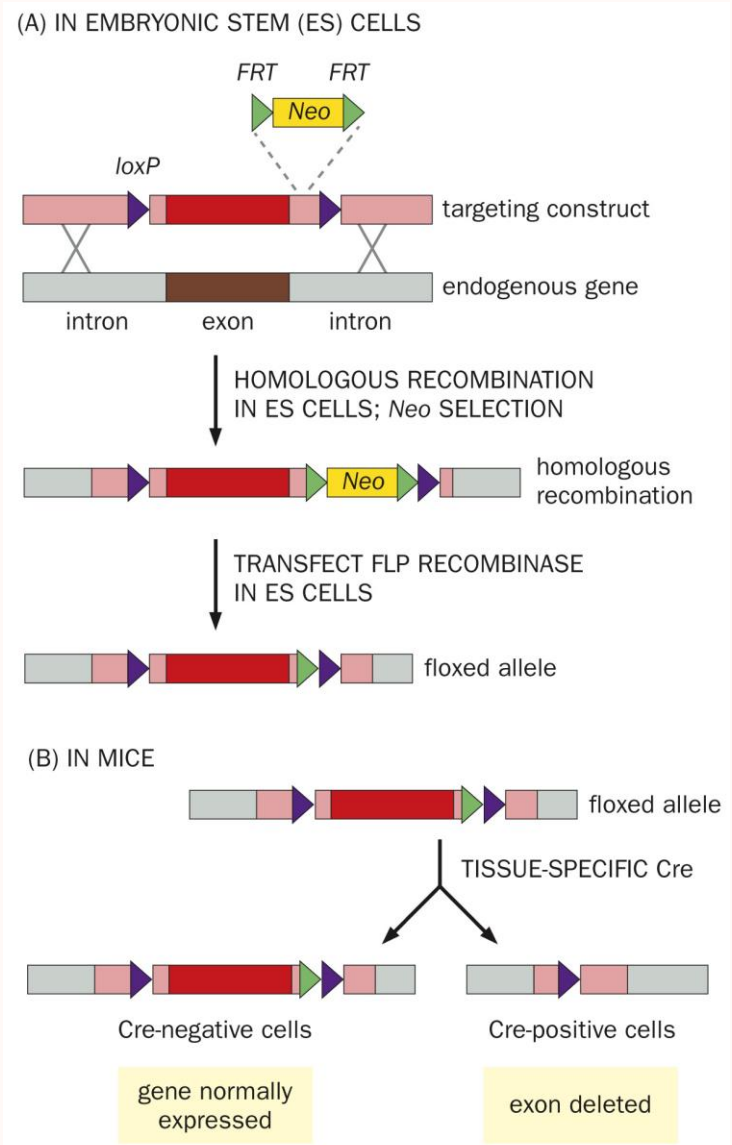

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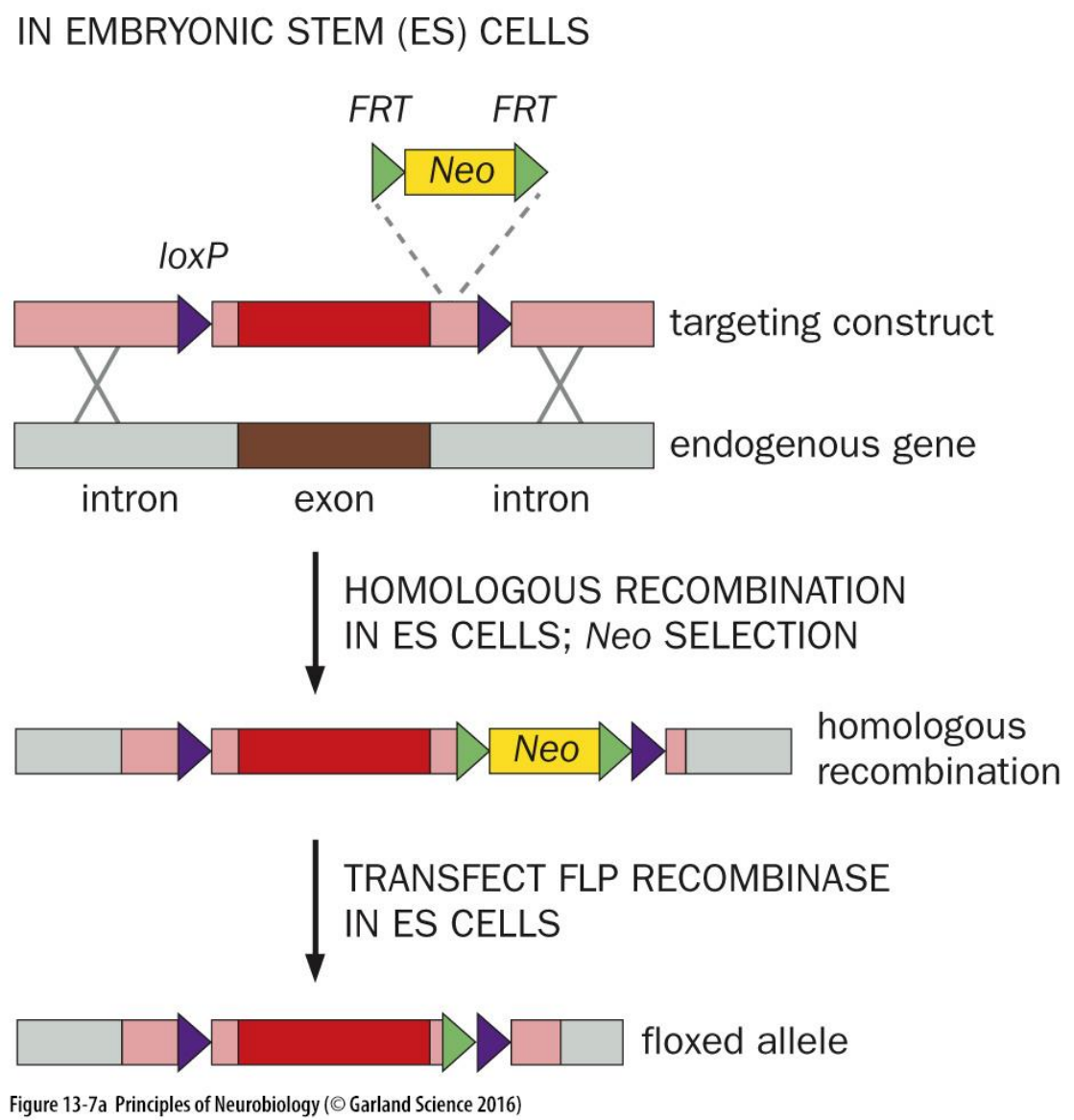

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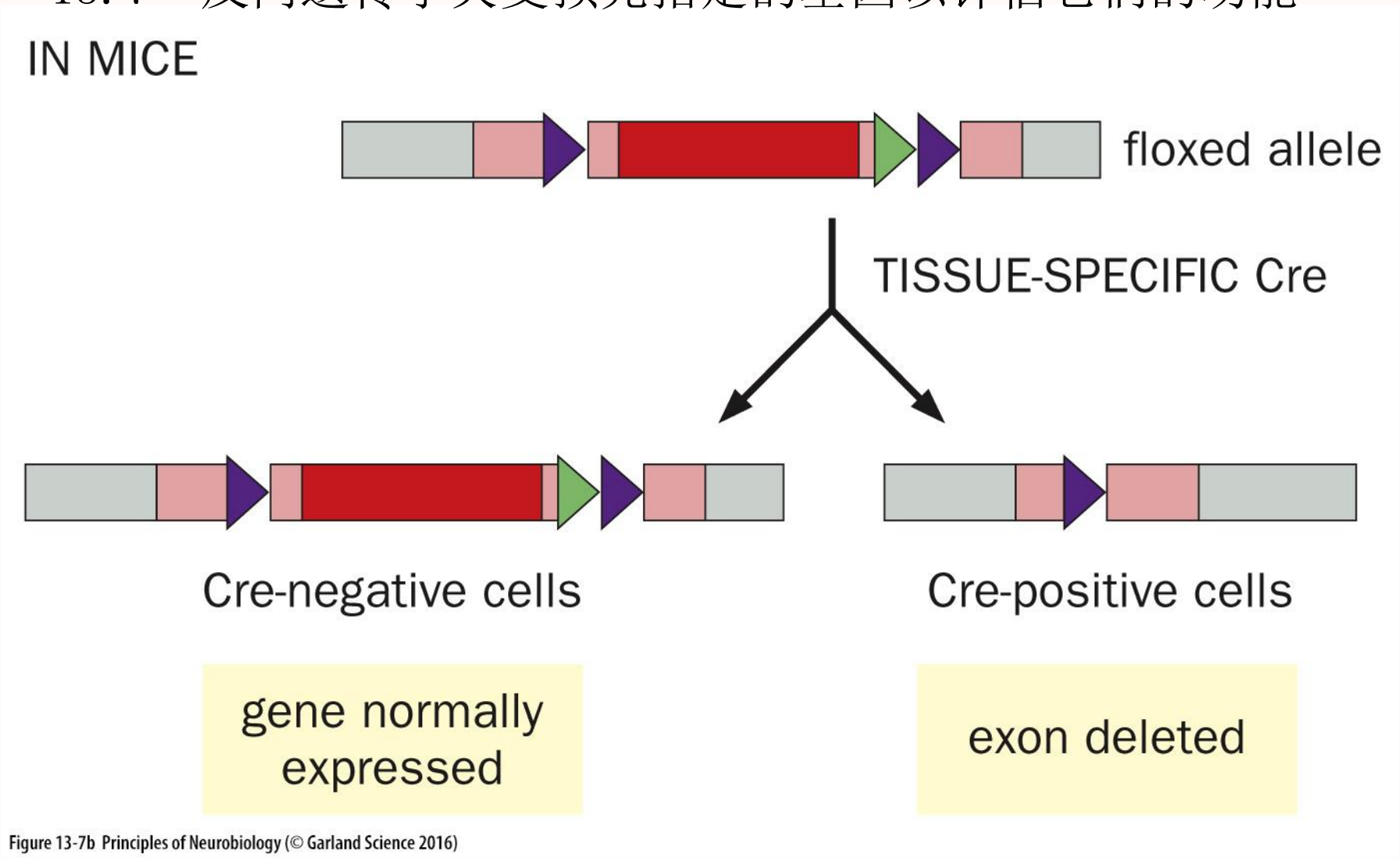

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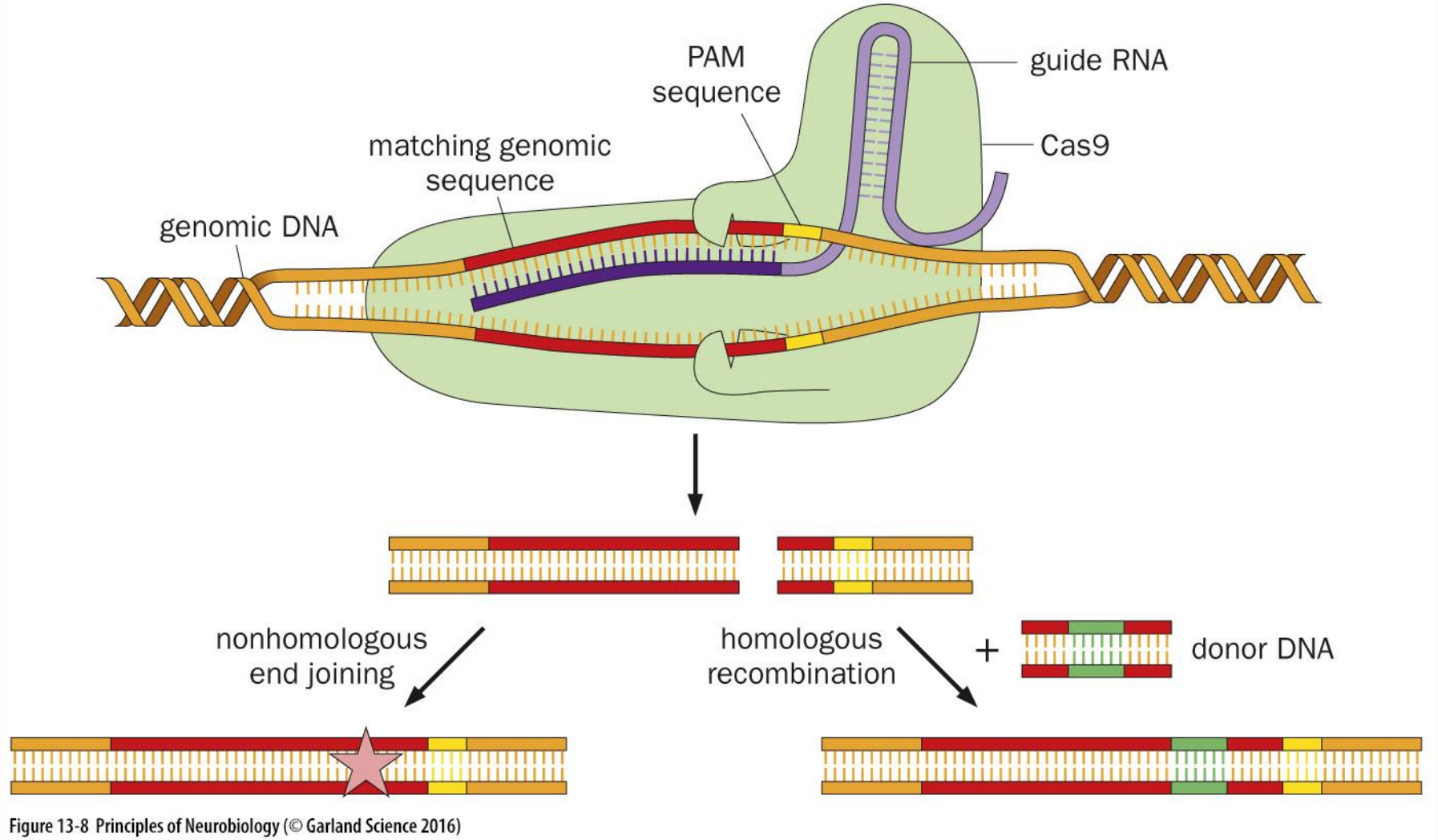

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GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

13.8 RNA interference (RNAi)-mediated knockdown can also be used to assess gene function

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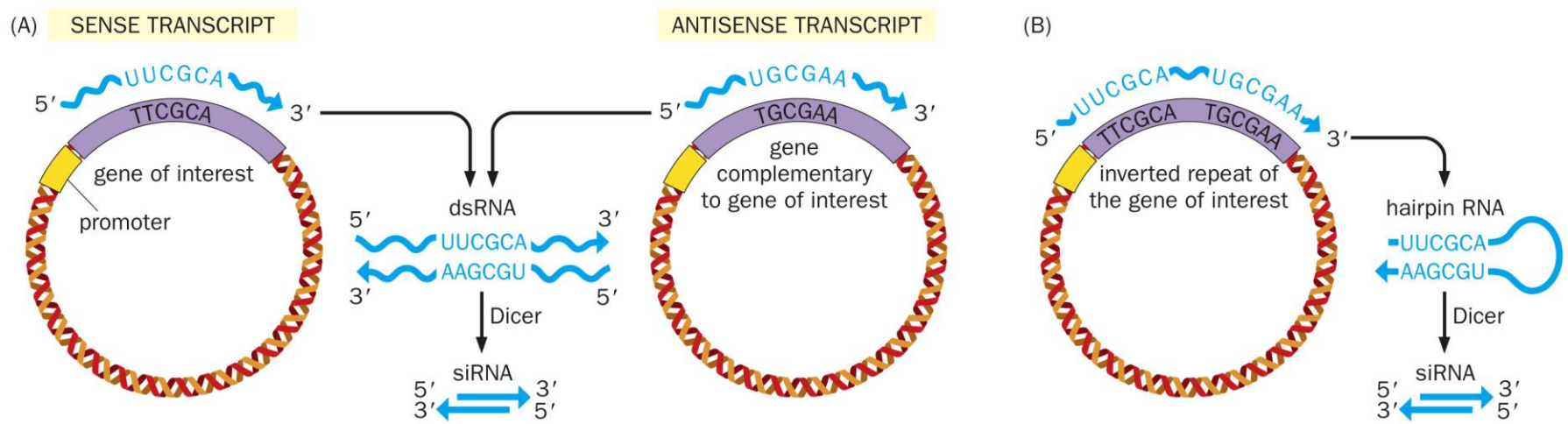

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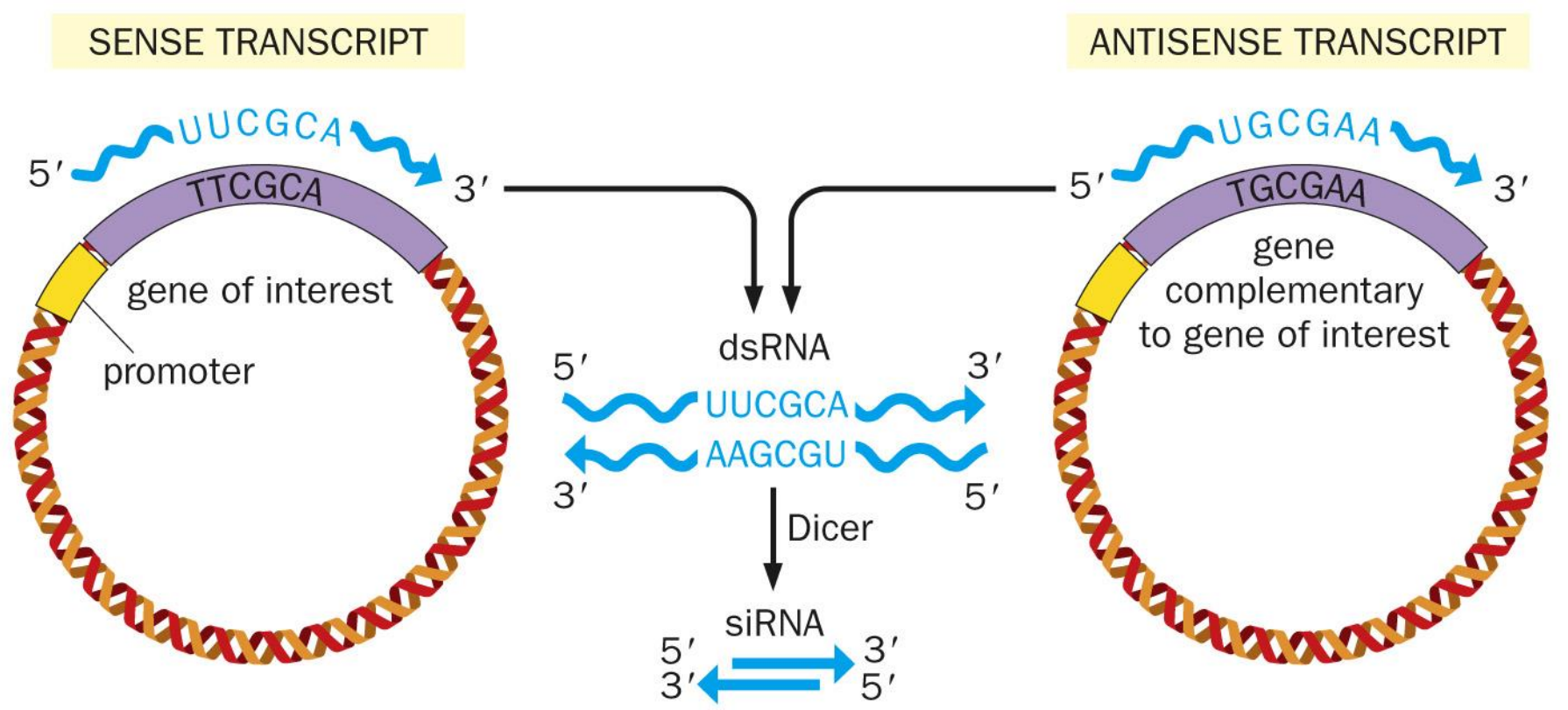

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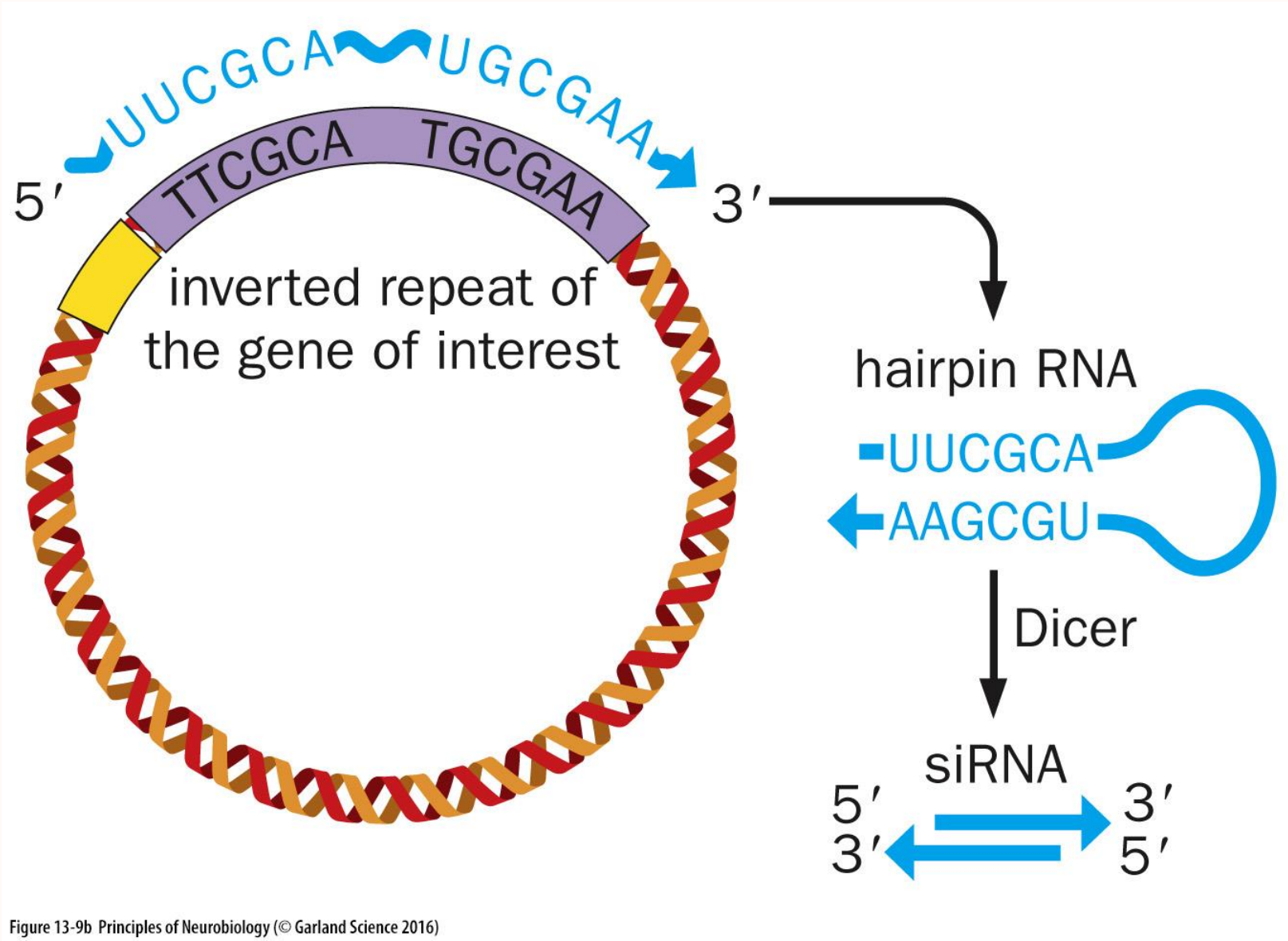

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GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

13.9 Genetic mosaic analysis can pinpoint which cell is critical for mediating gene action

13.9 遗传镶嵌分析可以确定对调节基因活动重要的细胞

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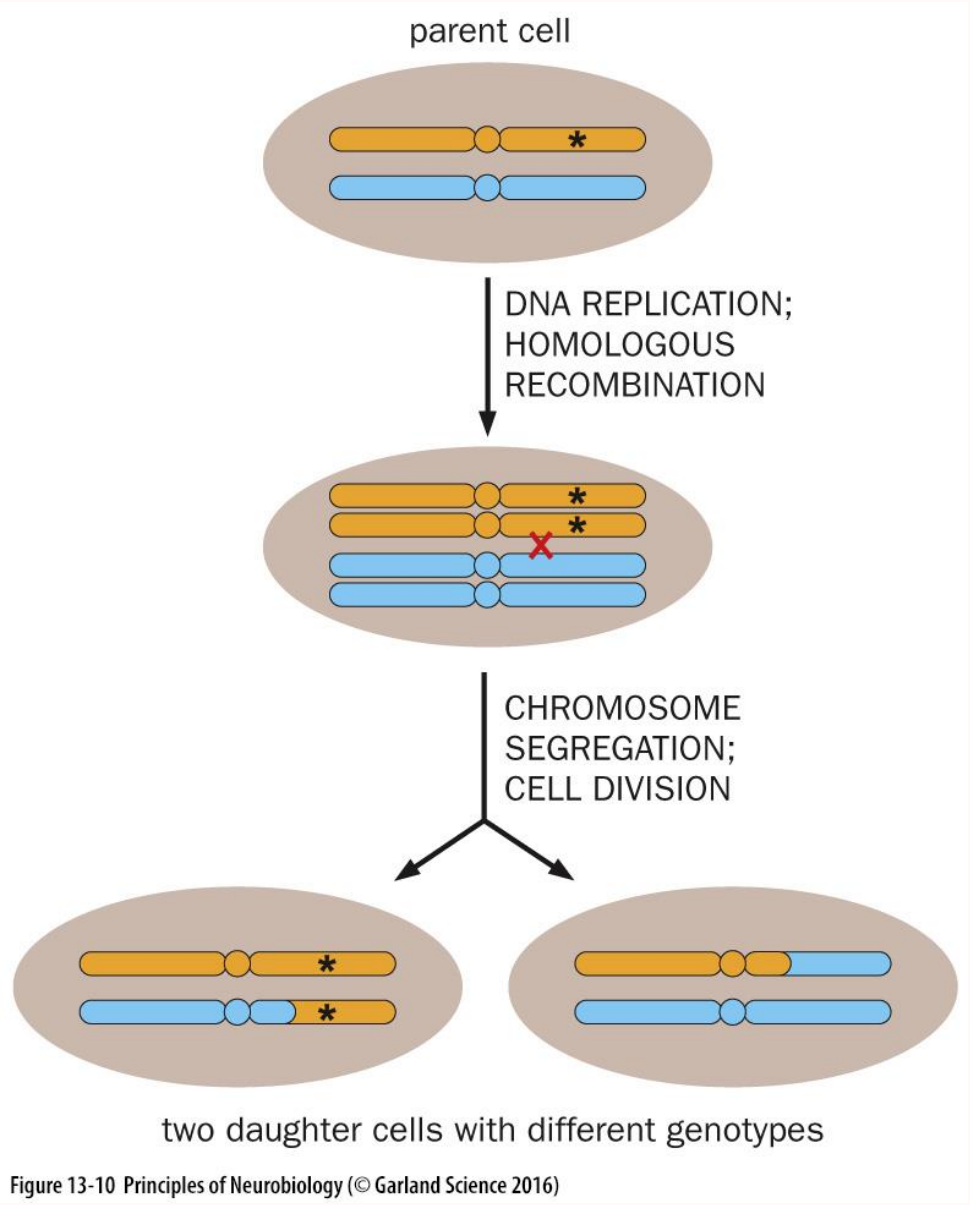

Figure 13-10 Principles of Neurobiology (© Garland Science 2016)

GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

13.10 Transgene expression can be controlled in both space and time in transgenic animals

13.10 转基因的表达可以在时间空间水平中控制

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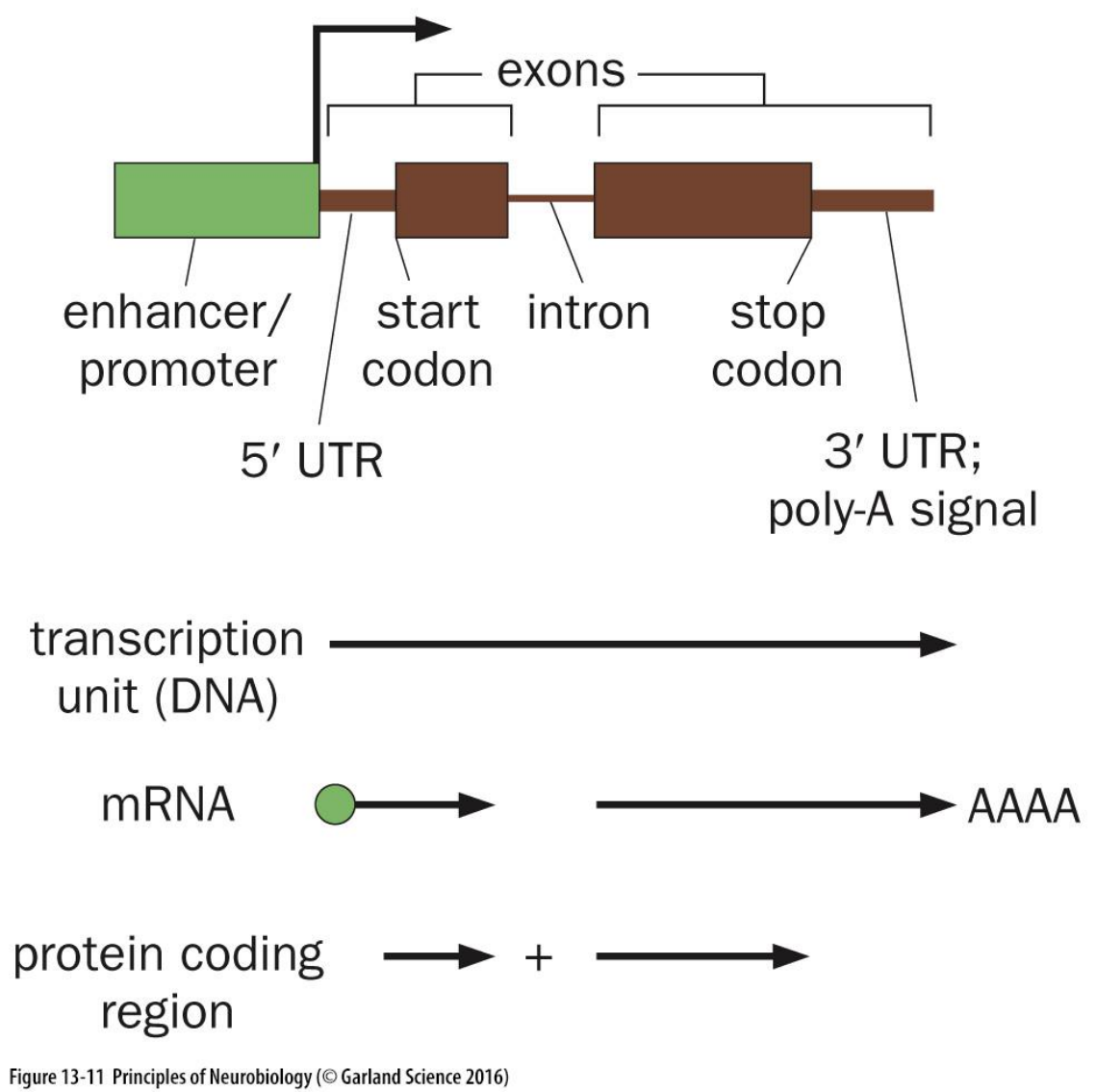

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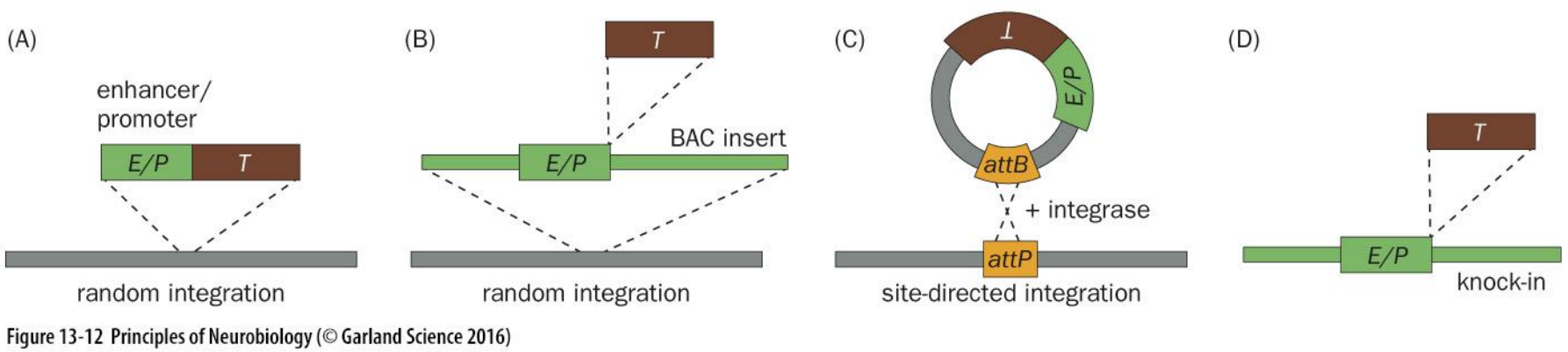

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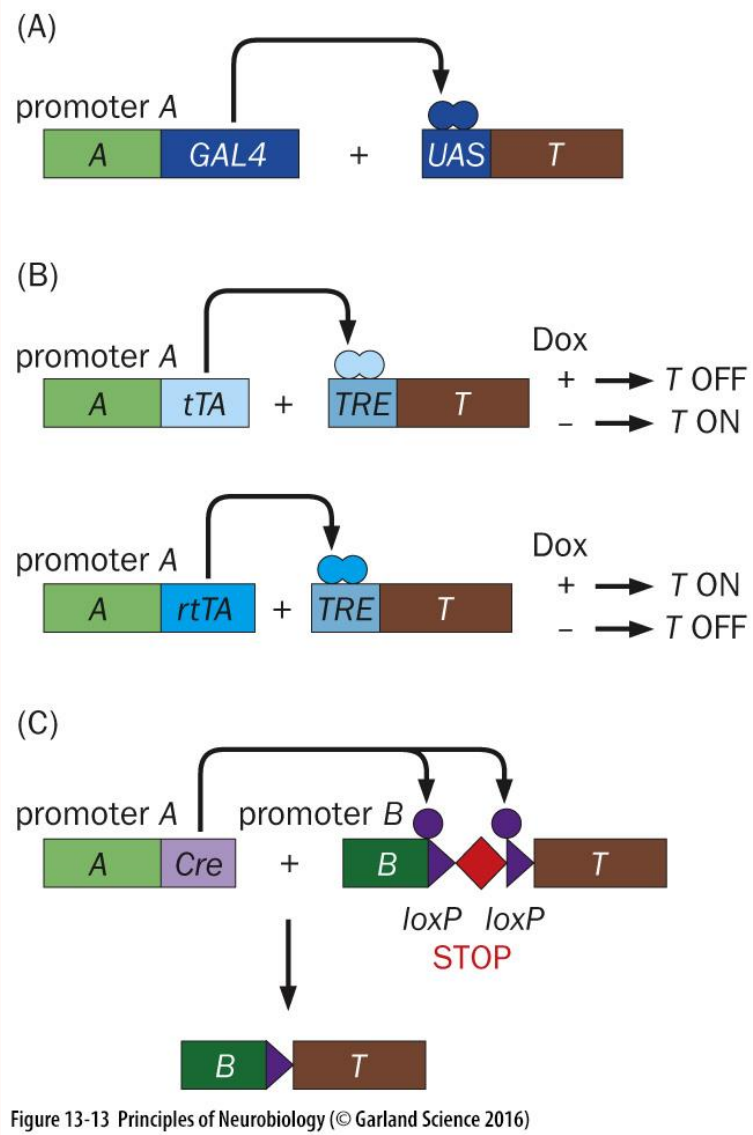

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GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

13.11 Transgene expression can also be achieved by viral transduction and other transient methods

13.11 转基因表达也可以通过病毒转导和其他瞬时表达的方法实现

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Table 13–1: Properties of commonly used viral vectors for gene expression in the nervous system

Property	Adeno-associated virus (AAV)	Lentivirus	Herpes simplex virus (HSV)
Genetic material	single-strand DNA	RNA	double-strand DNA
Capacity	~ 5 kilobases	~ 8 kilobases	~150 kilobases
Speed of expression	weeks	weeks	days
Duration of expression	years	years	weeks to months
Tropism (cell types susceptible to viral transduction)	from broad to highly preferential depending on the serotype	usually pseudotyped[1] with coat proteins from other viruses for broad tropism	broad tropism for neurons

[1] To pseudotype a virus, the gene encoding the endogenous coat protein is deleted, and viruses are assembled in cell lines that co-express genes encoding a coat protein from a different virus.

Data from Luo L, Callaway EM & Svoboda K [2008] *Neuron* 57:634–660.

Table 13-1 Principles of Neurobiology (© Garland Science 2016)

GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

13.12 Accessing specific neuronal types facilitates functional circuit dissection

13.12 利用特定种类神经元研究功能环路

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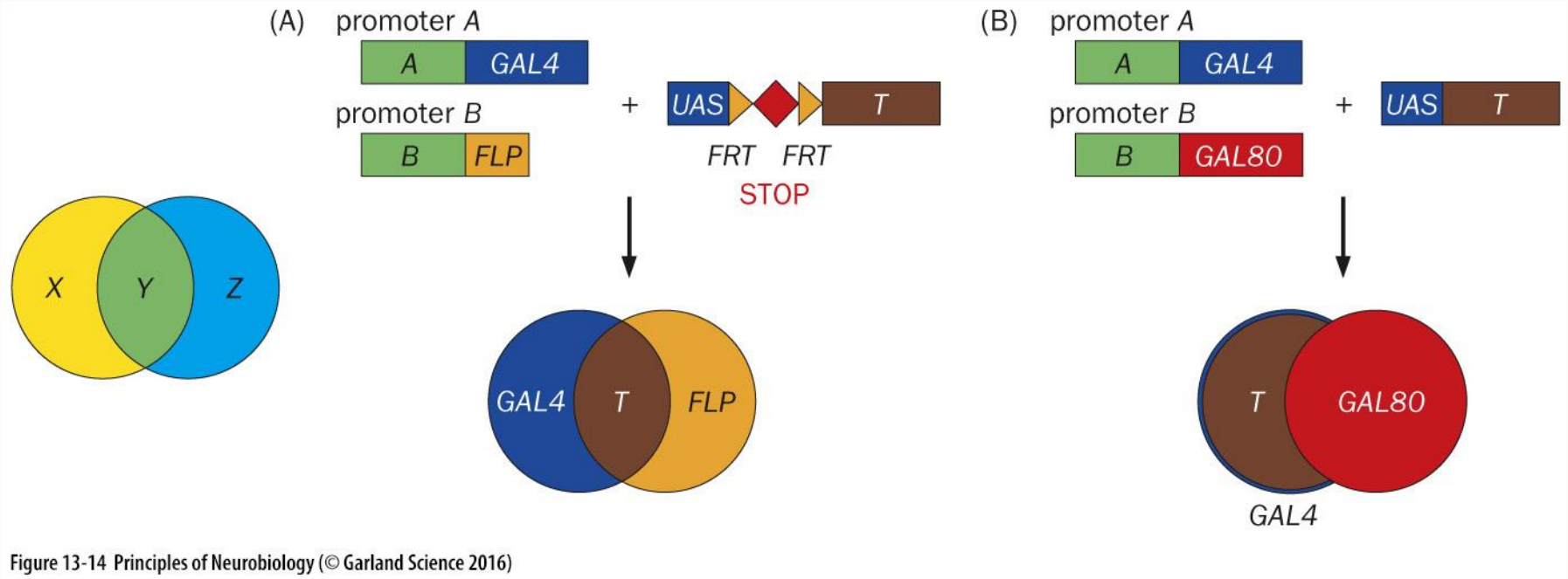

Figure 13-14 Principles of Neurobiology (© Garland Science 2016)

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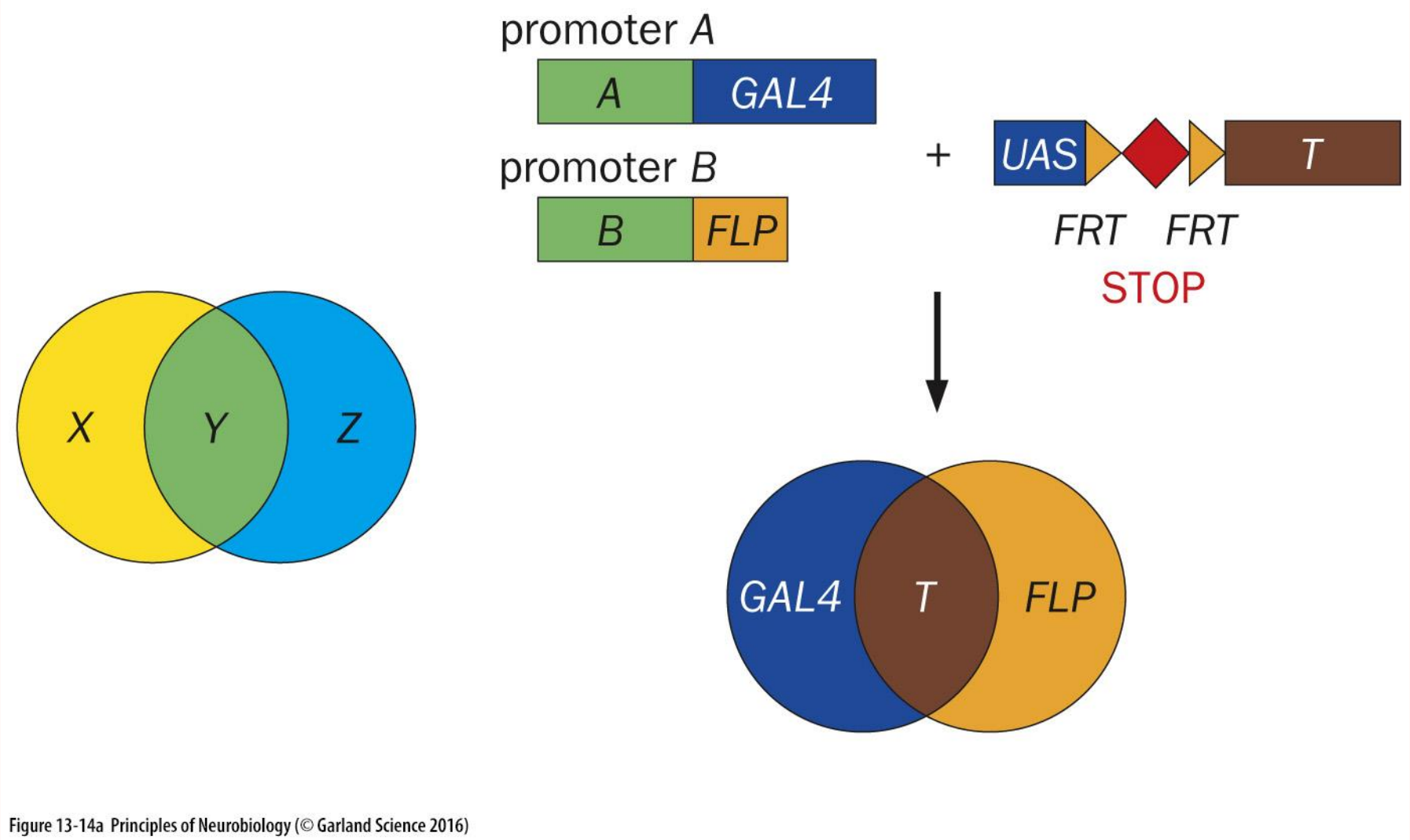

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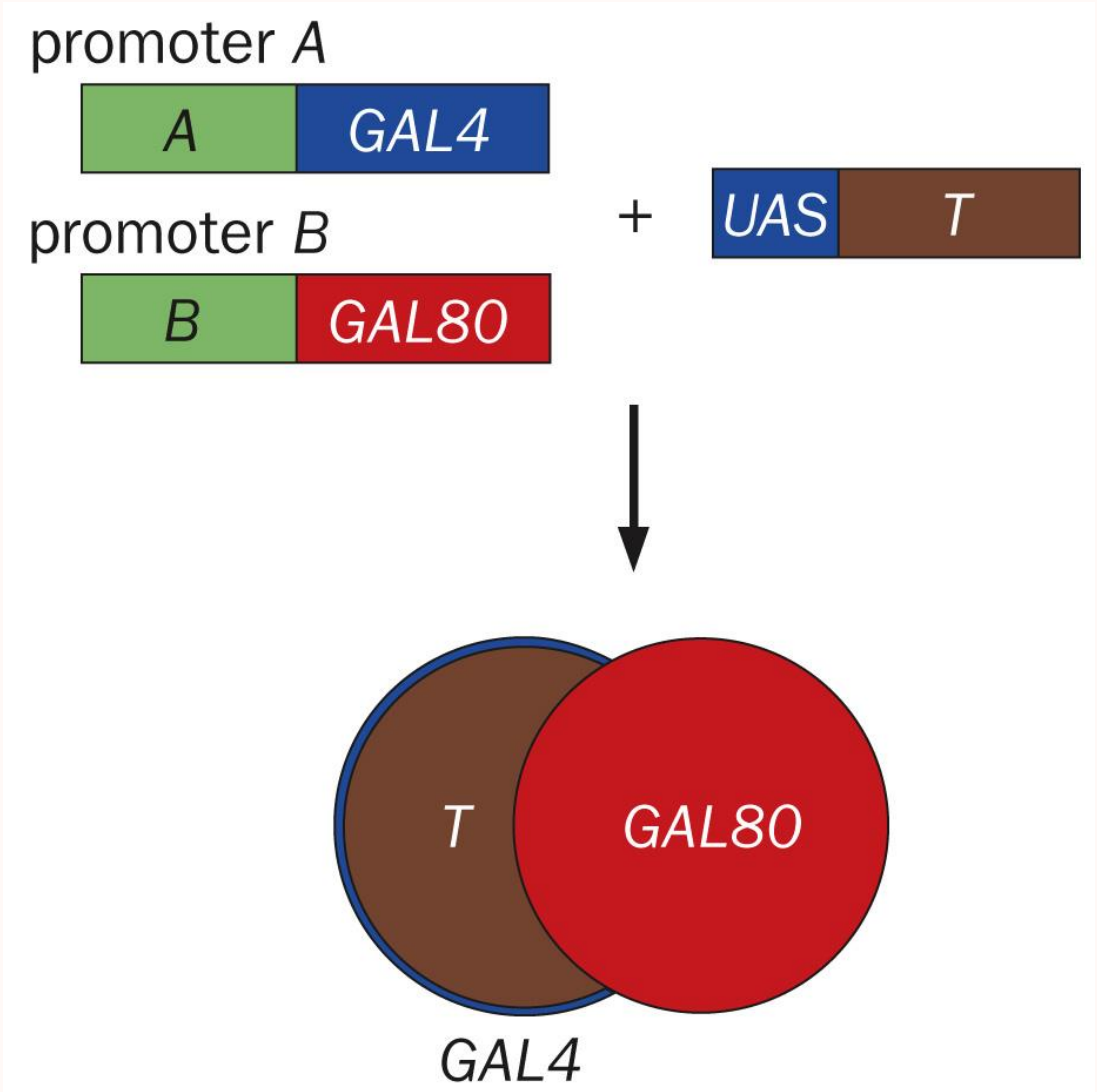

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GENETIC AND MOLECULAR TECHNIQUES

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13.13 Gene expression patterns can be determined by multiple powerful techniques

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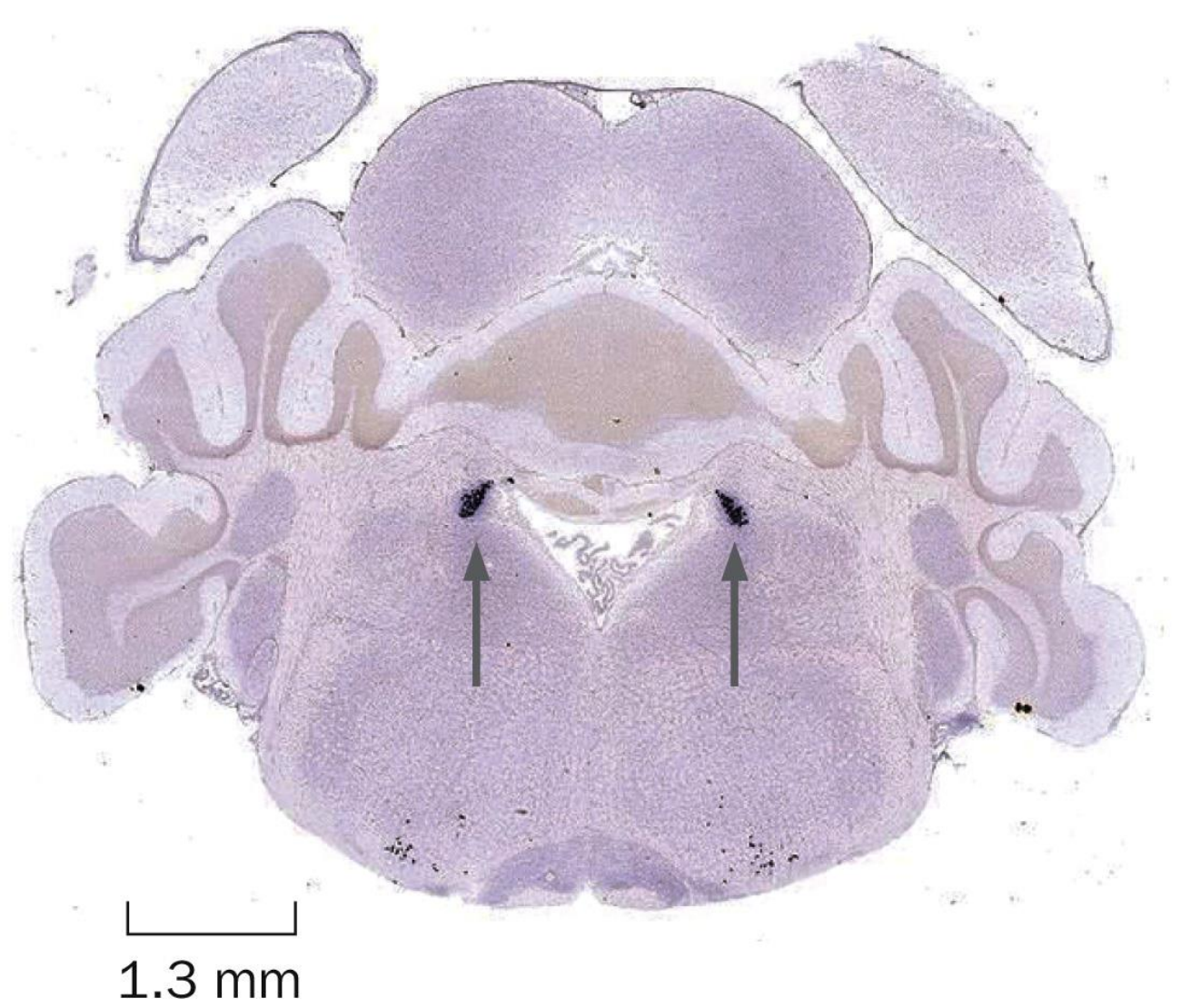

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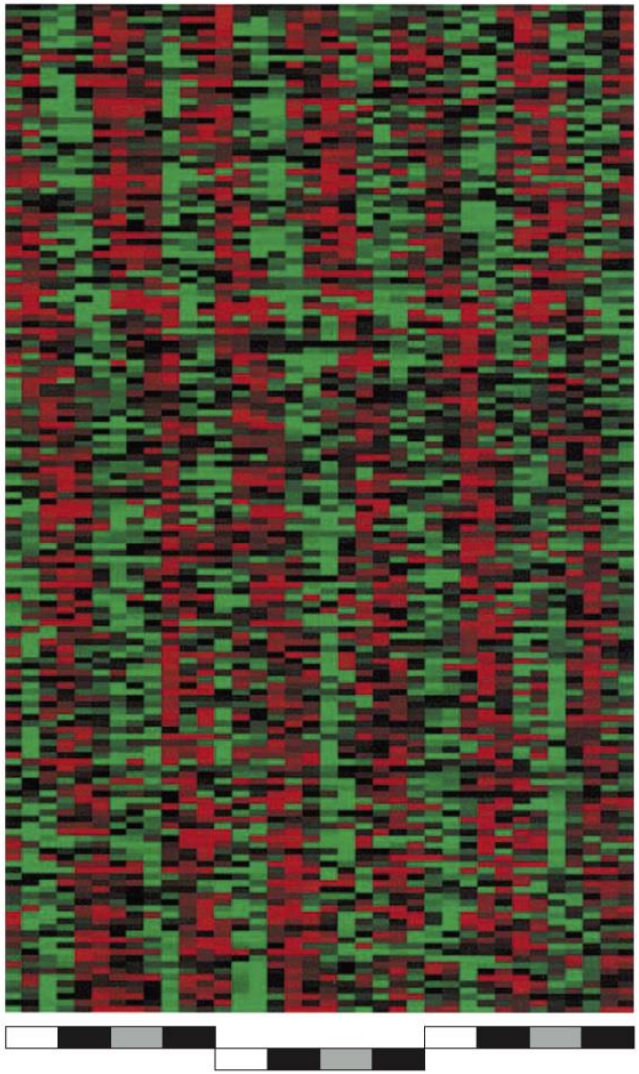

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GENETIC AND MOLECULAR TECHNIQUES

遗传和分子学技术

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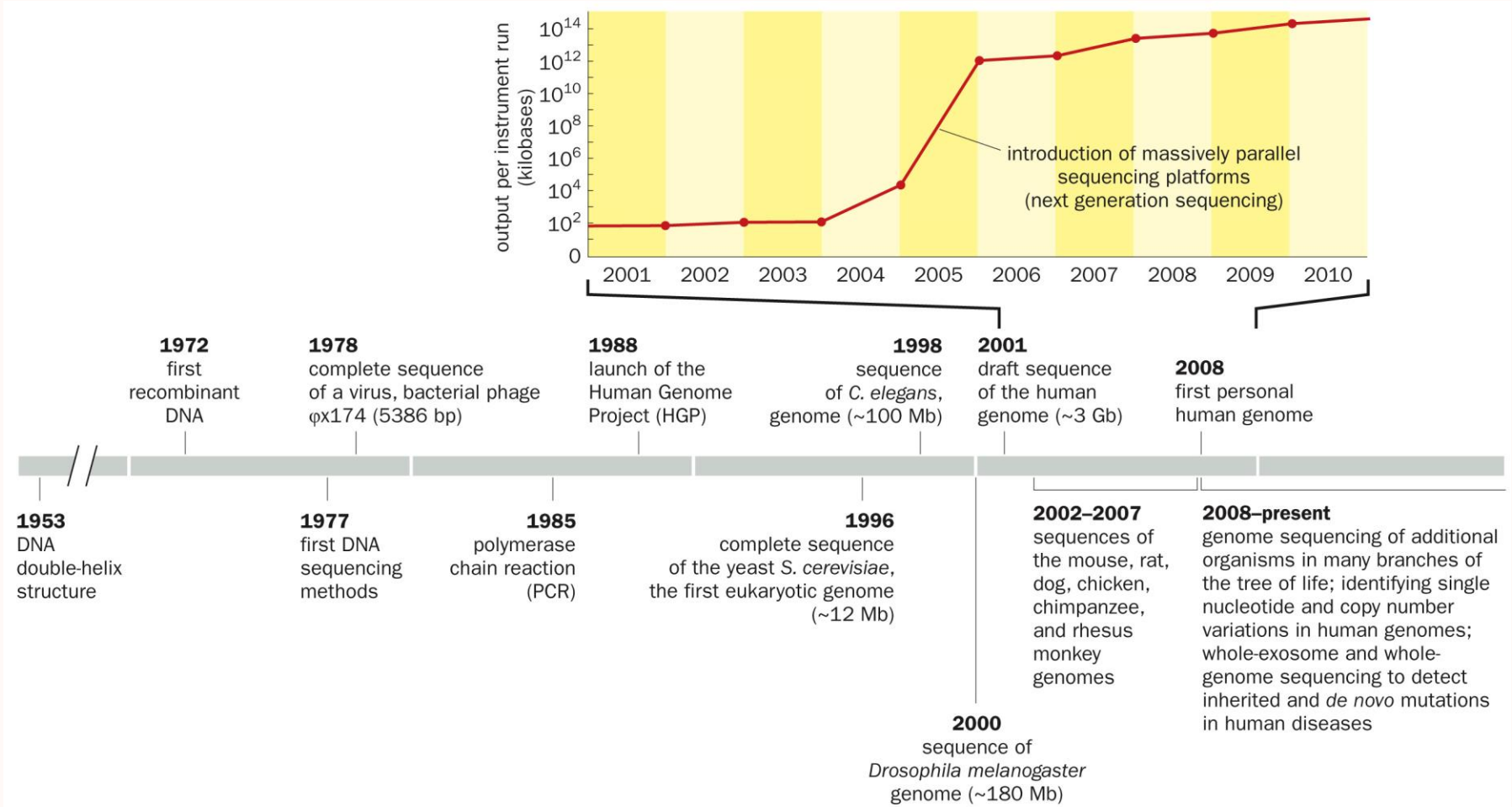

Figure 13-17 Principles of Neurobiology (© Garland Science 2016)

ANATOMICAL TECHNIQUES

基于解剖结构的技术

13.15 Histological analyses reveal the gross organization of the nervous system

13.16 Visualizing individual neurons opens new vistas in understanding the nervous system

13.15 组织学分析揭露神经系统的结构

13.16 可视化单个神经元开辟了理解神经系统的新的前景

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13.17 Fine structure studies can identify key facets of molecular organization within neurons

13.18 Mapping neuronal projections allows the tracking of information flow across different brain regions

13.19 Mapping synaptic connections reveals neural circuitry

13.17 精细结构的研究可以验证神经元内分子组织的关键

13.18 了解神经投射可以追踪不同脑区的信息流动

13.19 了解突触间连接可以揭示神经环路

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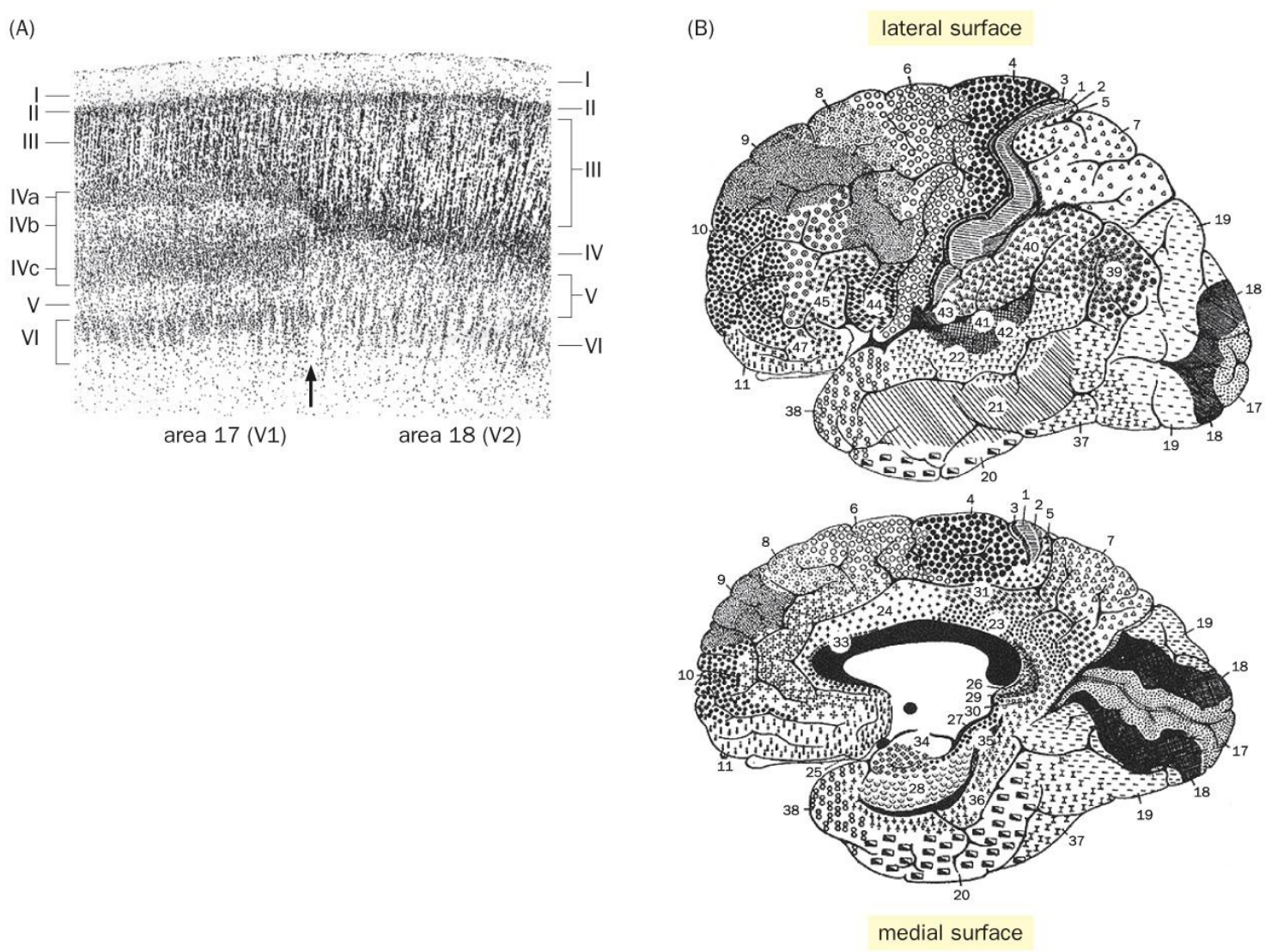

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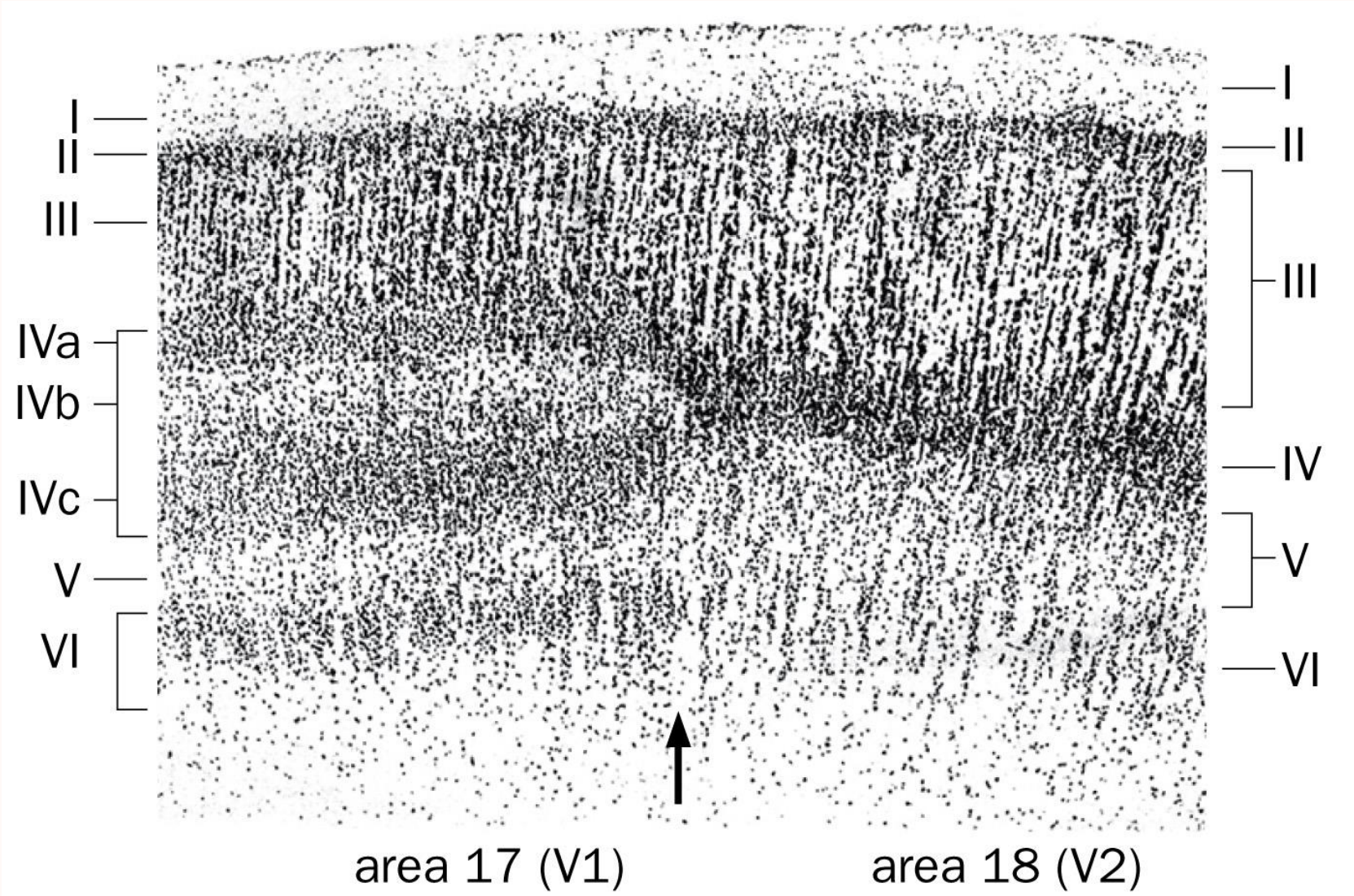

Figure 13-18a Principles of Neurobiology (© Garland Science 2016)

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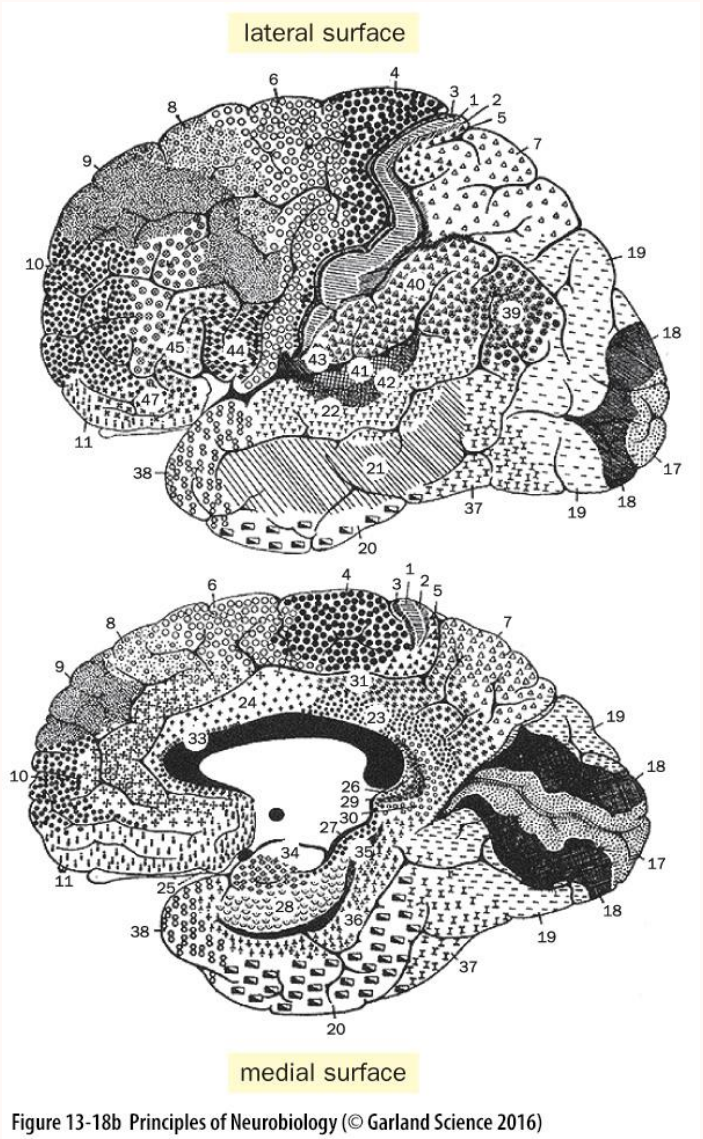

Figure 13-18b Principles of Neurobiology (© Garland Science 2016)

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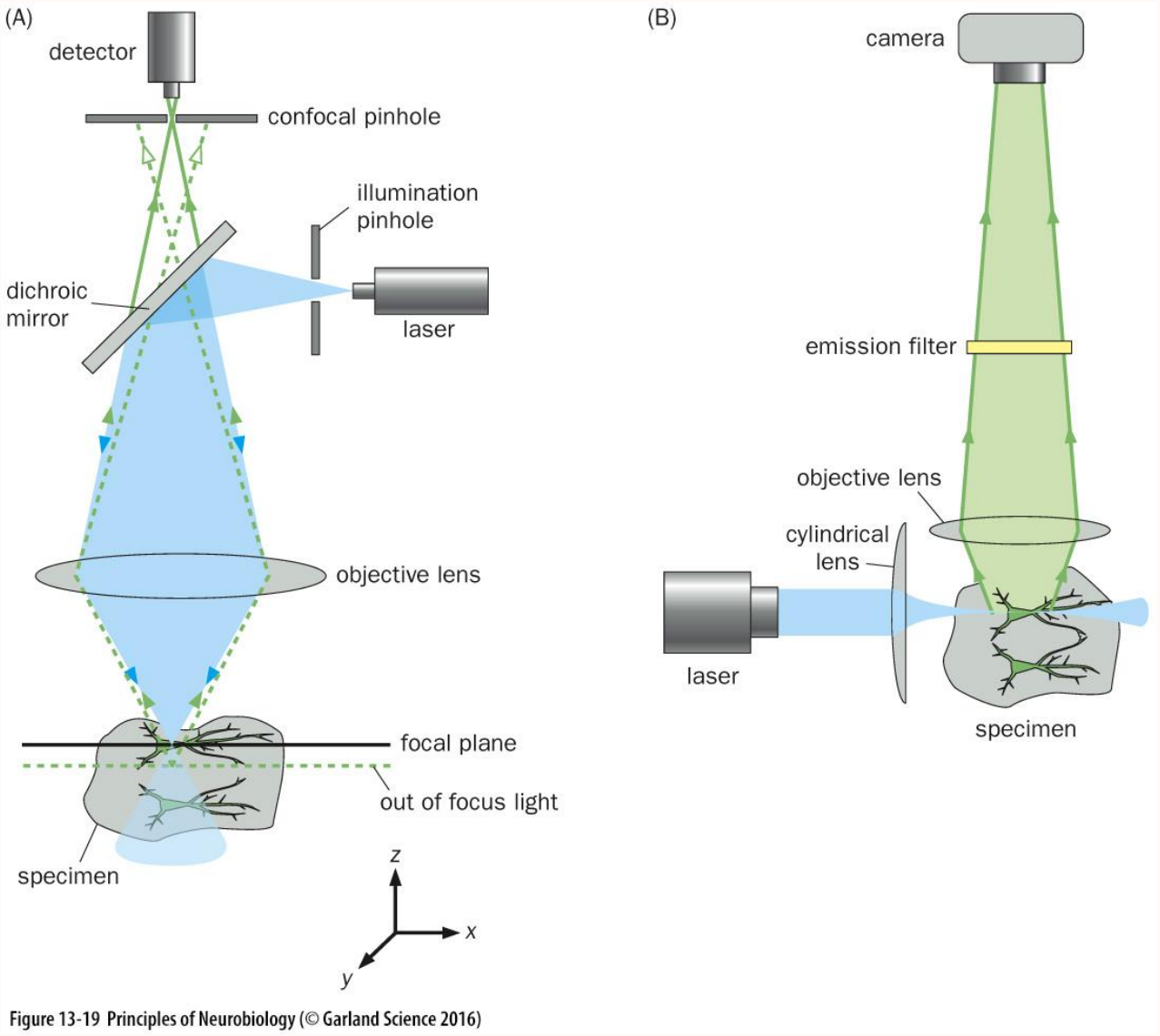

Figure 13-19 Principles of Neurobiology (© Garland Science 2016)

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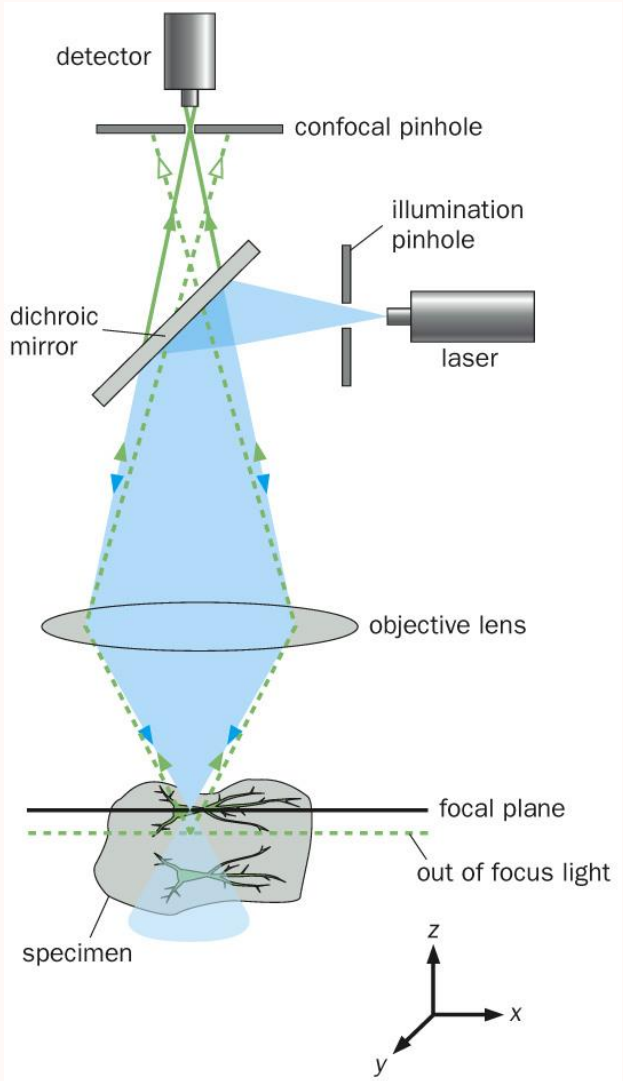

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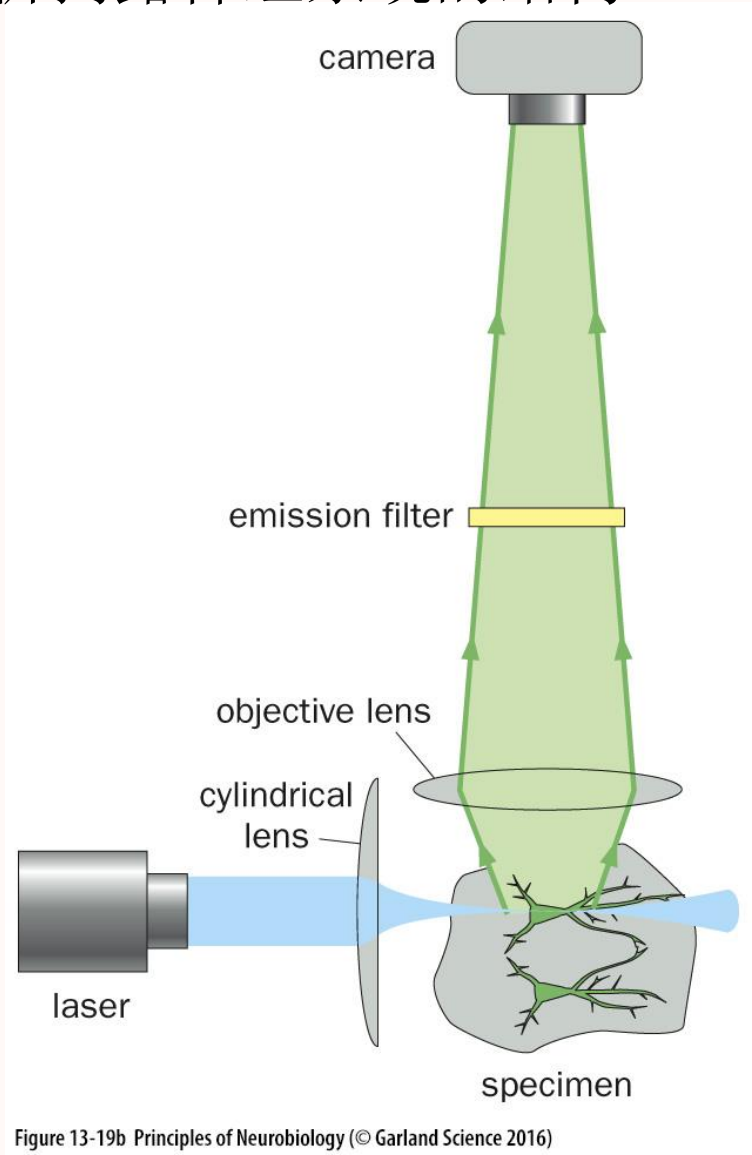

Figure 13-19b Principles of Neurobiology (© Garland Science 2016)

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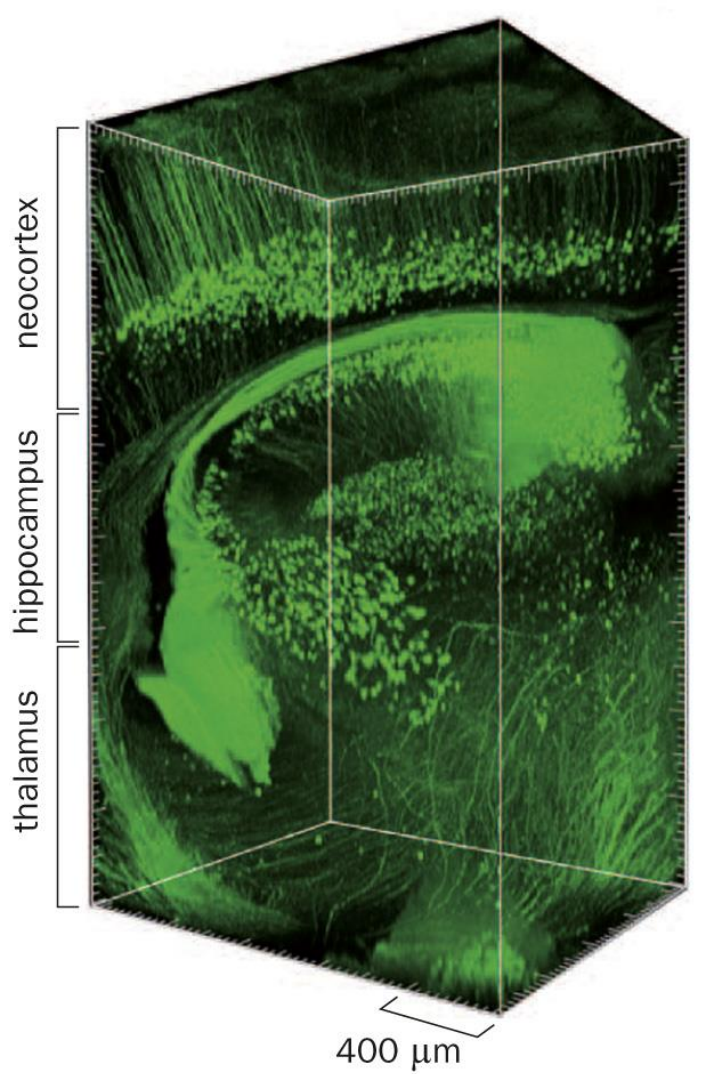

Figure 13-20 Principles of Neurobiology (© Garland Science 2016)

ANATOMICAL TECHNIQUES

基于解剖结构的技术

13.16 Visualizing individual neurons opens new vistas in understanding the nervous system

13.16 可视化单个神经元开辟了理解神经系统的新的前景

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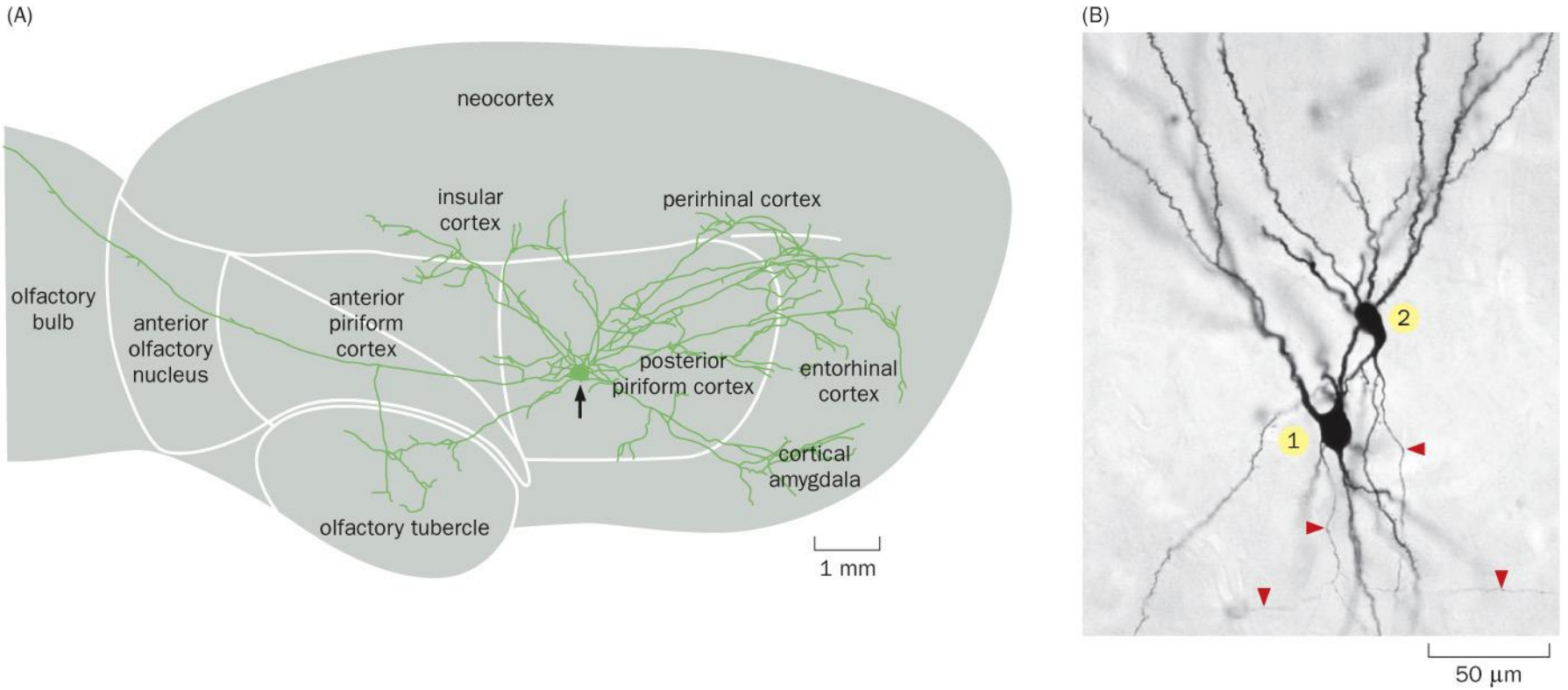

Figure 13-21 Principles of Neurobiology (© Garland Science 2016)

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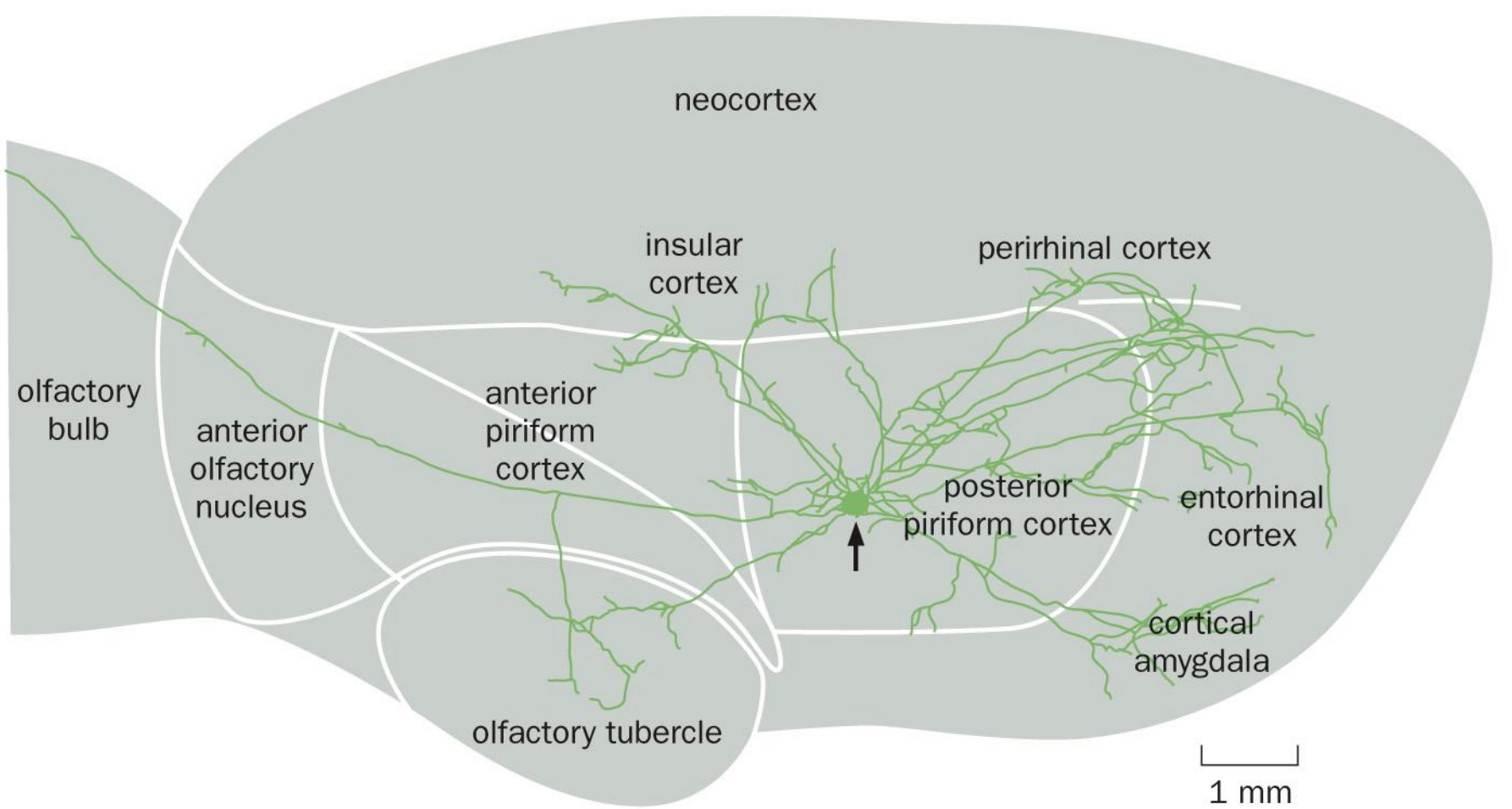

Figure 13-21a Principles of Neurobiology (© Garland Science 2016)

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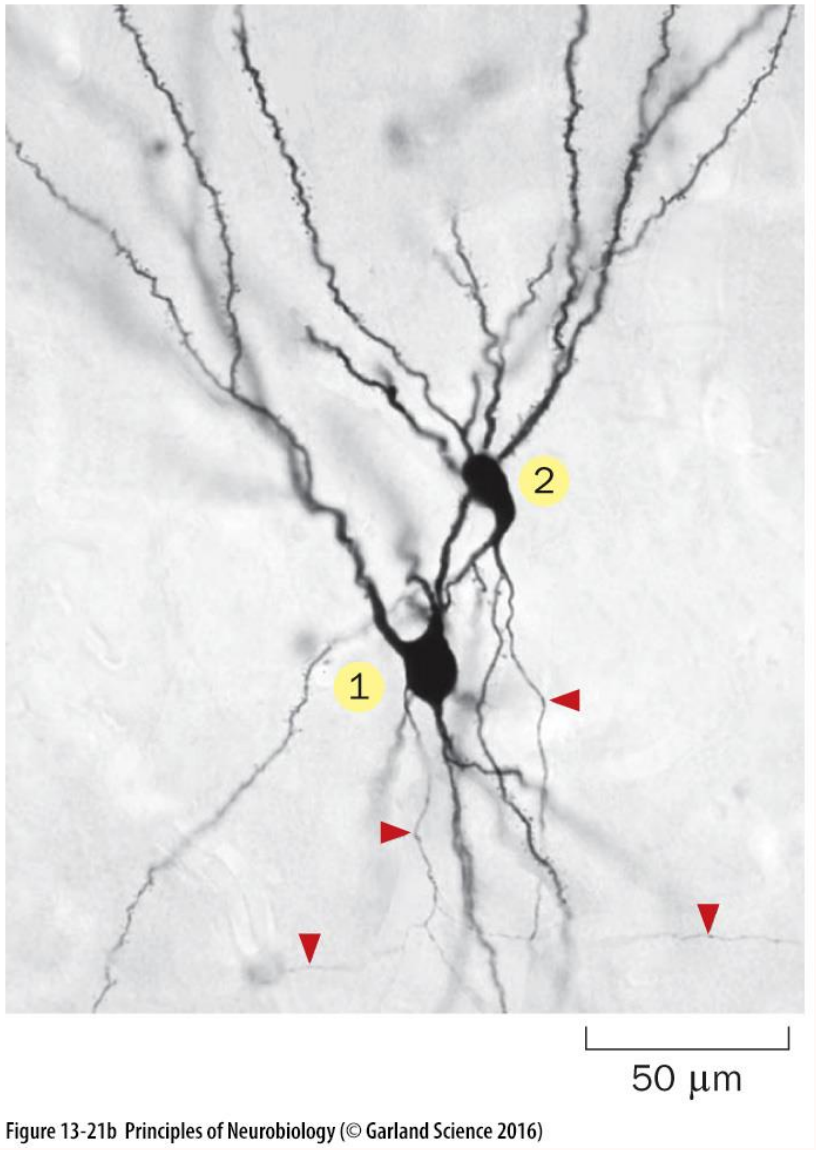

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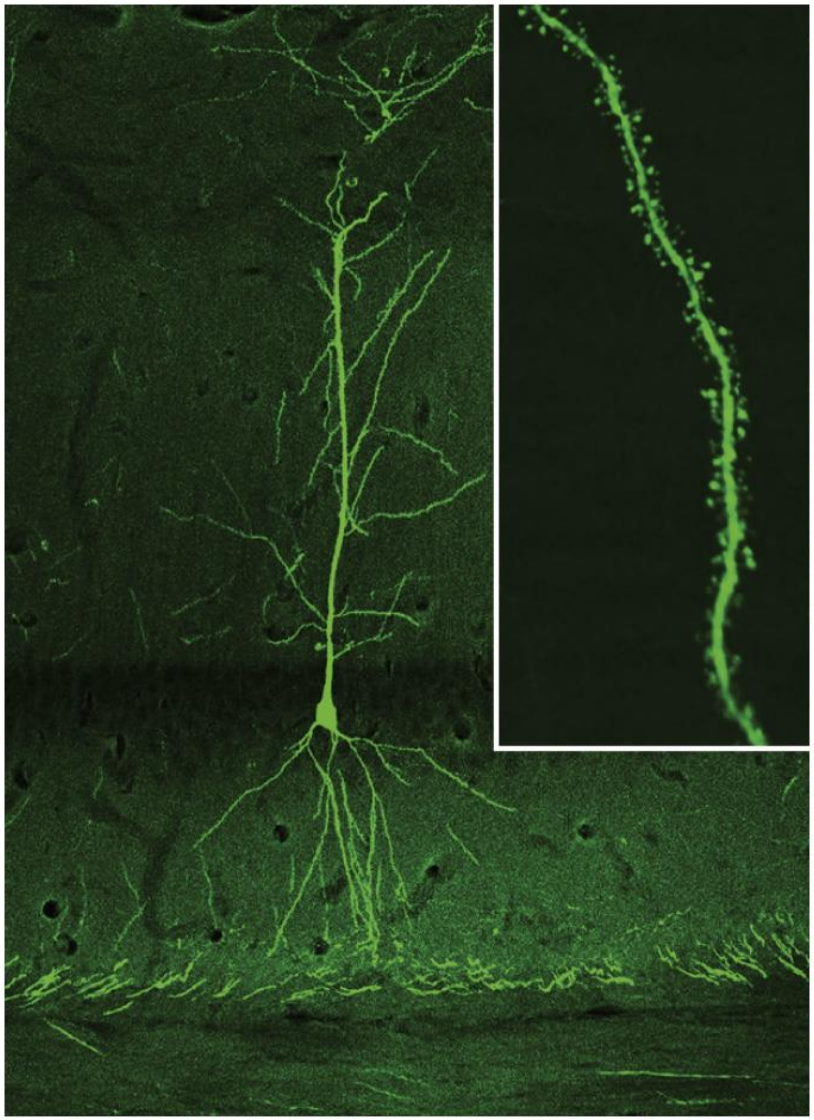

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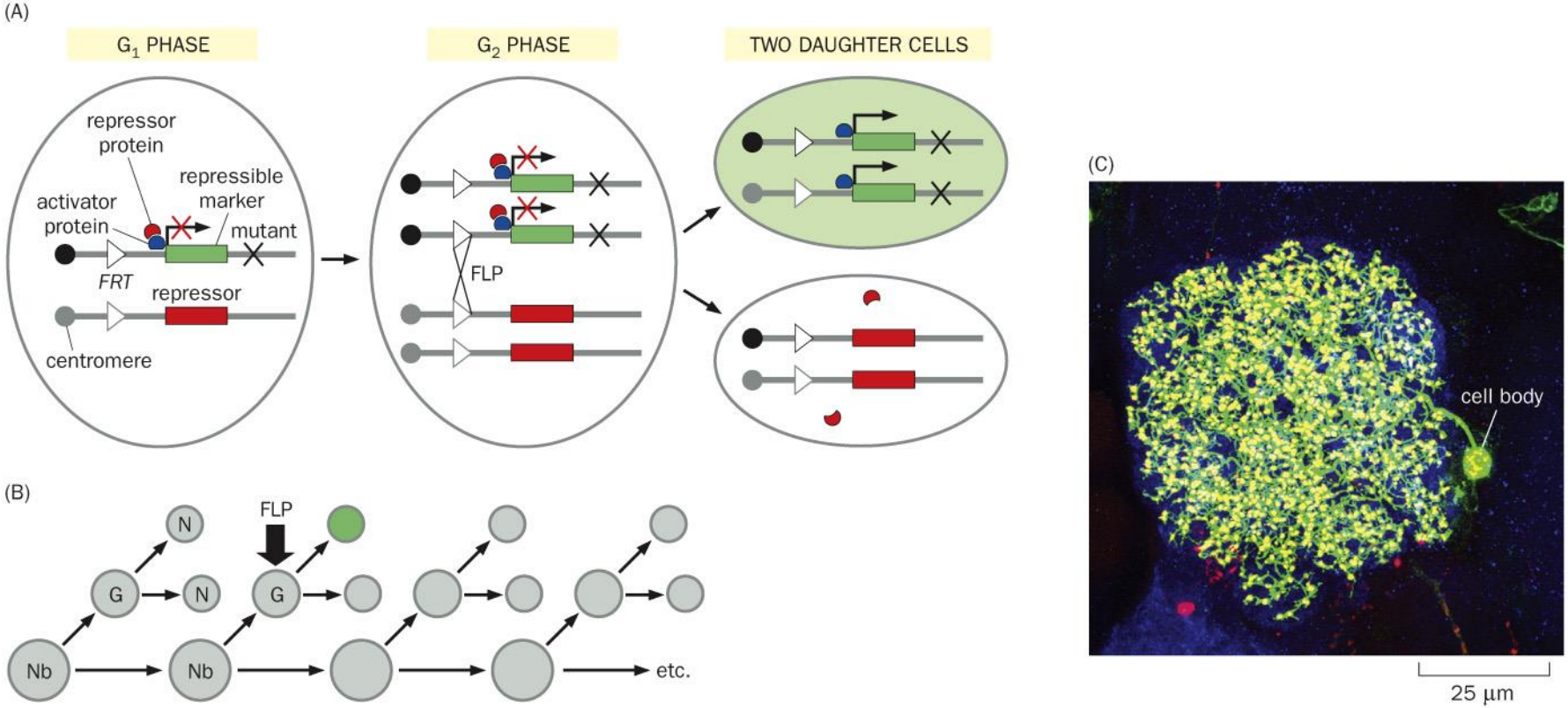

Figure 13-23 Principles of Neurobiology (© Garland Science 2016)

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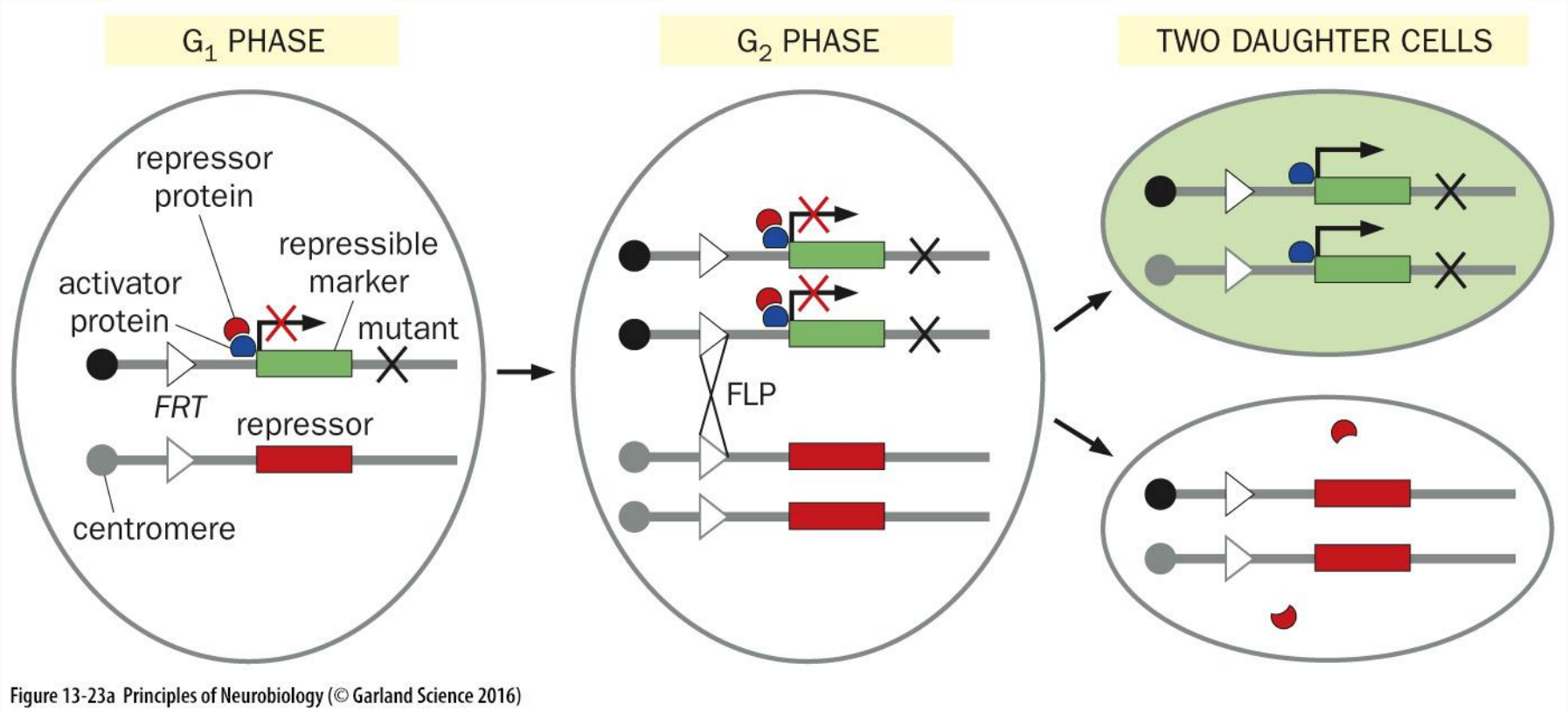

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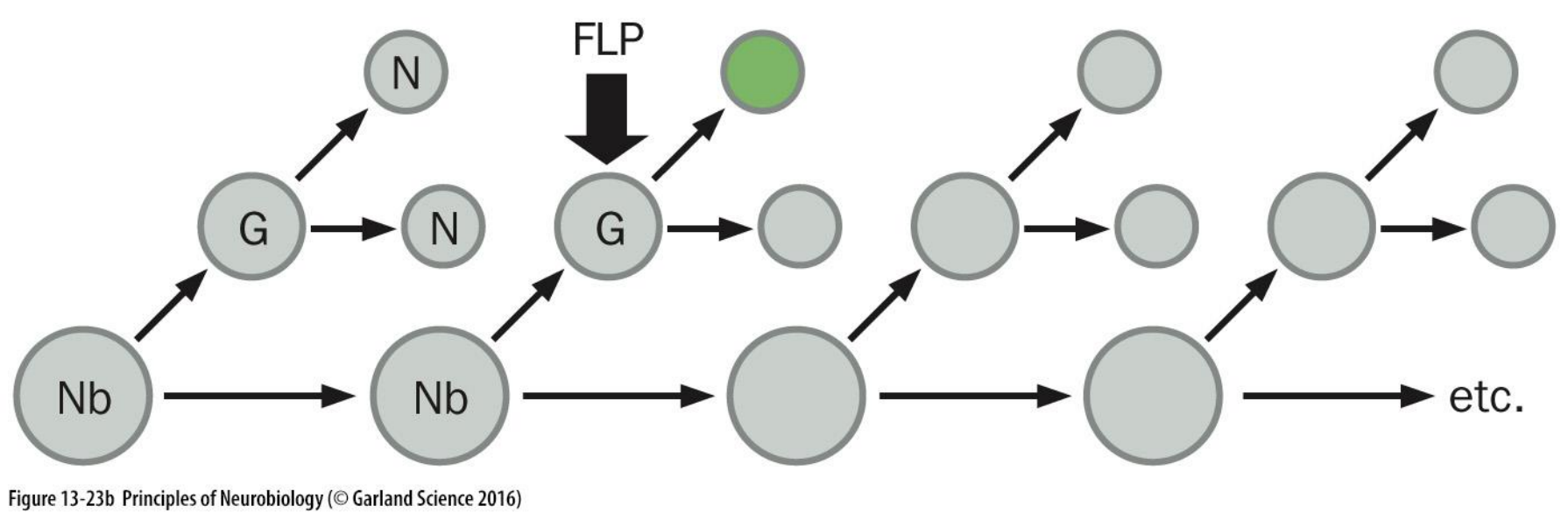

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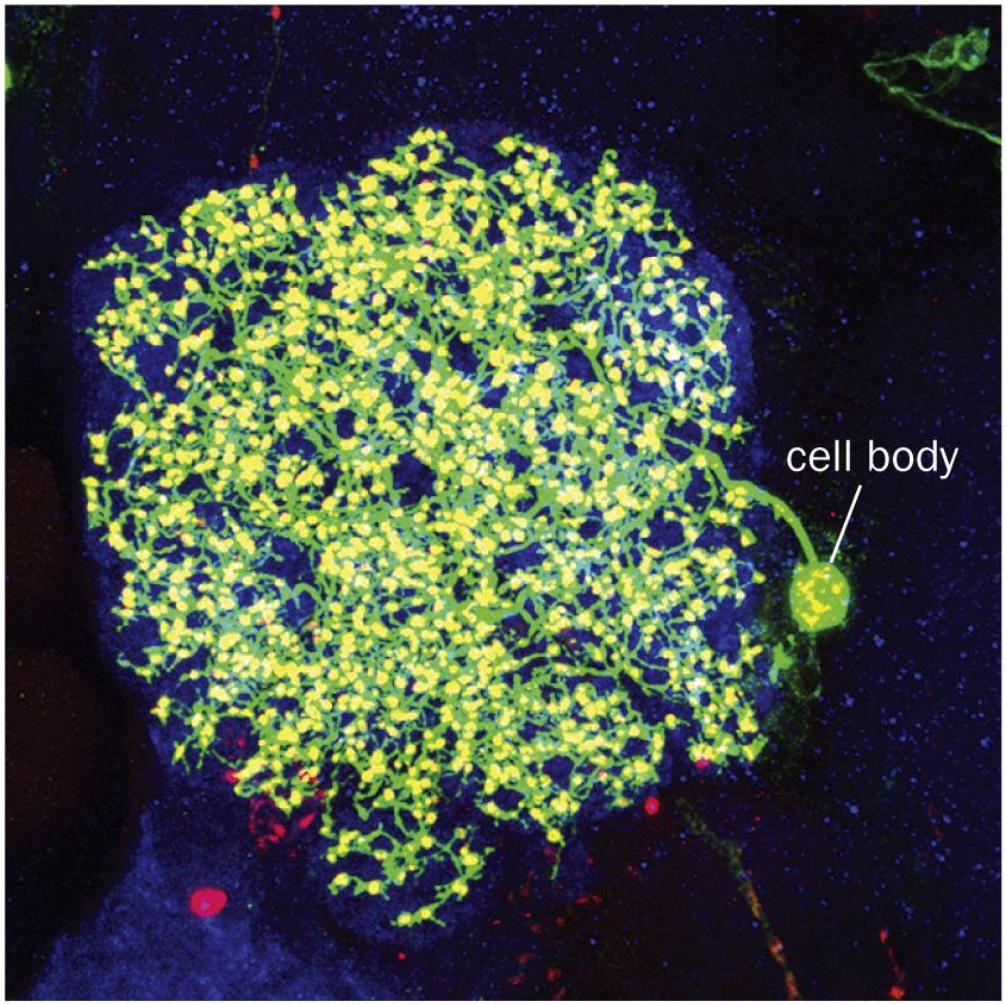

Figure 13-23c Principles of Neurobiology (© Garland Science 2016)

ANATOMICAL TECHNIQUES

基于解剖结构的技术

13.17 Fine structure studies can identify key facets of molecular organization within neurons

13.17 精细结构的研究可以验证神经元内分子组织的关键

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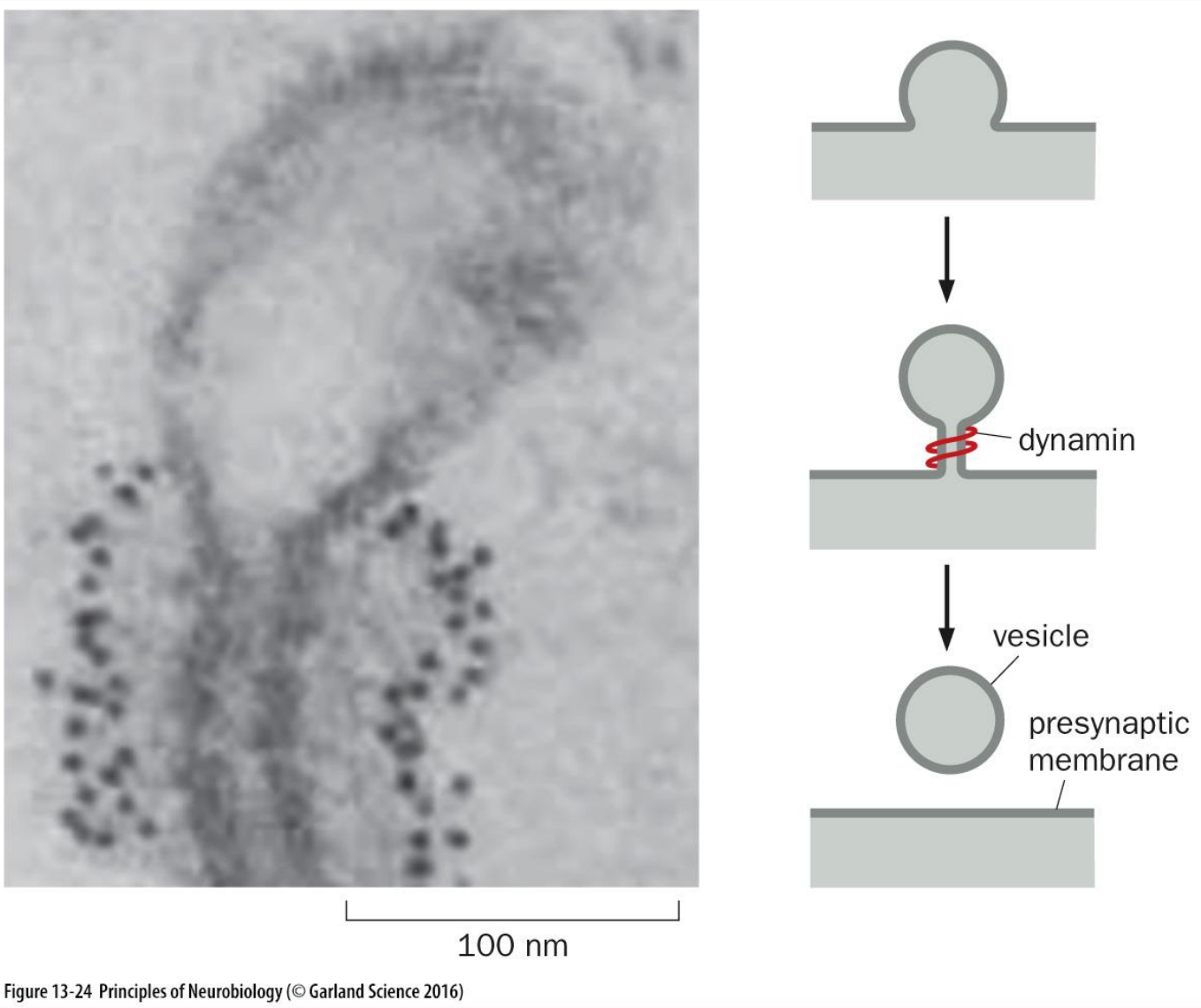

Figure 13-24 Principles of Neurobiology (© Garland Science 2016)

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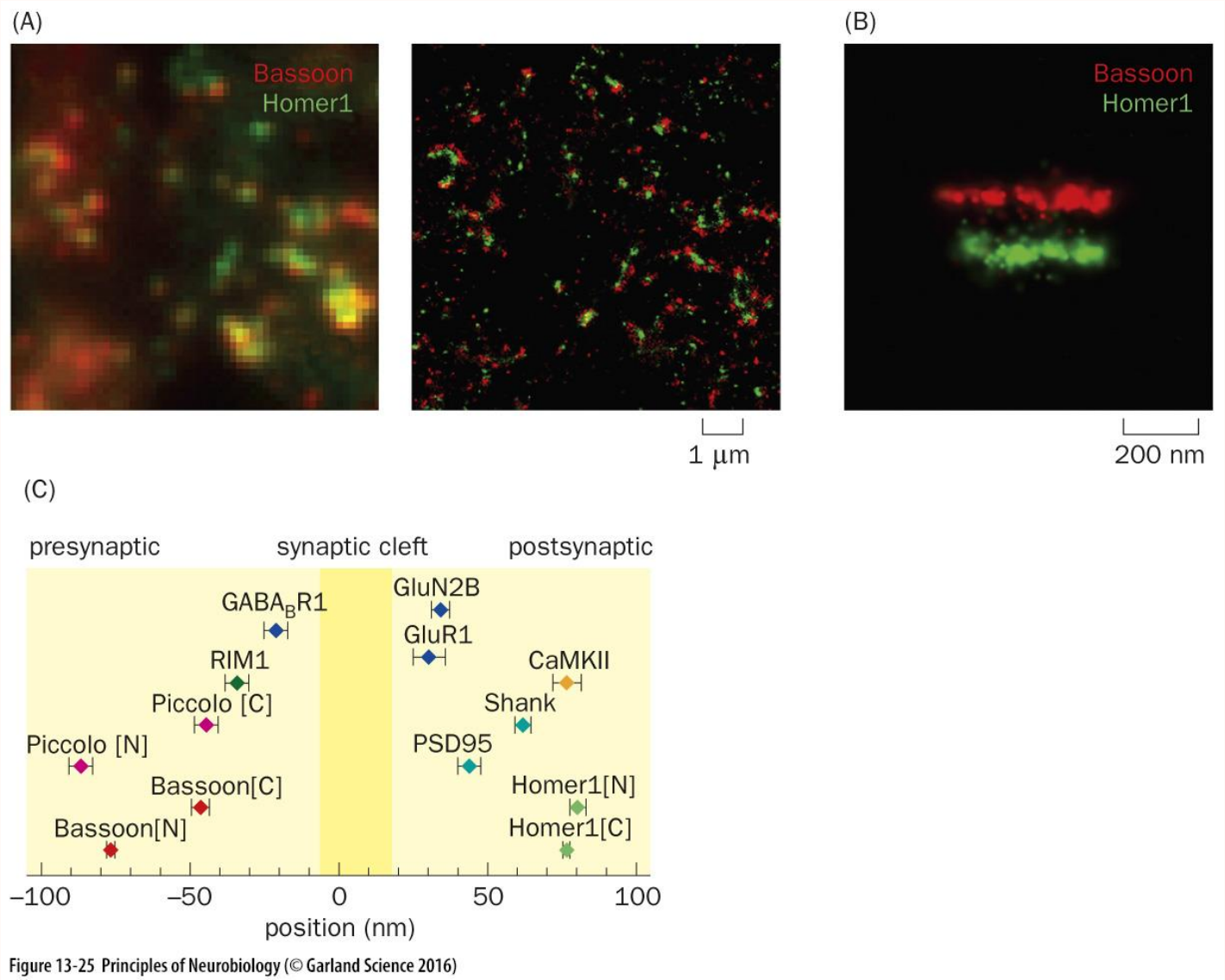

Figure 13-25 Principles of Neurobiology (© Garland Science 2016)

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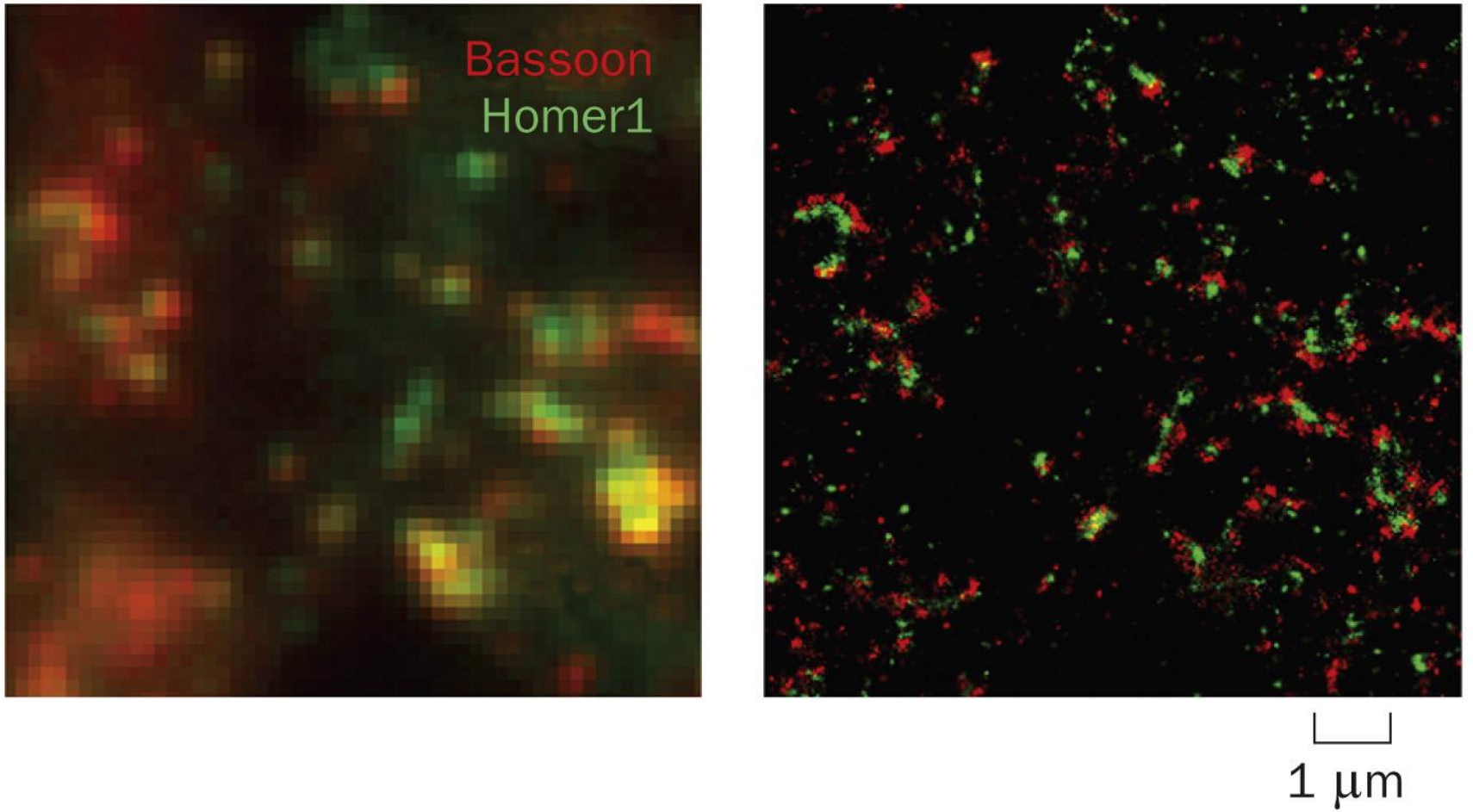

Figure 13-25a Principles of Neurobiology (© Garland Science 2016)

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Figure 13-25b Principles of Neurobiology (© Garland Science 2016)

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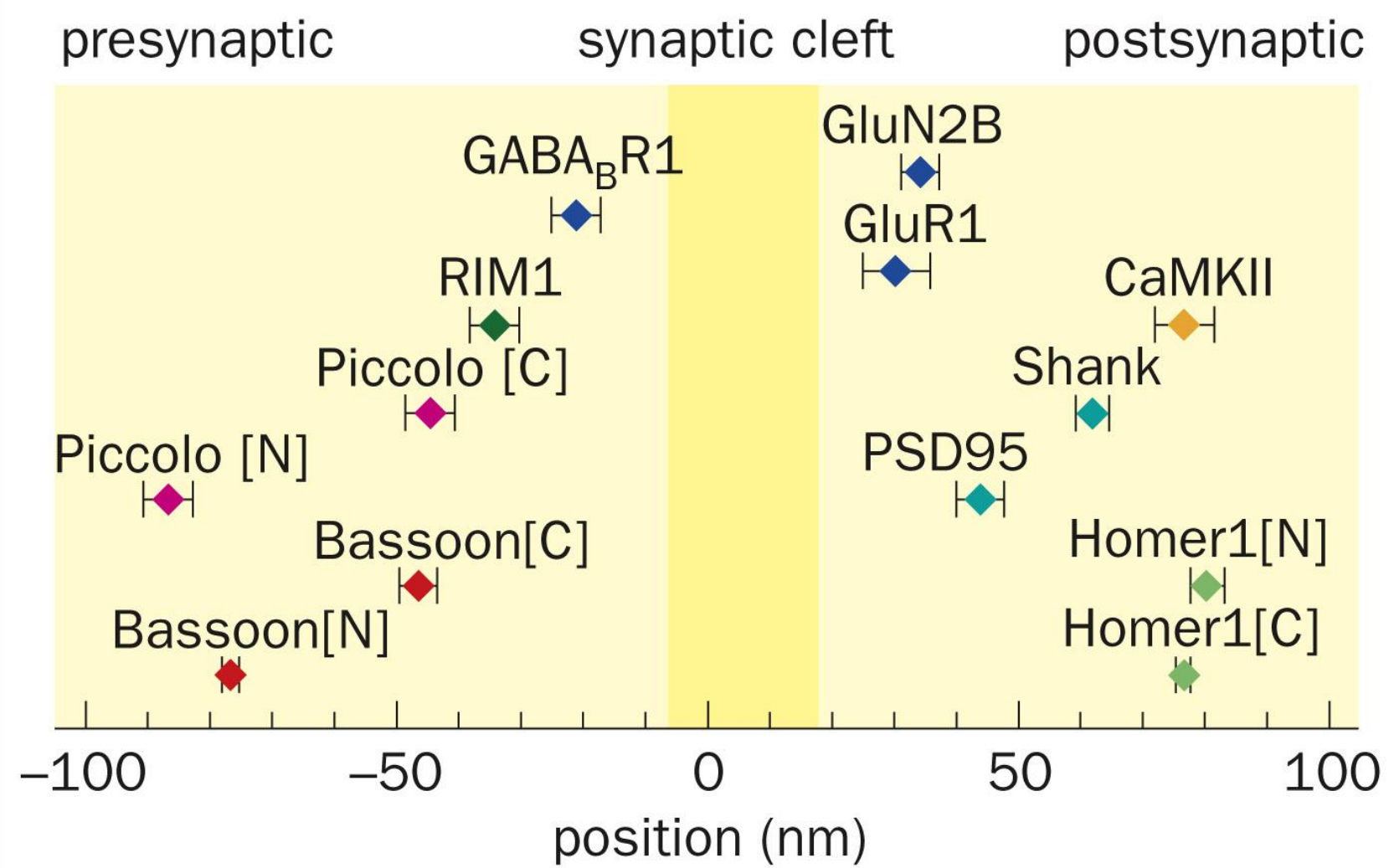

Figure 13-25c Principles of Neurobiology (© Garland Science 2016)

ANATOMICAL TECHNIQUES

基于解剖结构的技术

13.18 Mapping neuronal projections allows the tracking of information flow across different brain regions

13.18　了解神经投射可以追踪不同脑区的信息流动

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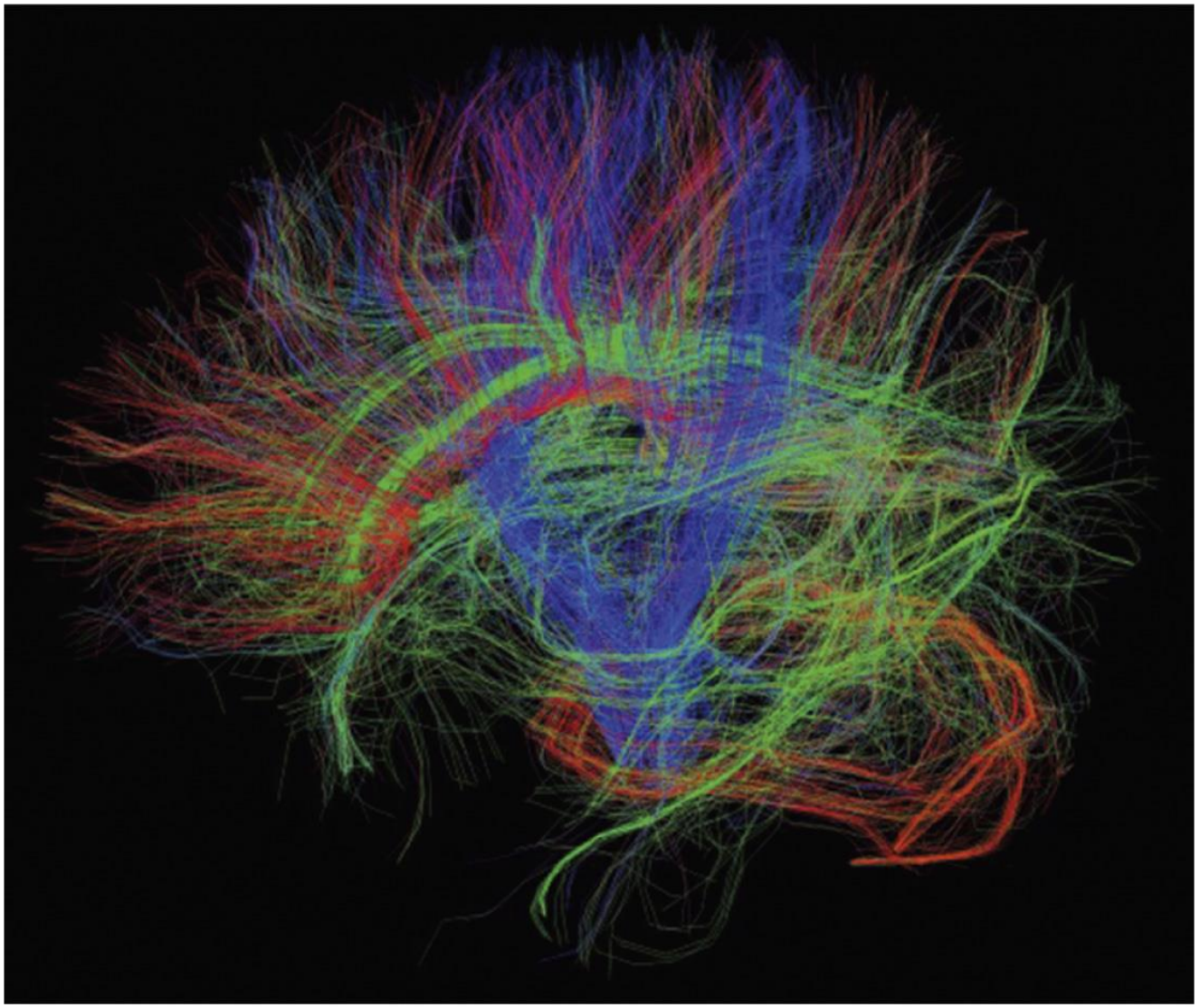

Figure 13-26 Principles of Neurobiology (© Garland Science 2016)

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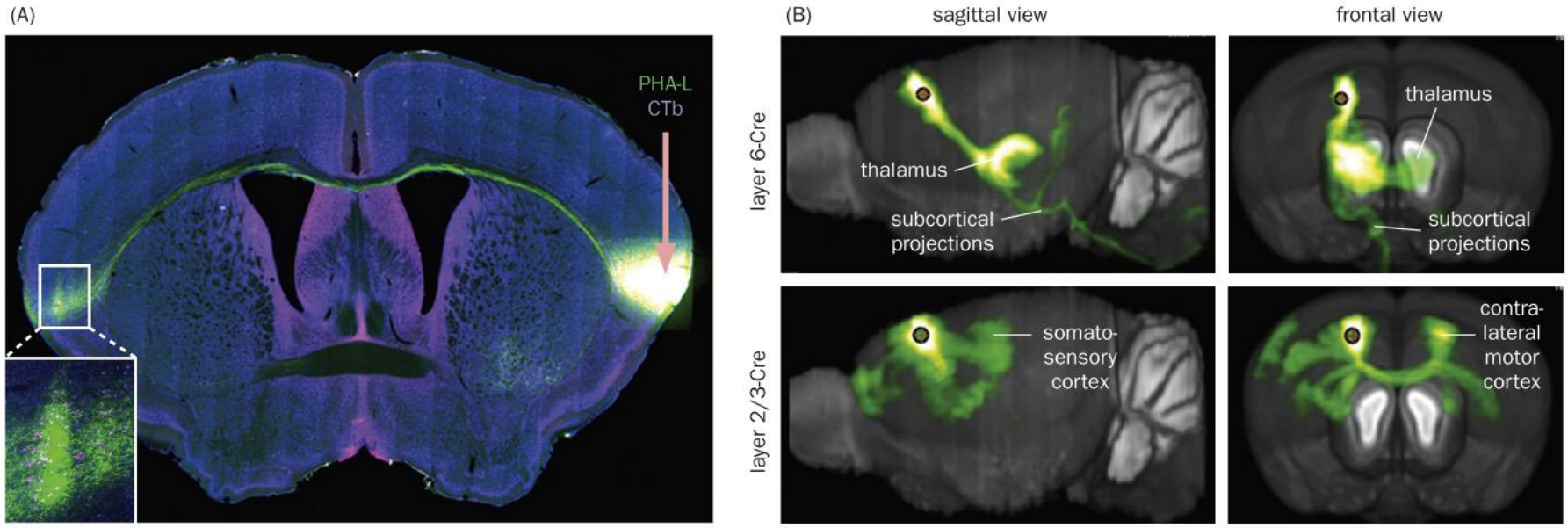

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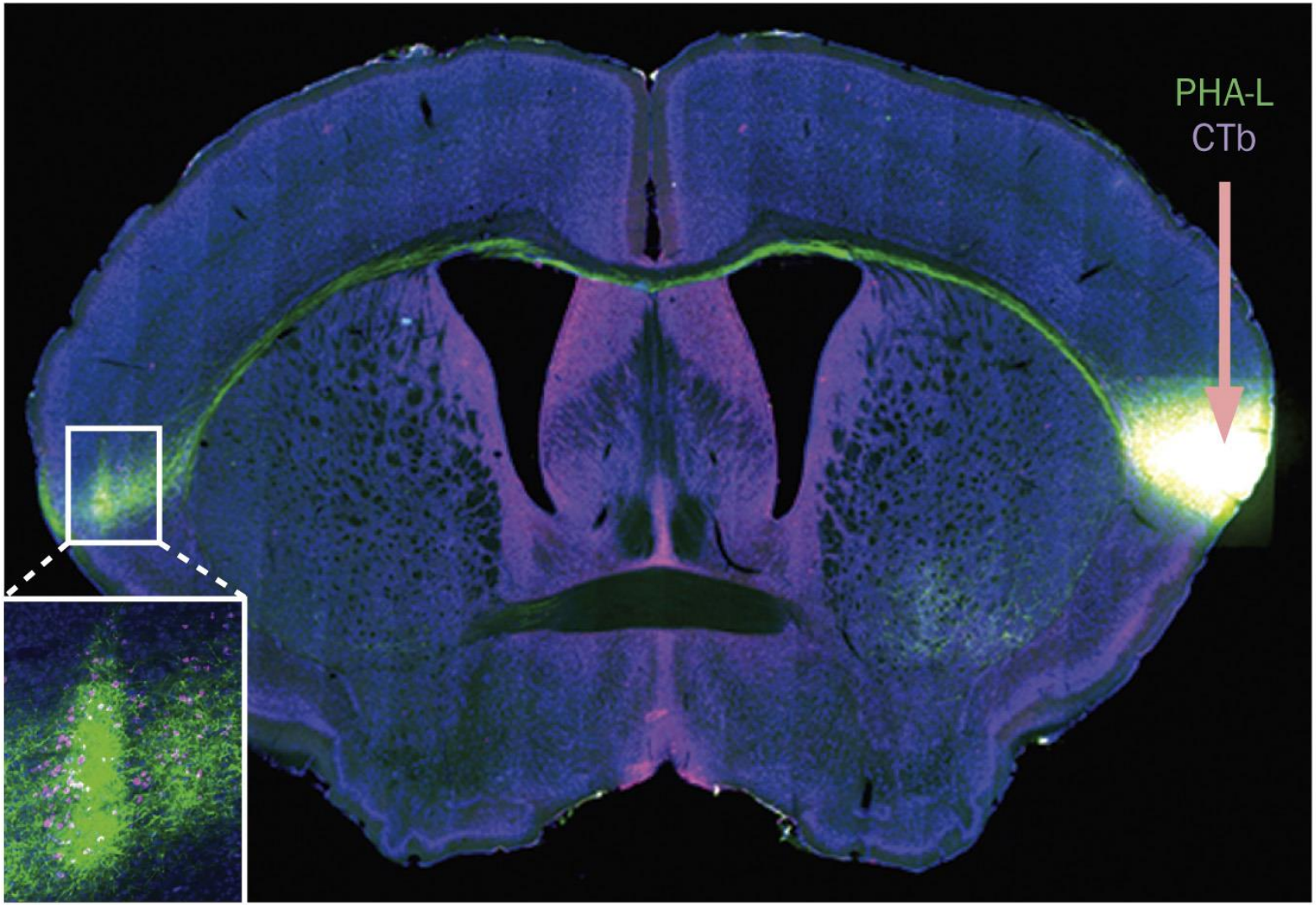

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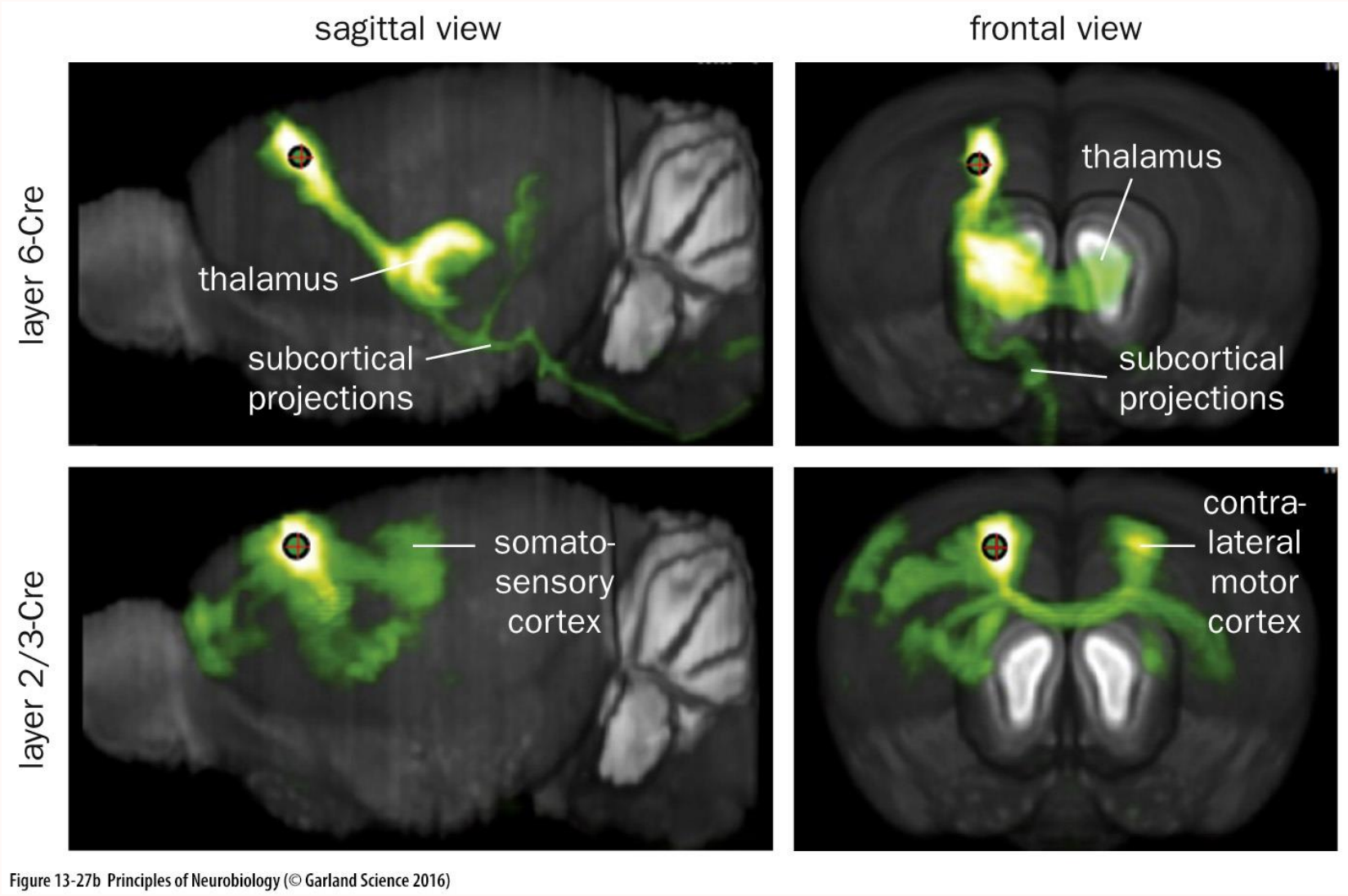

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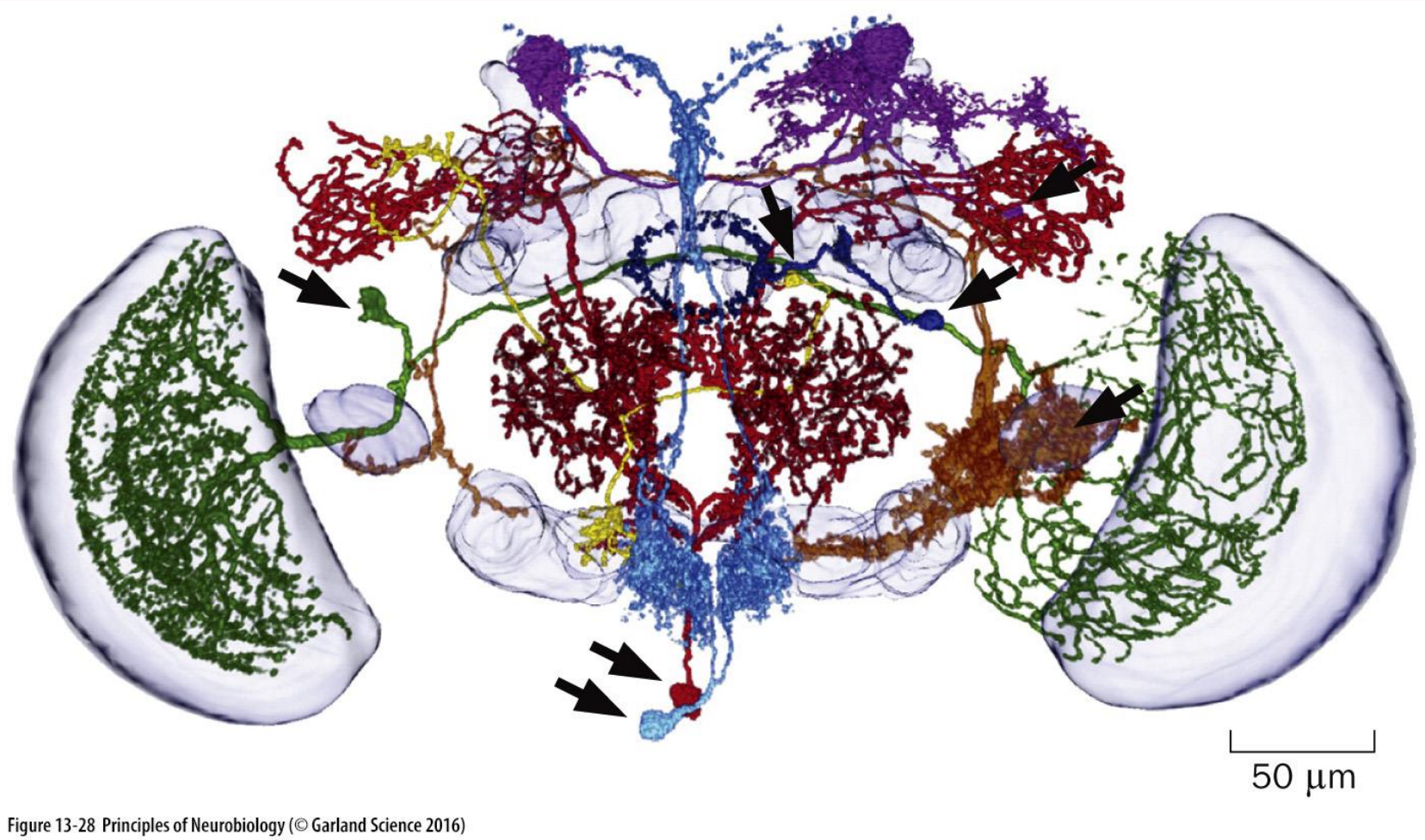

Figure 13-28 Principles of Neurobiology (© Garland Science 2016)

ANATOMICAL TECHNIQUES

基于解剖结构的技术

13.19 Mapping synaptic connections reveals neural circuitry

13.19 了解突触间连接可以揭示神经环路

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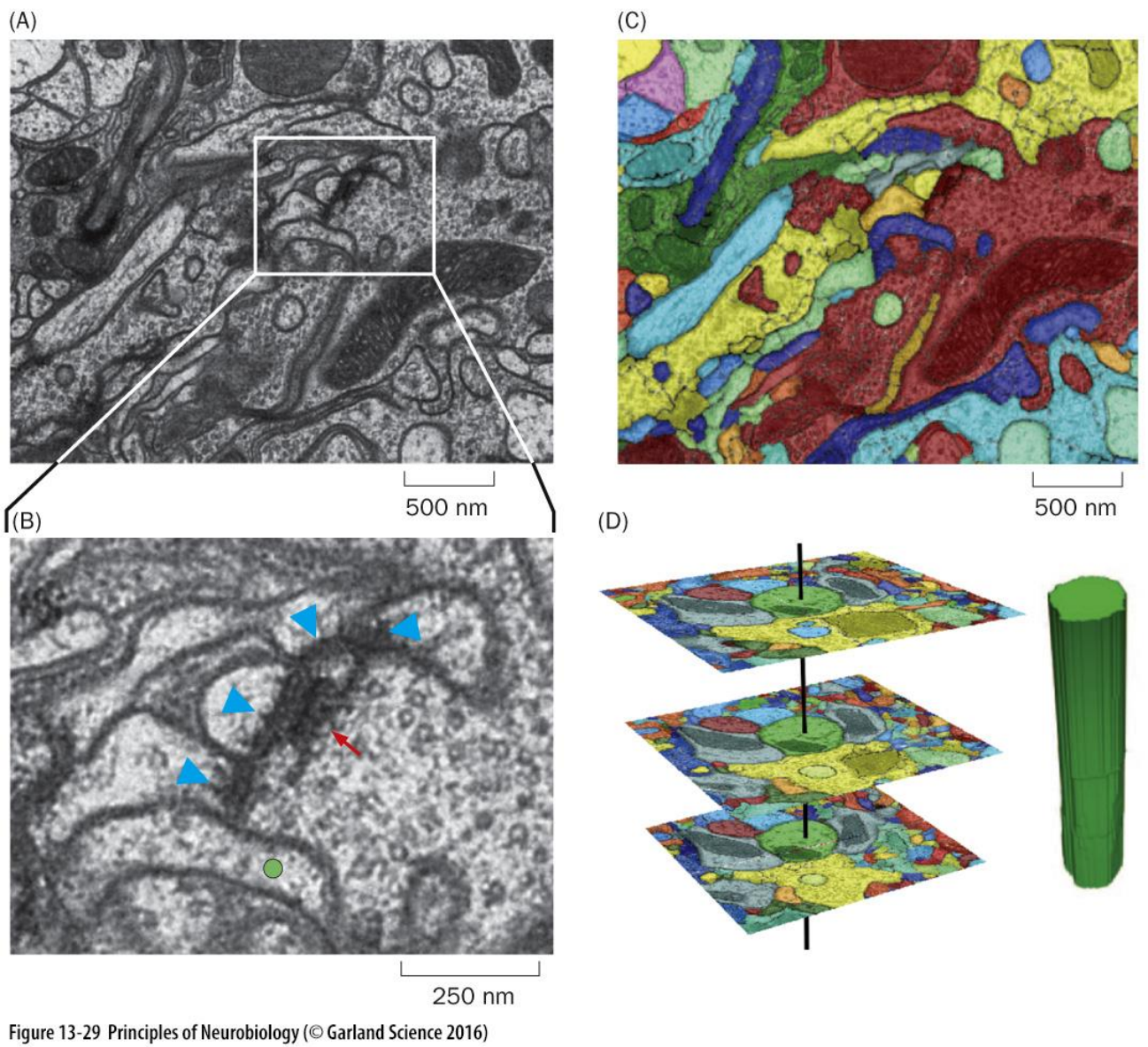

Figure 13-29 Principles of Neurobiology (© Garland Science 2016)

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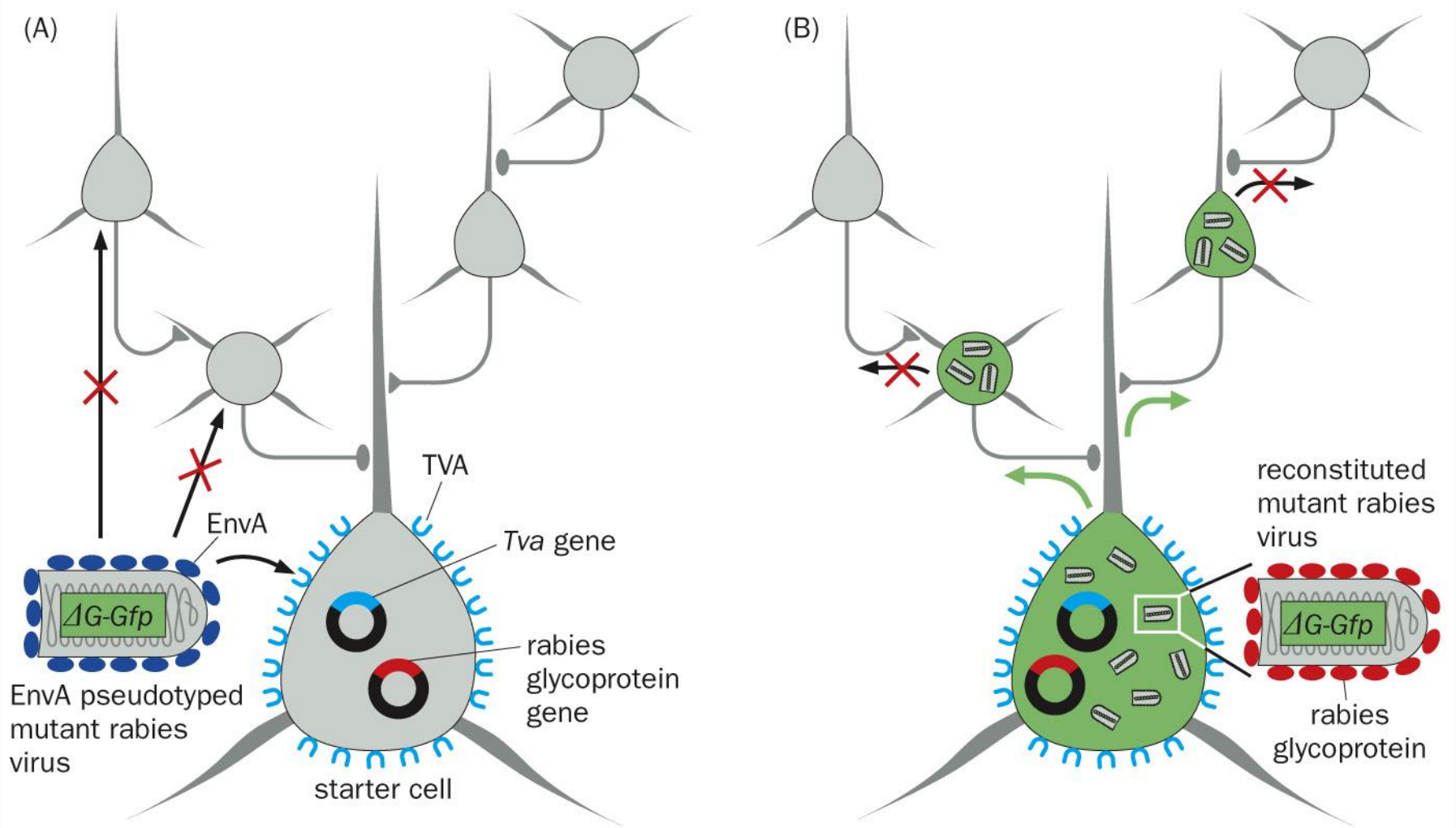

Figure 13-30 Principles of Neurobiology (© Garland Science 2016)

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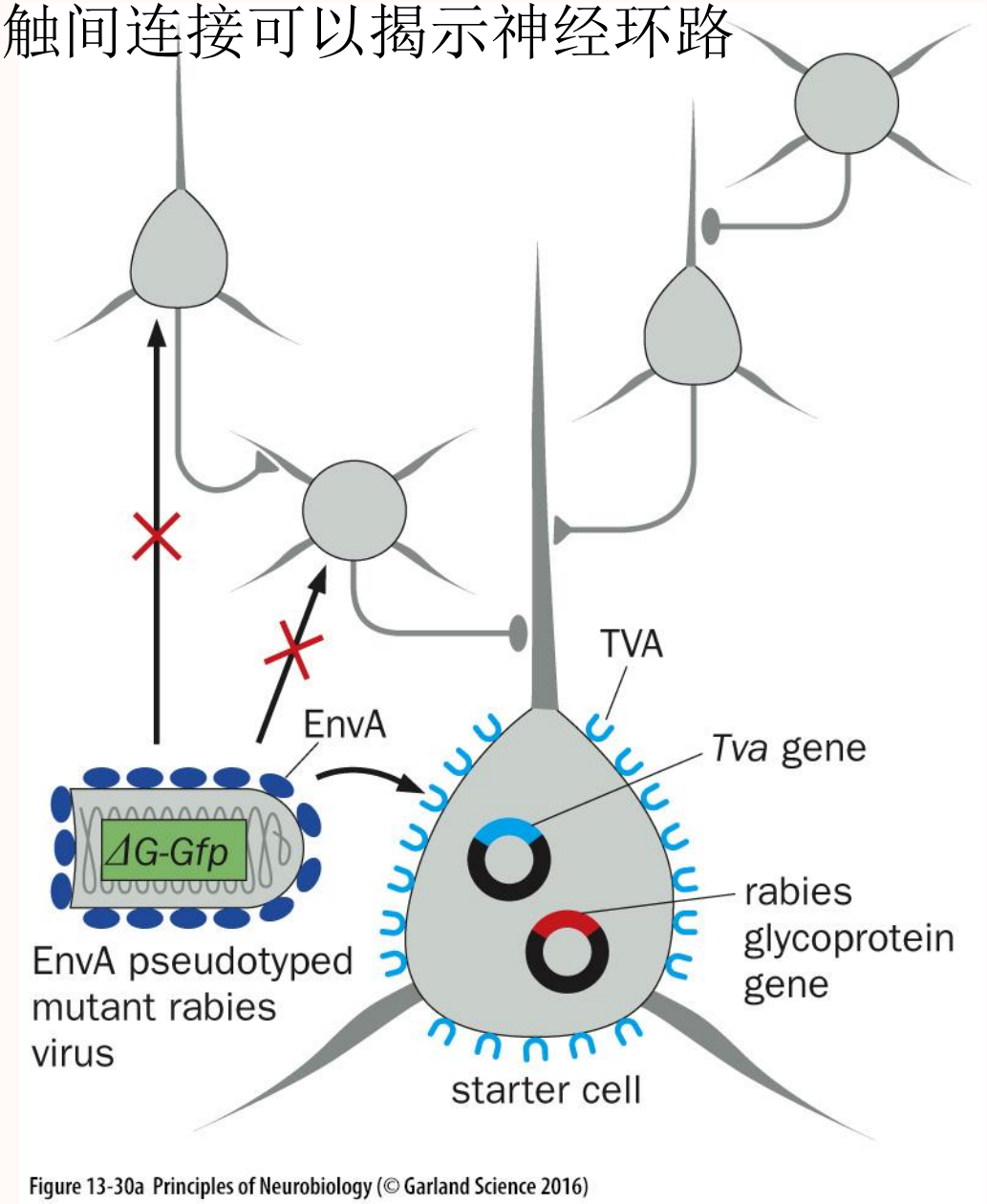

Figure 13-30a Principles of Neurobiology (© Garland Science 2016)

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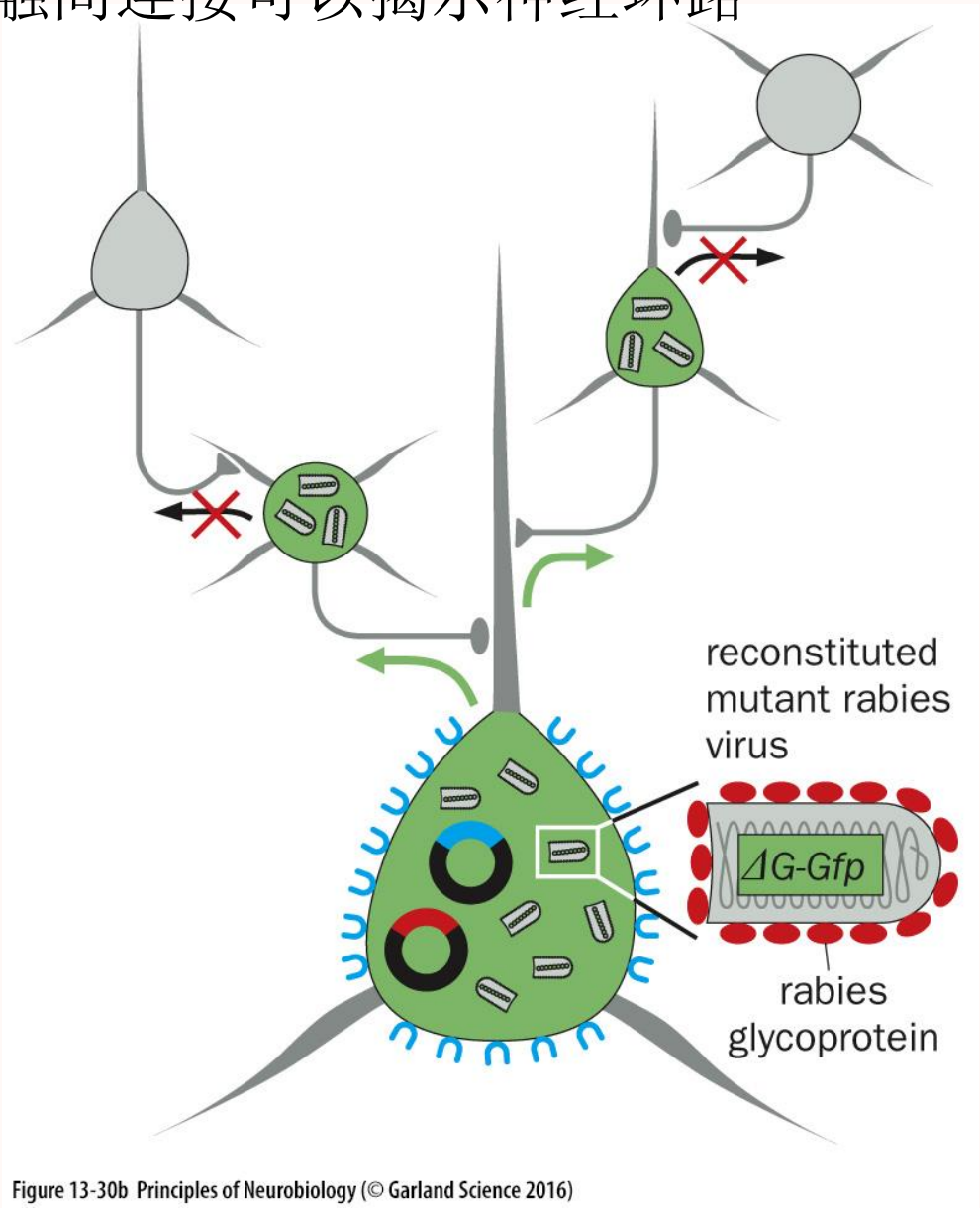

Figure 13-30b Principles of Neurobiology (© Garland Science 2016)

RECORDING AND MANIPULATING NEURONAL ACTIVITY

记录和操控神经活动

13.20 Extracellular recordings can detect the firing of individual neurons

13.21 Intracellular and whole-cell patch recordings can measure synaptic input in addition to firing patterns

13.22 Optical imaging can measure the activity of many neurons simultaneously

13.23 Neuronal inactivation can be used to reveal which neurons are essential for circuit function and behavior

13.20 利用细胞外记录方法检测单个神经元的发放
13.21 利用细胞内记录和全细胞膜片钳记录检测突触输入和神经元发放
13.22 光学成像方法可以同时监测多个神经元共同的活动
13.23 失活神经元来揭示对于神经环路功能和行为重要的神经元

13.24 Neuronal activation can establish sufficiency of neuronal activity in circuit function and behavior

13.25 Optogenetics allows control of the activity of genetically targeted neurons with millisecond precision

13.26 Synaptic connections can be mapped by physiological and optogenetic methods

13.24 激活神经元可以产生足够的能引起神经环路功能和行的神经活动

13.25 光遗传学可以在毫秒级时间内控制特定遗传编码的神经元

13.26 利用生理学和光遗传学方法了解突触间连接

RECORDING AND MANIPULATING NEURONAL ACTIVITY

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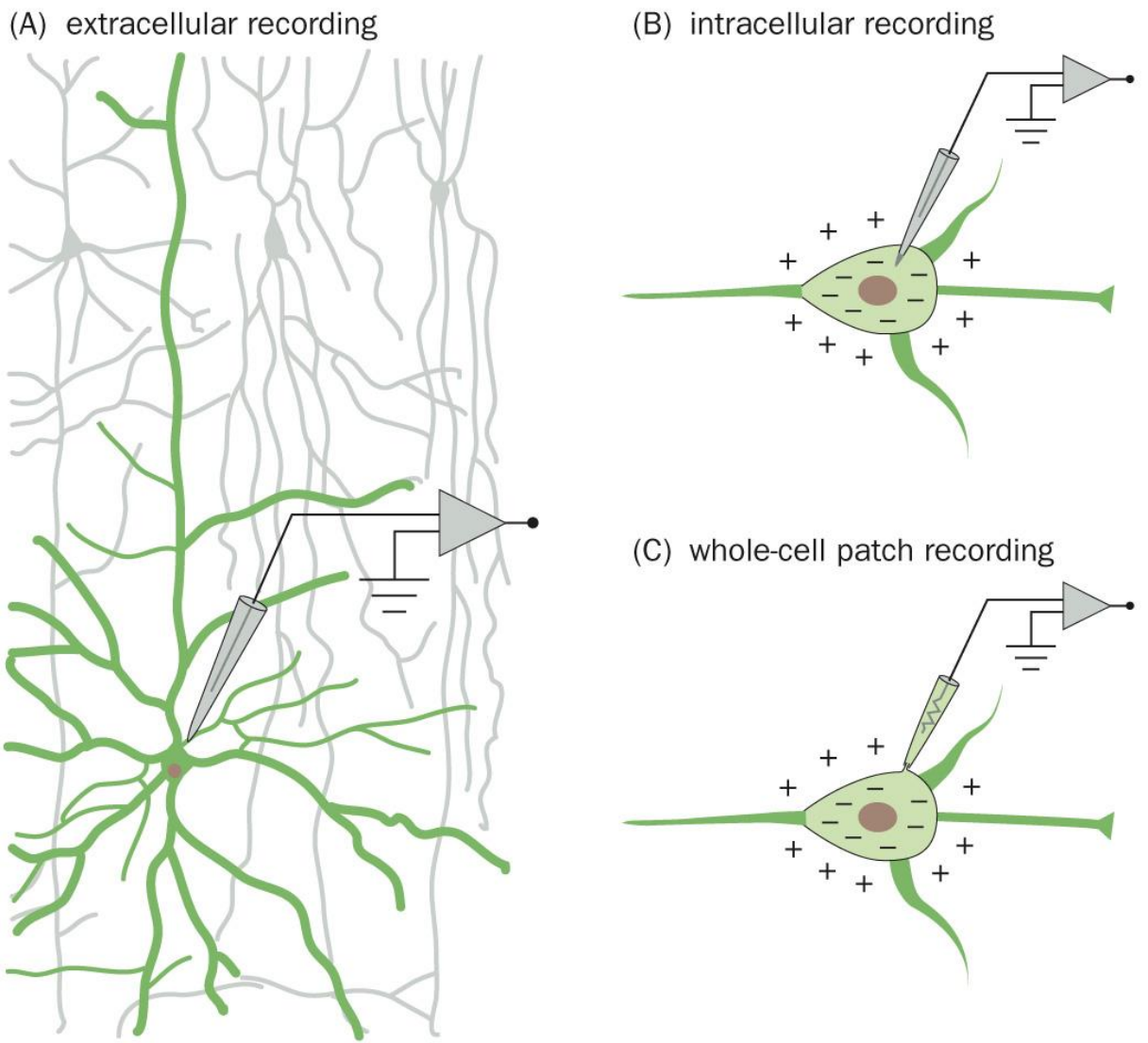

Figure 13-31 Principles of Neurobiology (© Garland Science 2016)

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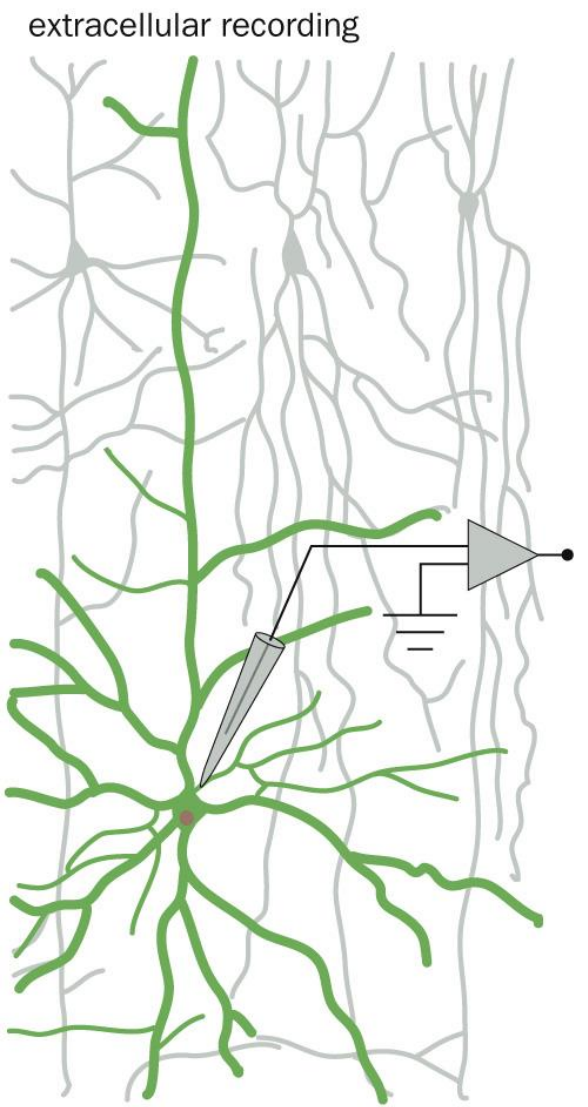

Figure 13-31a Principles of Neurobiology (© Garland Science 2016)

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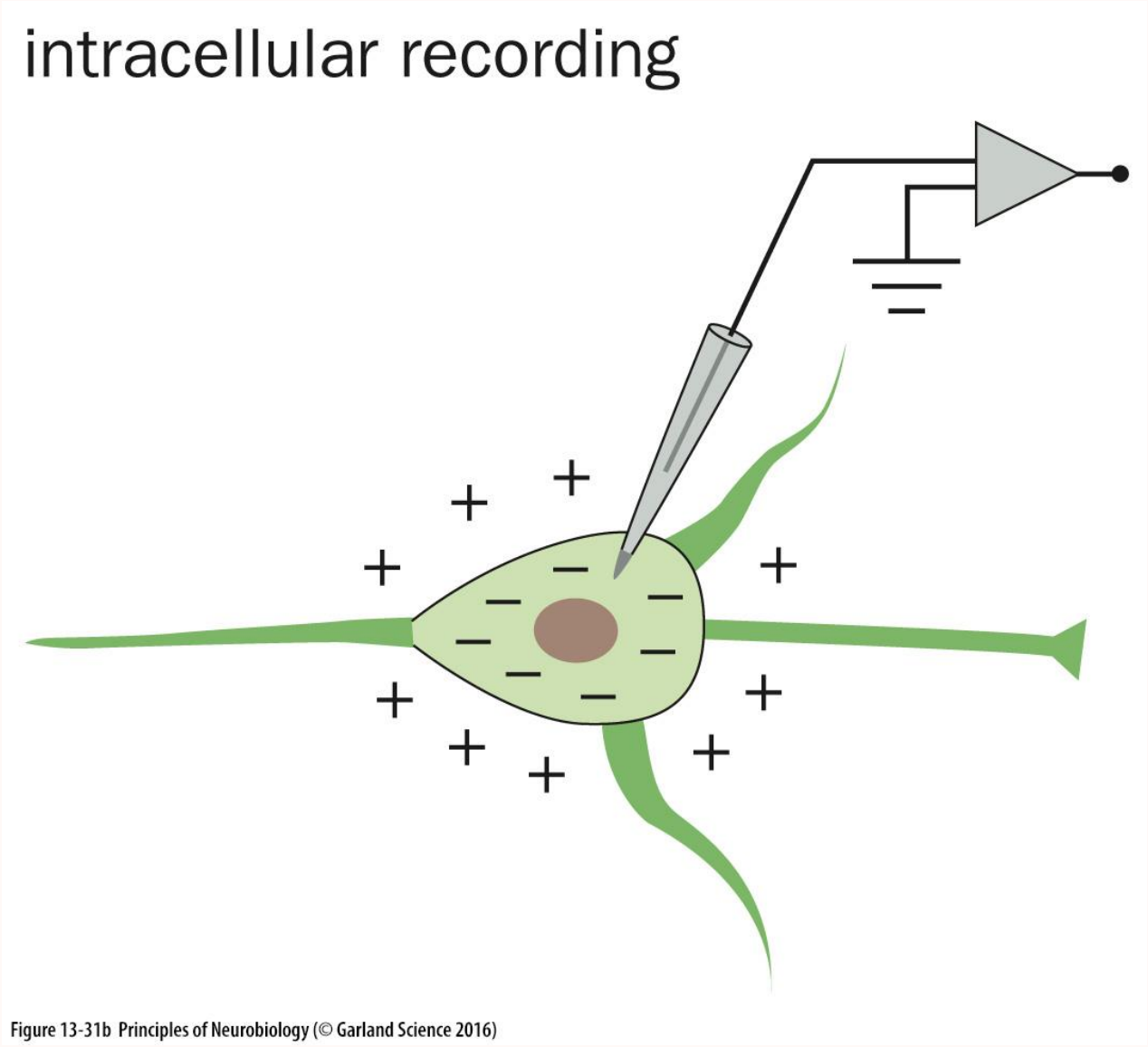

Figure 13-31b Principles of Neurobiology (© Garland Science 2016)

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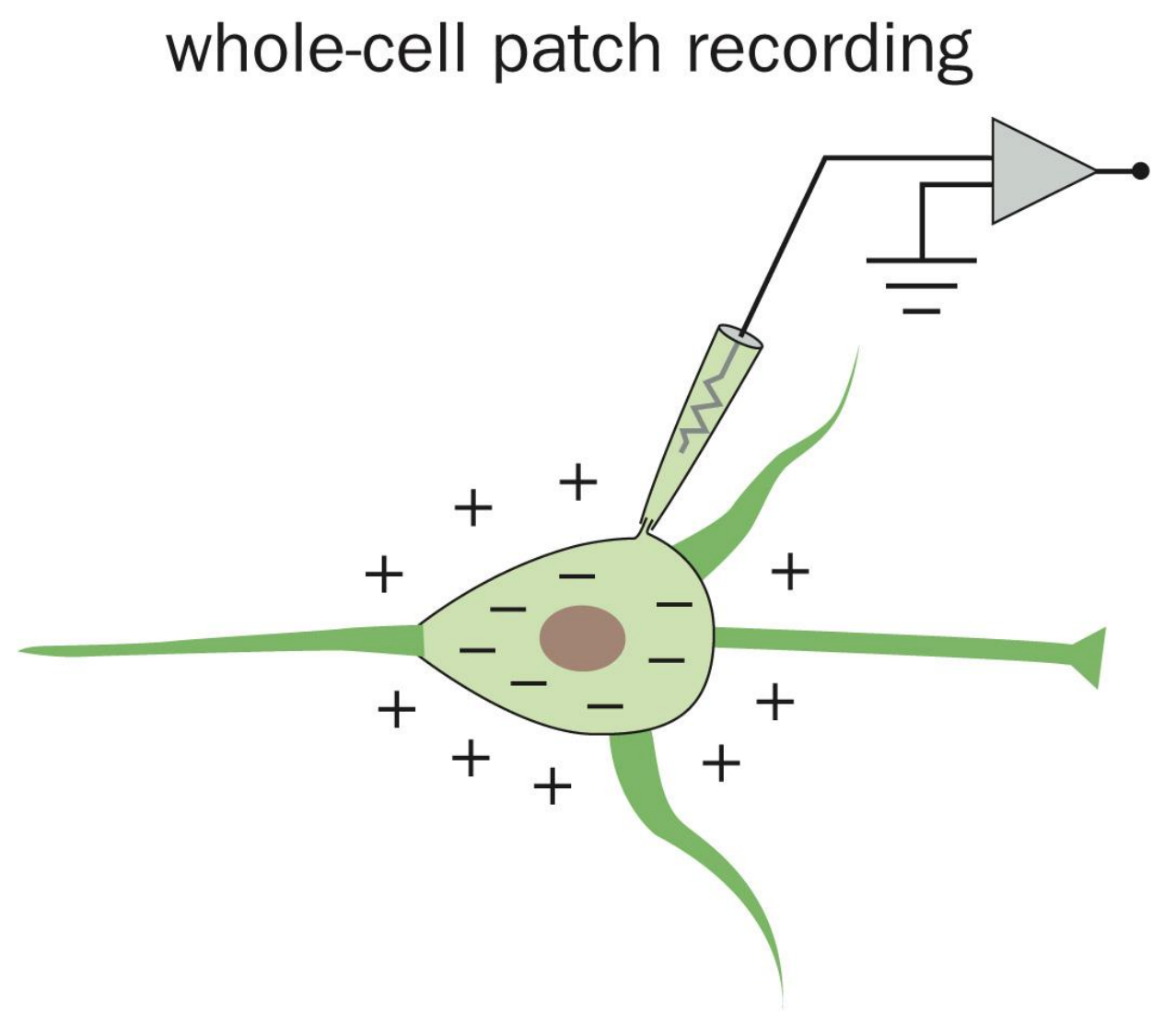

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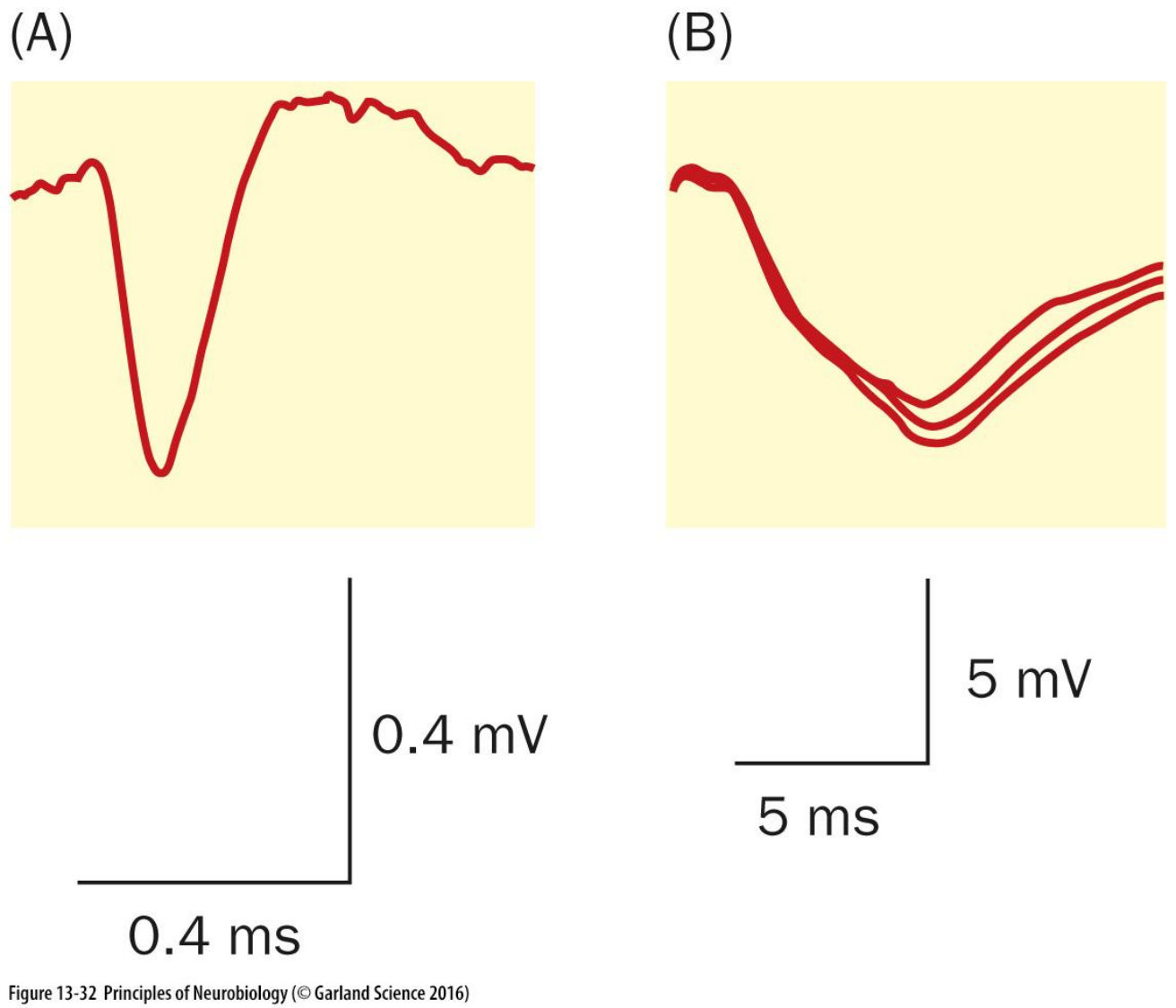

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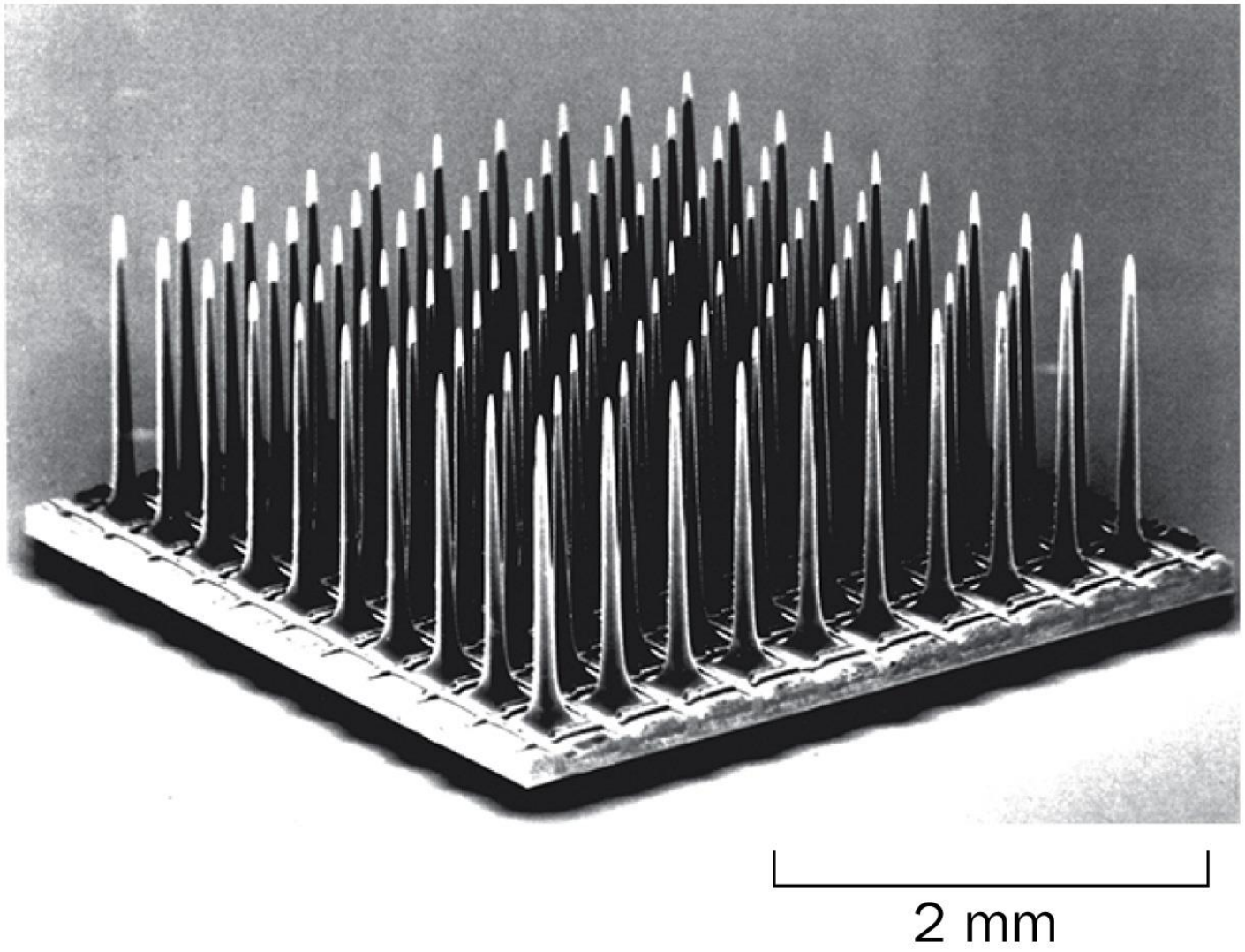

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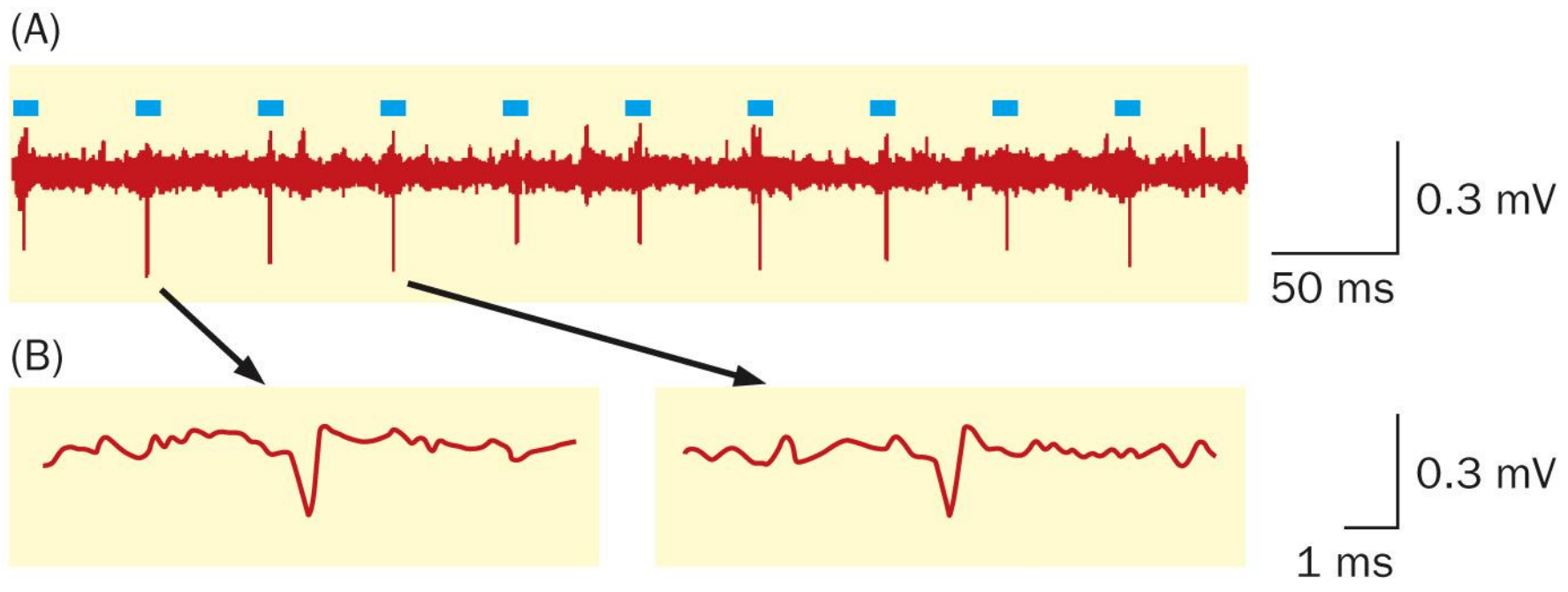

Figure 13-34 Principles of Neurobiology (© Garland Science 2016)

RECORDING AND MANIPULATING NEURONAL ACTIVITY

记录和操控神经活动

13.21 Intracellular and whole-cell patch recordings can measure synaptic input in addition to firing patterns

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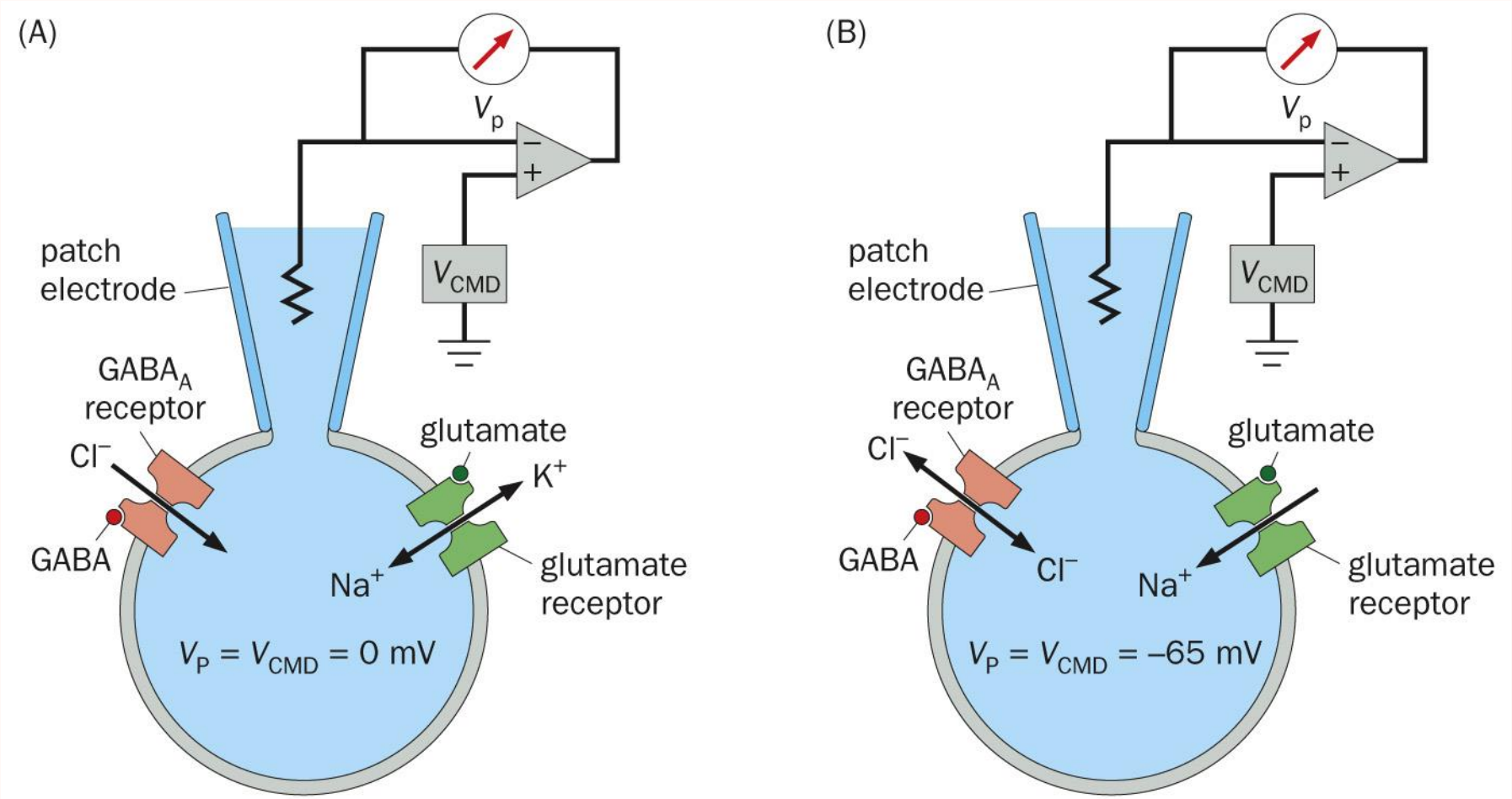

Figure 13-35 Principles of Neurobiology (© Garland Science 2016)

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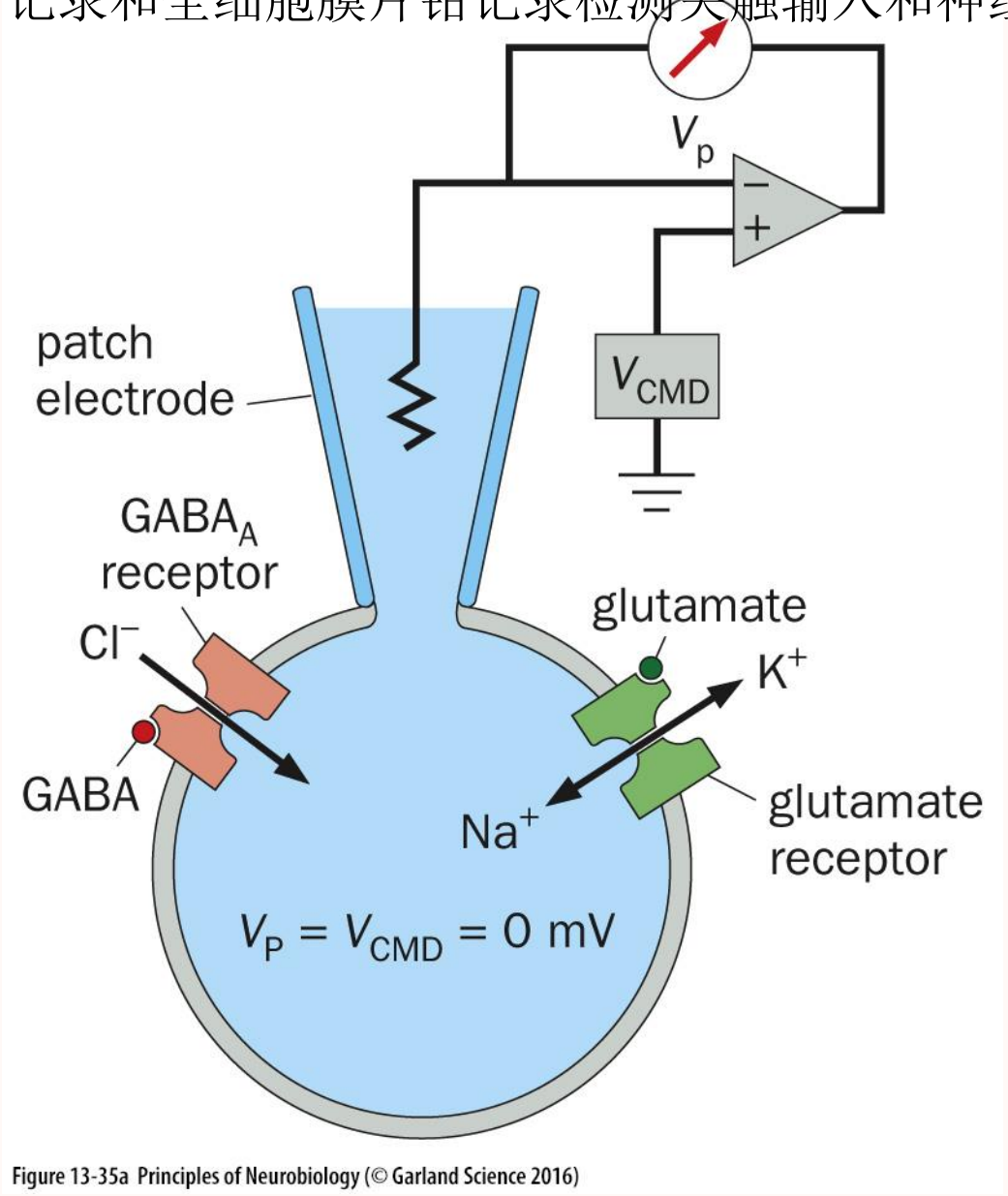

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13.21 Intracellular and whole-cell patch recordings can measure synaptic input in addition to firing patterns

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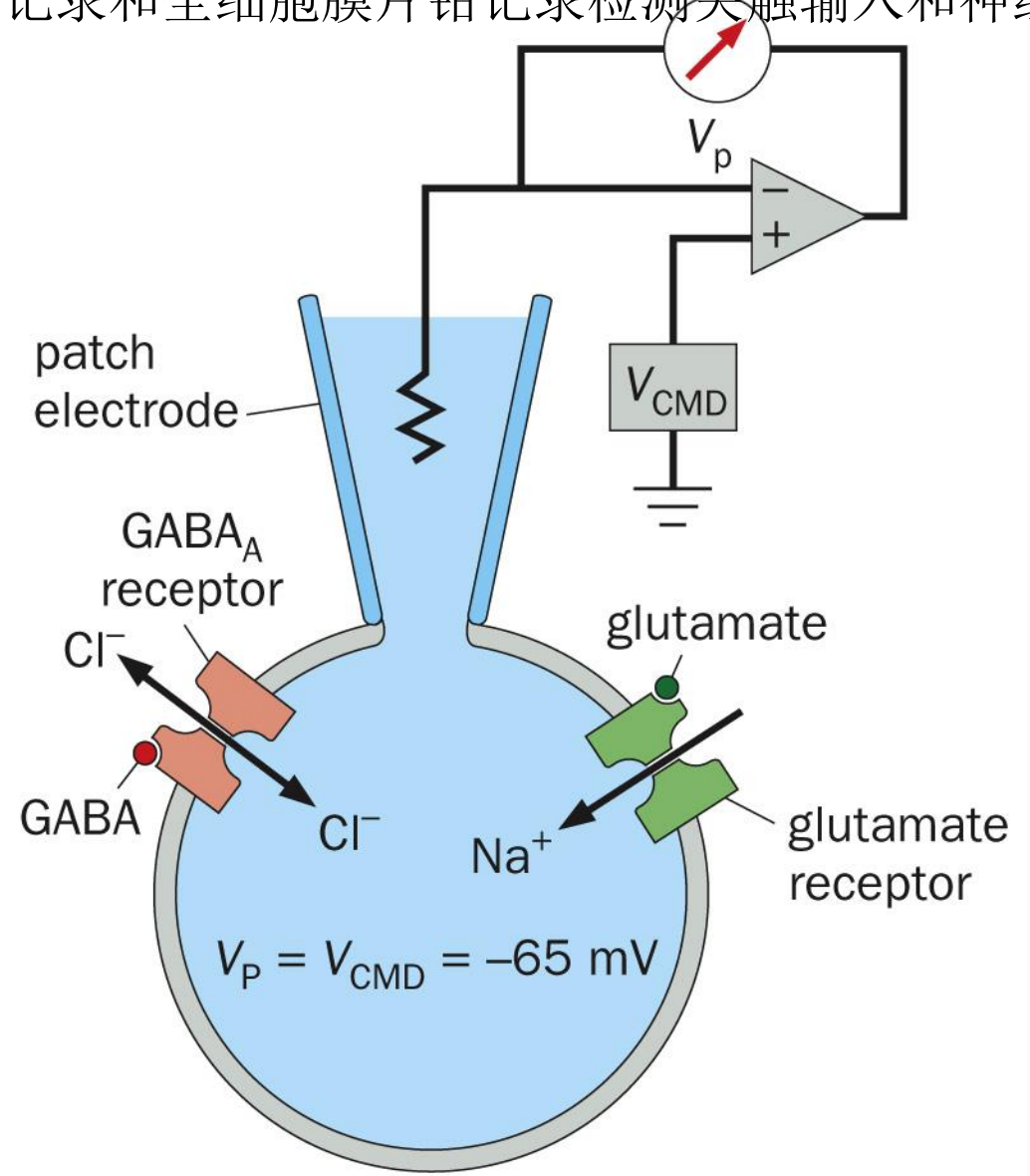

Figure 13-35b Principles of Neurobiology (© Garland Science 2016)

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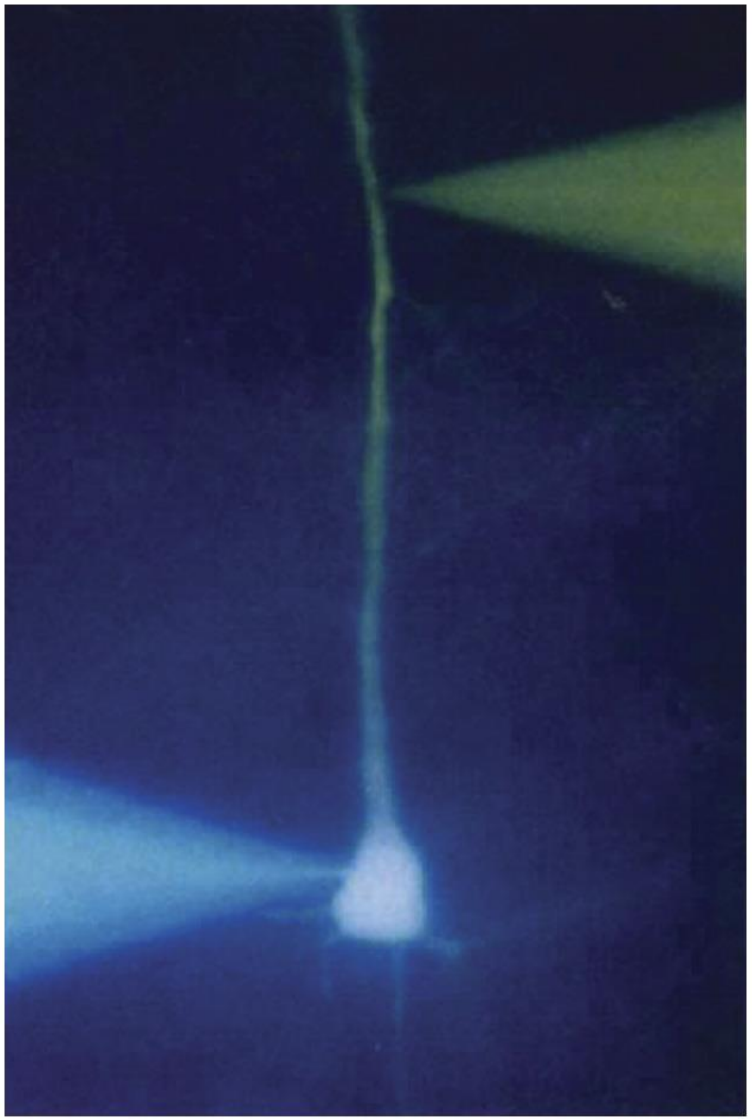

Figure 13-36 Principles of Neurobiology (© Garland Science 2016)

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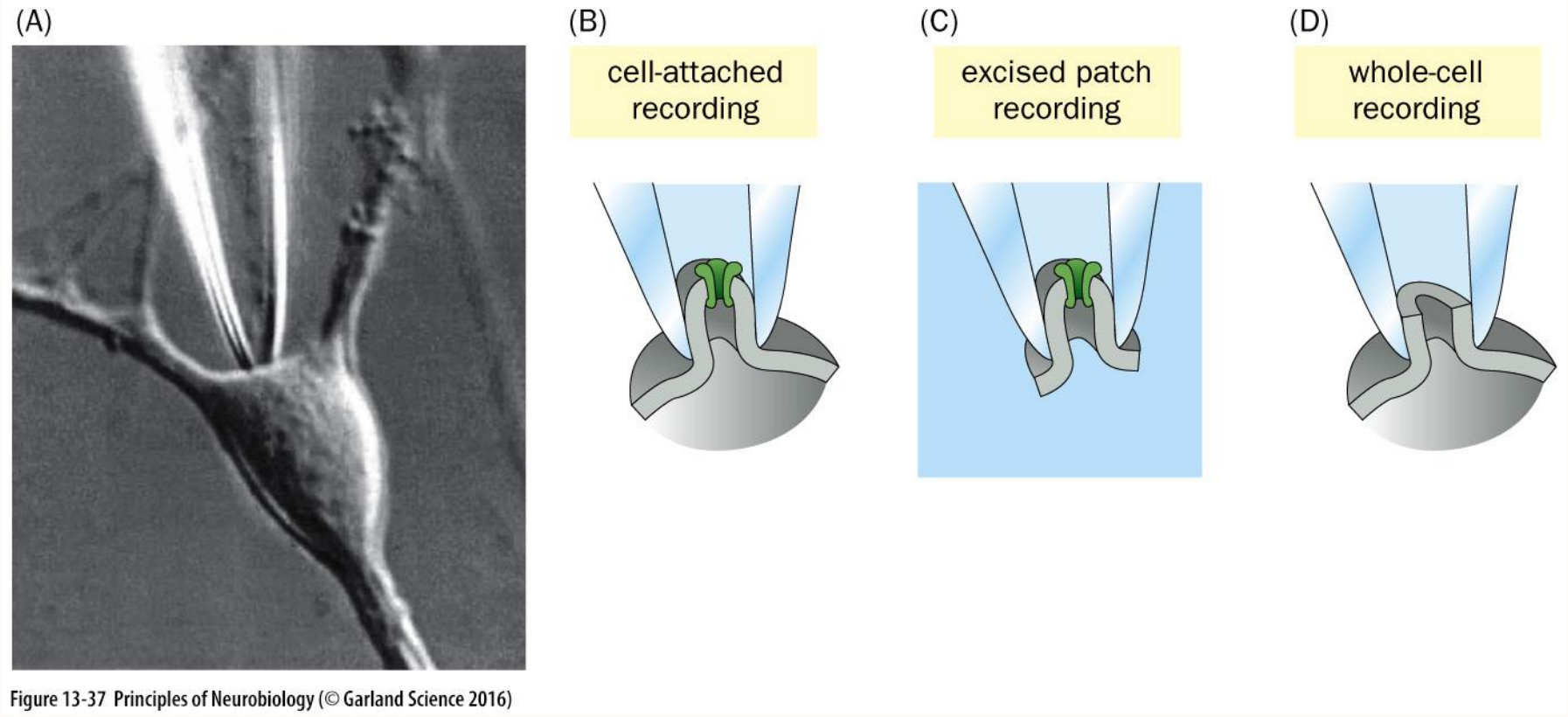

Figure 13-37 Principles of Neurobiology (© Garland Science 2016)

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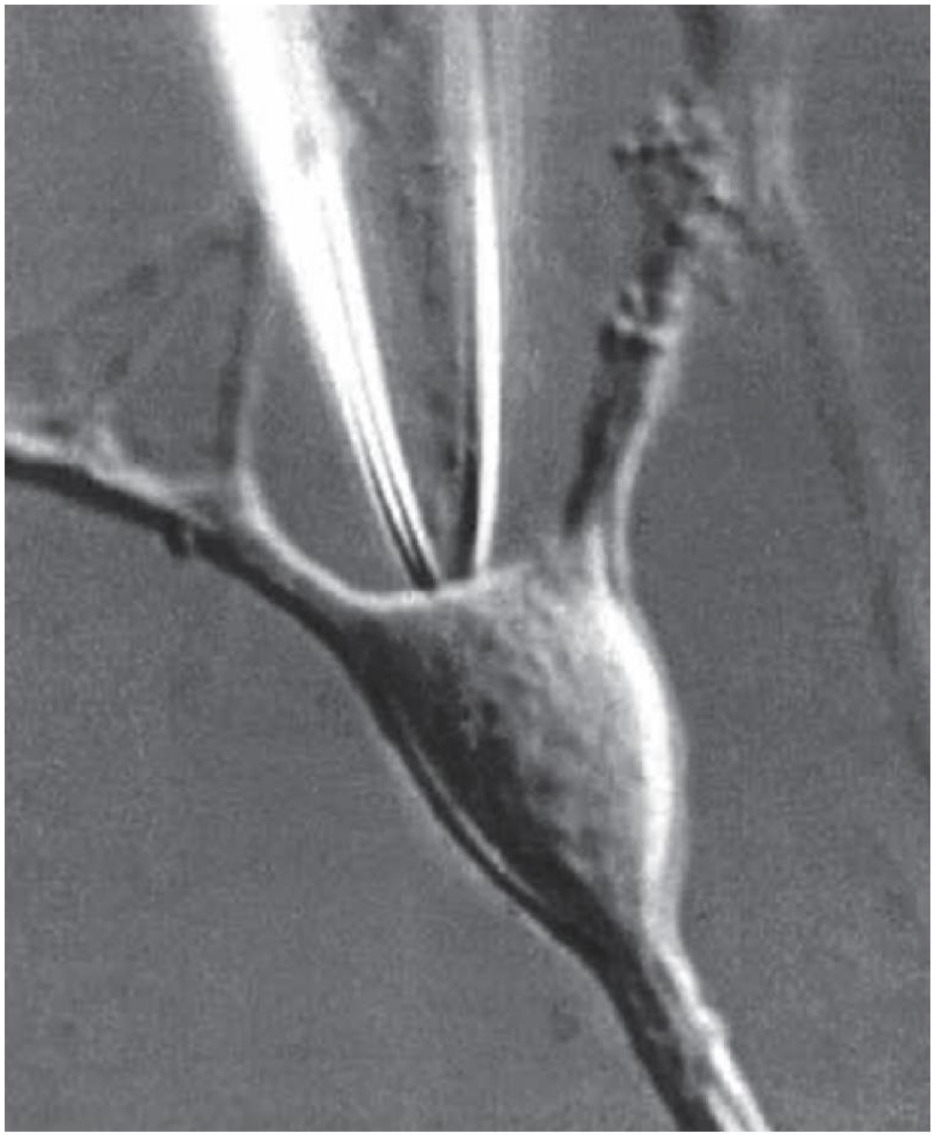

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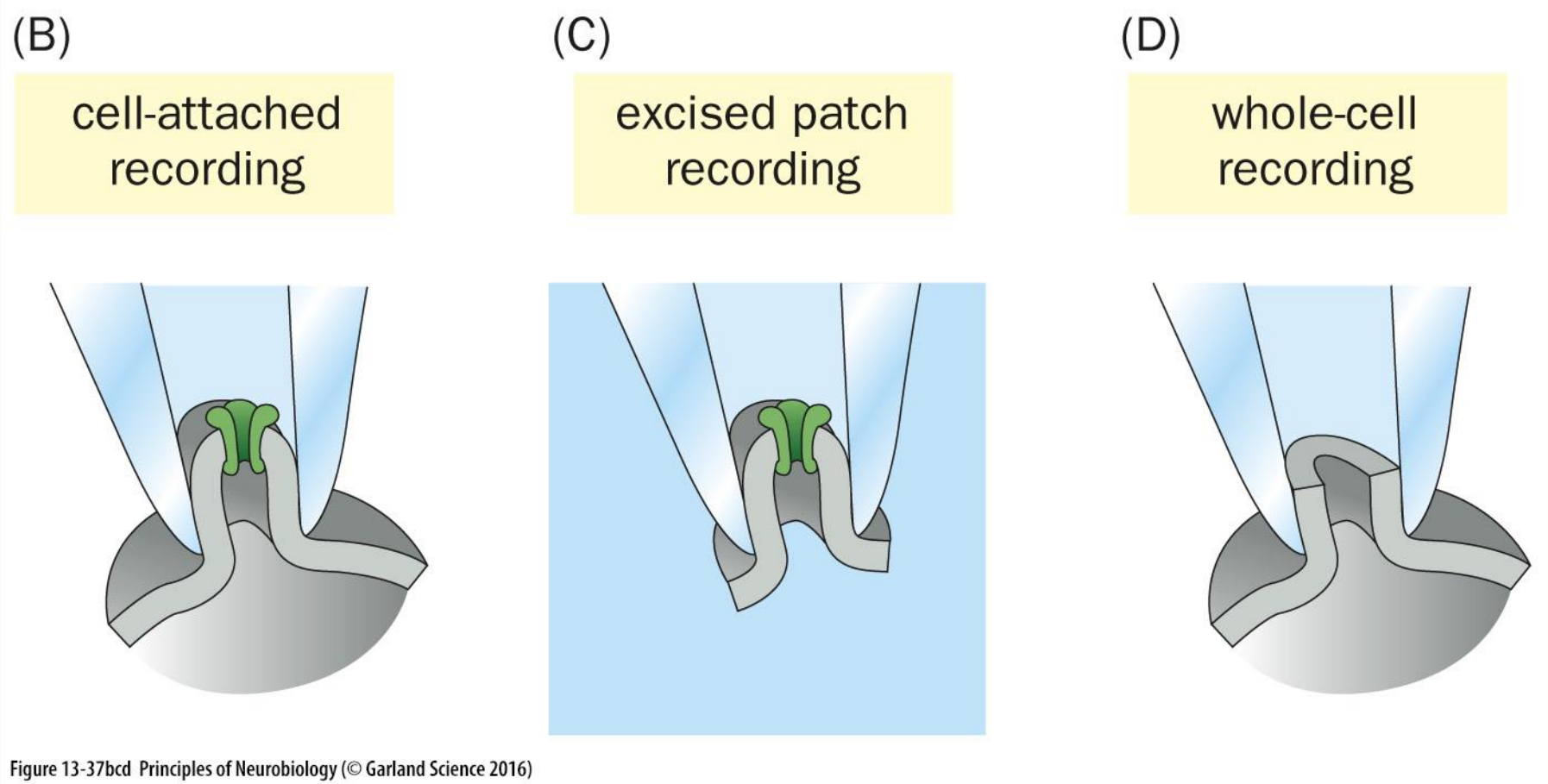

Figure 13-37bcd Principles of Neurobiology (© Garland Science 2016)

RECORDING AND MANIPULATING NEURONAL ACTIVITY

记录和操控神经活动

13.22 Optical imaging can measure the activity of many neurons simultaneously

13.22 光学成像方法可以同时监测多个神经元共同的活动

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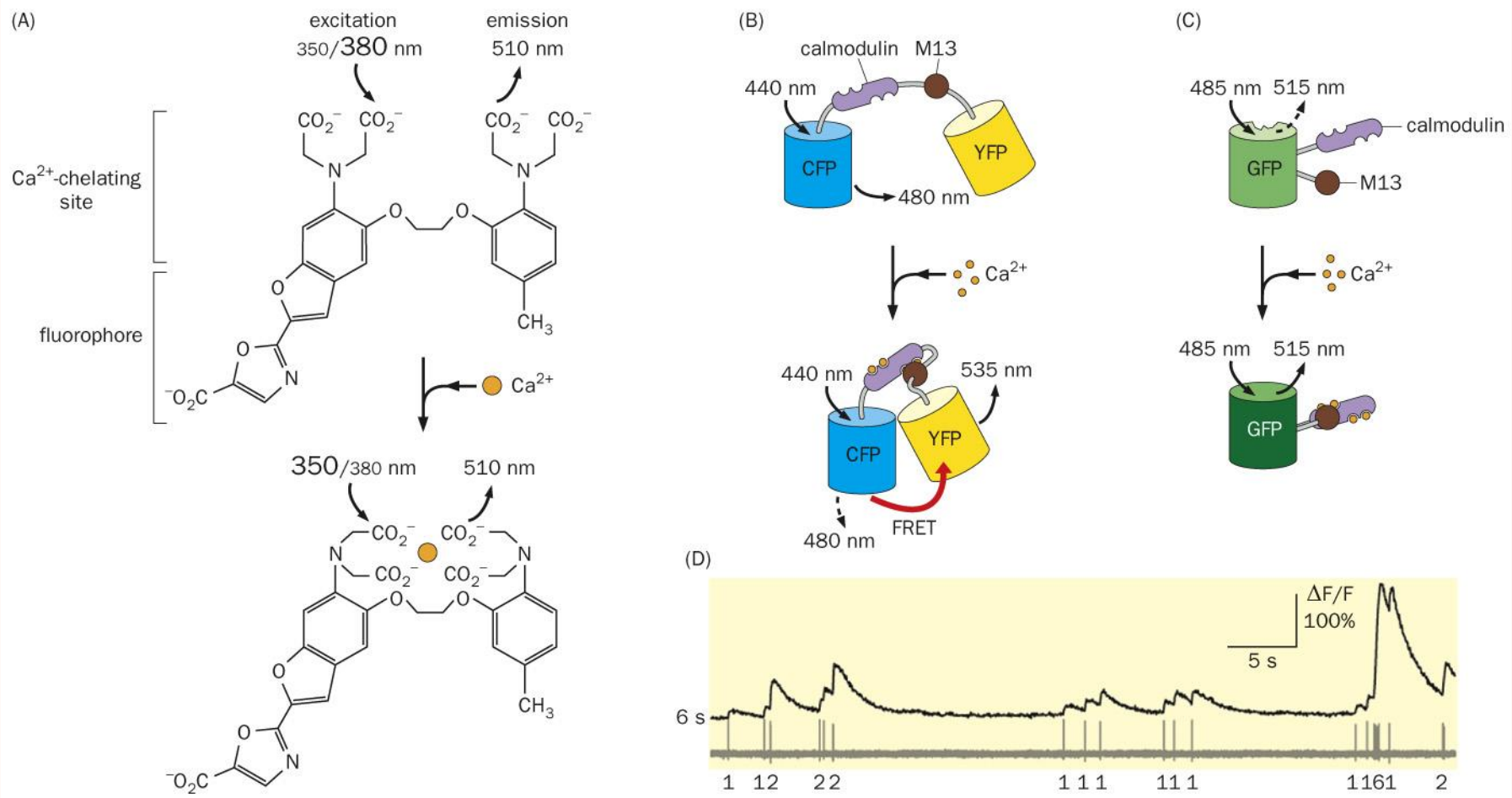

Figure 13-38 Principles of Neurobiology (© Garland Science 2016)

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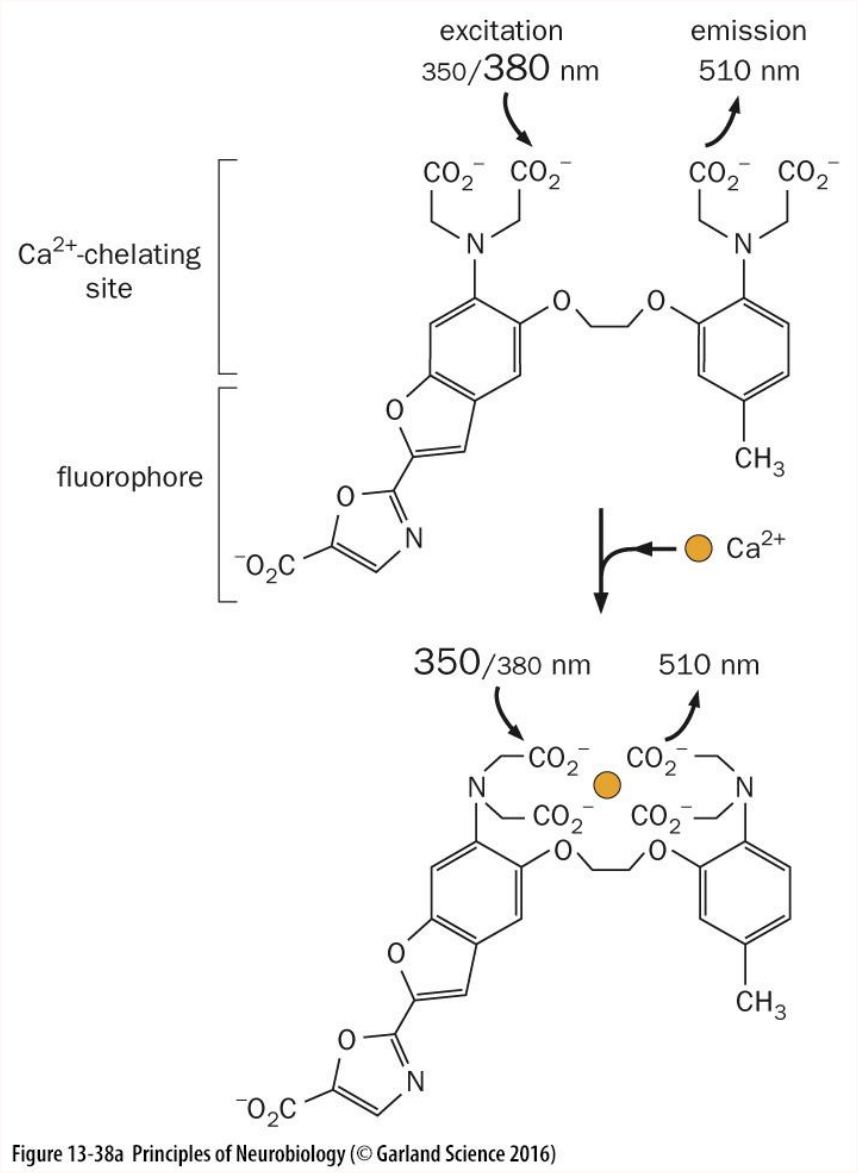

Figure 13-38a Principles of Neurobiology (© Garland Science 2016)

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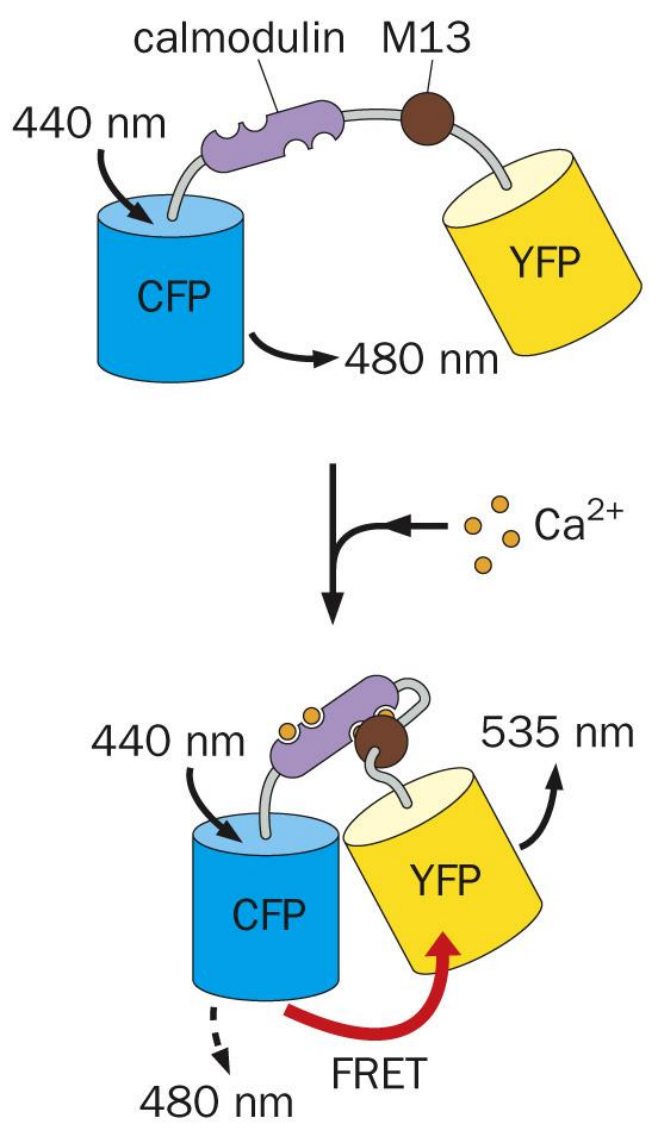

Figure 13-38b Principles of Neurobiology (© Garland Science 2016)

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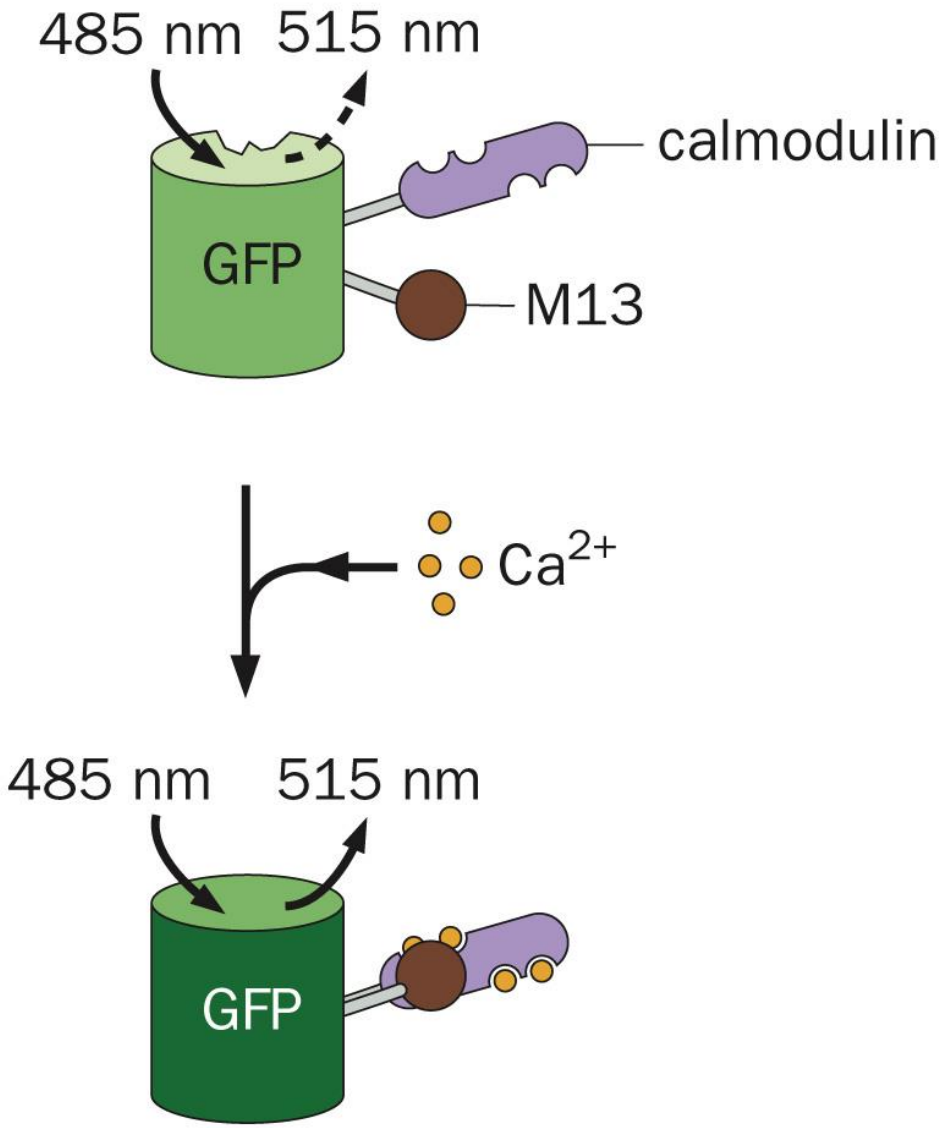

Figure 13-38c Principles of Neurobiology (© Garland Science 2016)

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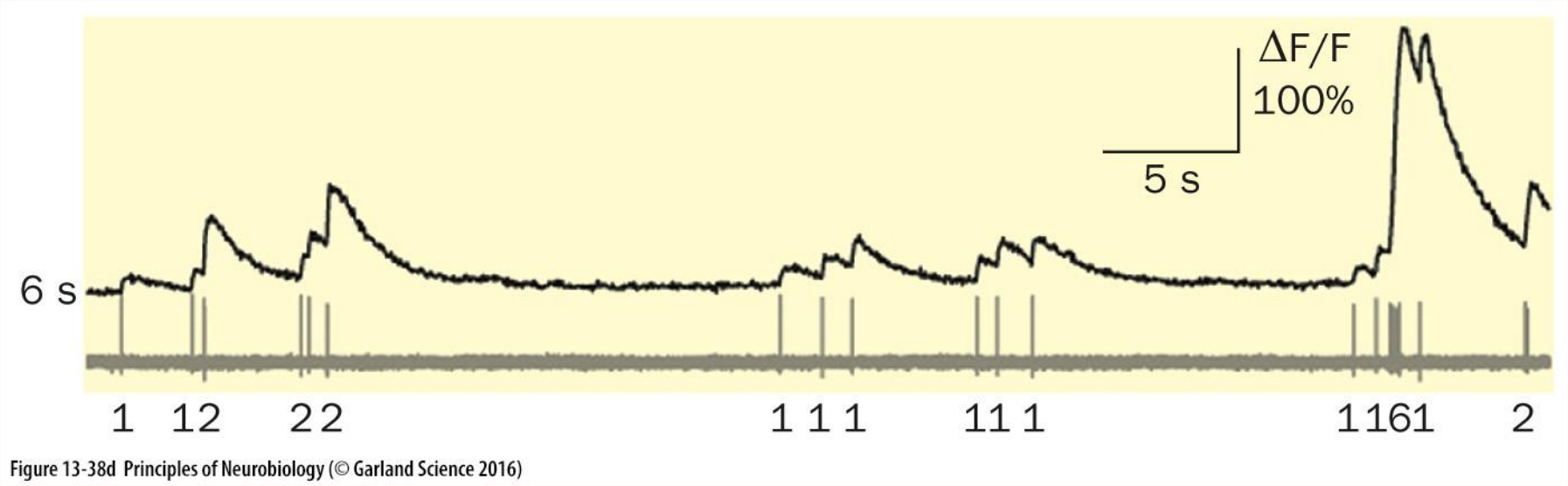

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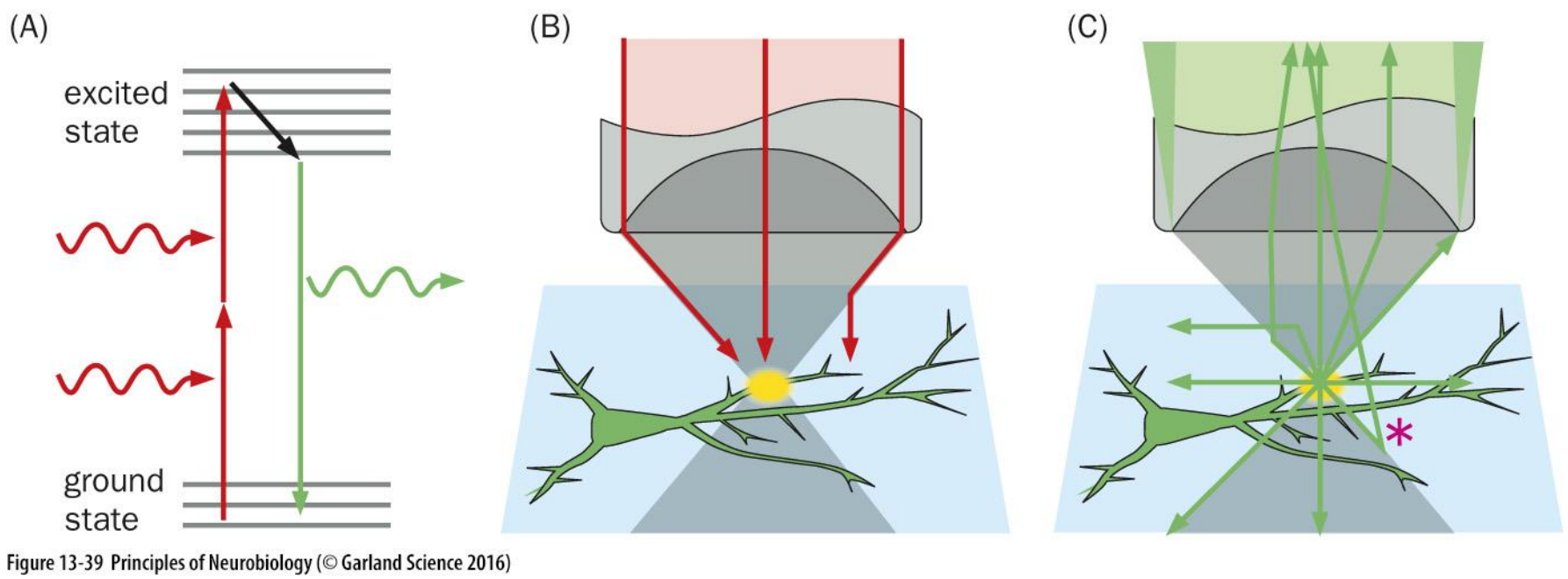

Figure 13-39 Principles of Neurobiology (© Garland Science 2016)

13.22 Optical imaging can measure the activity of many neurons simultaneously

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Table 13–2: Comparison of electrophysiological and optical imaging methods for recording neuronal activity

Property	Electrophysiology		Optical imaging with Ca^{2+} indicators[1]
	Extracellular recording	Intracellular recording	
Sensitivity to electrical signal	spikes	spikes and sub-threshold activity	generally less sensitive[2]
Spatial resolution	cellular to network	cellular to subcellular[3]	cellular and subcellular
Temporal resolution	<1 millisecond	<1 millisecond	10s to 100s of milliseconds for a single imaging plane
Number of neurons recorded simultaneously	up to hundreds	at most a few	thousands or more
Stability during movement	good	poor	poor
Depth of recording	any depth	easier superficially	limited[4]
Duration of recording	days to weeks	10s of minutes	hours with chemical indicators; months with protein indicators
Cell-type-specific recording	poor	good	excellent with protein indicators
Biases	active neurons; dominant cell types	large cells	cells that take up or express the indicators well

[1] Most other indicators share similar properties.

[2] GCaMP6 can detect single action potentials, but cannot resolve high-frequency spikes (see Figure 13–38D).

[3] Whole-cell patch recording can be applied to large dendrites (see Figure 13–35).

[4] <10 μm with conventional fluorescence microscopy for cellular resolution; ~100 μm with confocal microscopy; ~500 μm with two-photon microscopy.

Table 13-2 Principles of Neurobiology (© Garland Science 2016)

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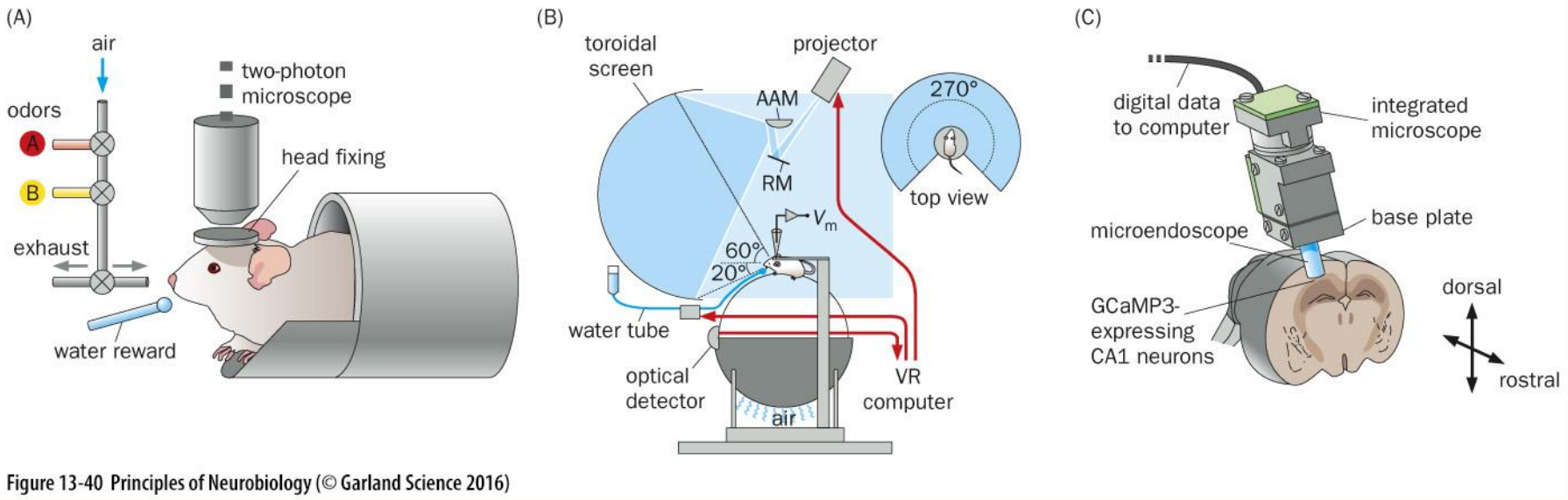

Figure 13-40 Principles of Neurobiology (© Garland Science 2016)

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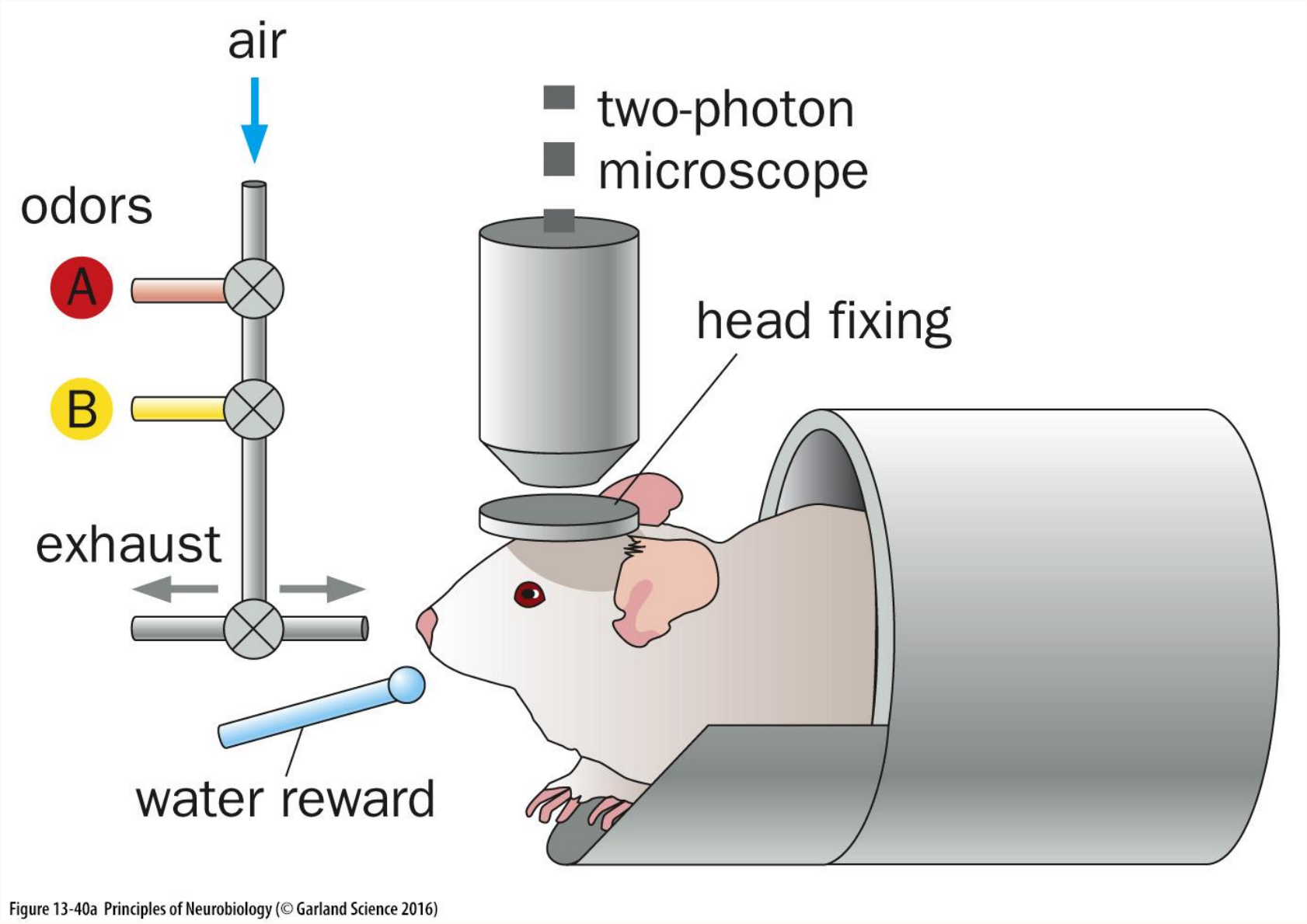

Figure 13-40a Principles of Neurobiology (© Garland Science 2016)

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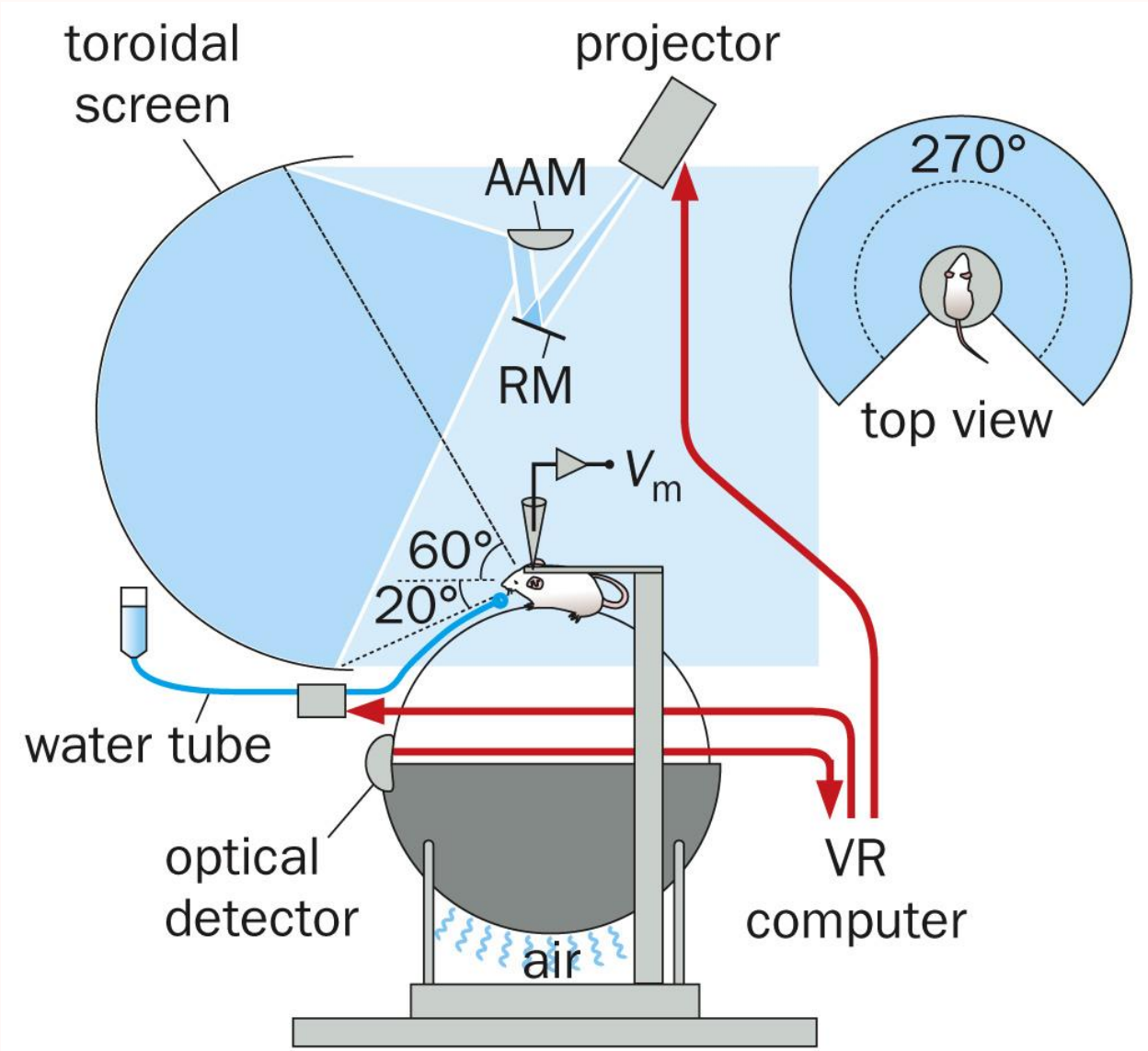

Figure 13-40b Principles of Neurobiology (© Garland Science 2016)

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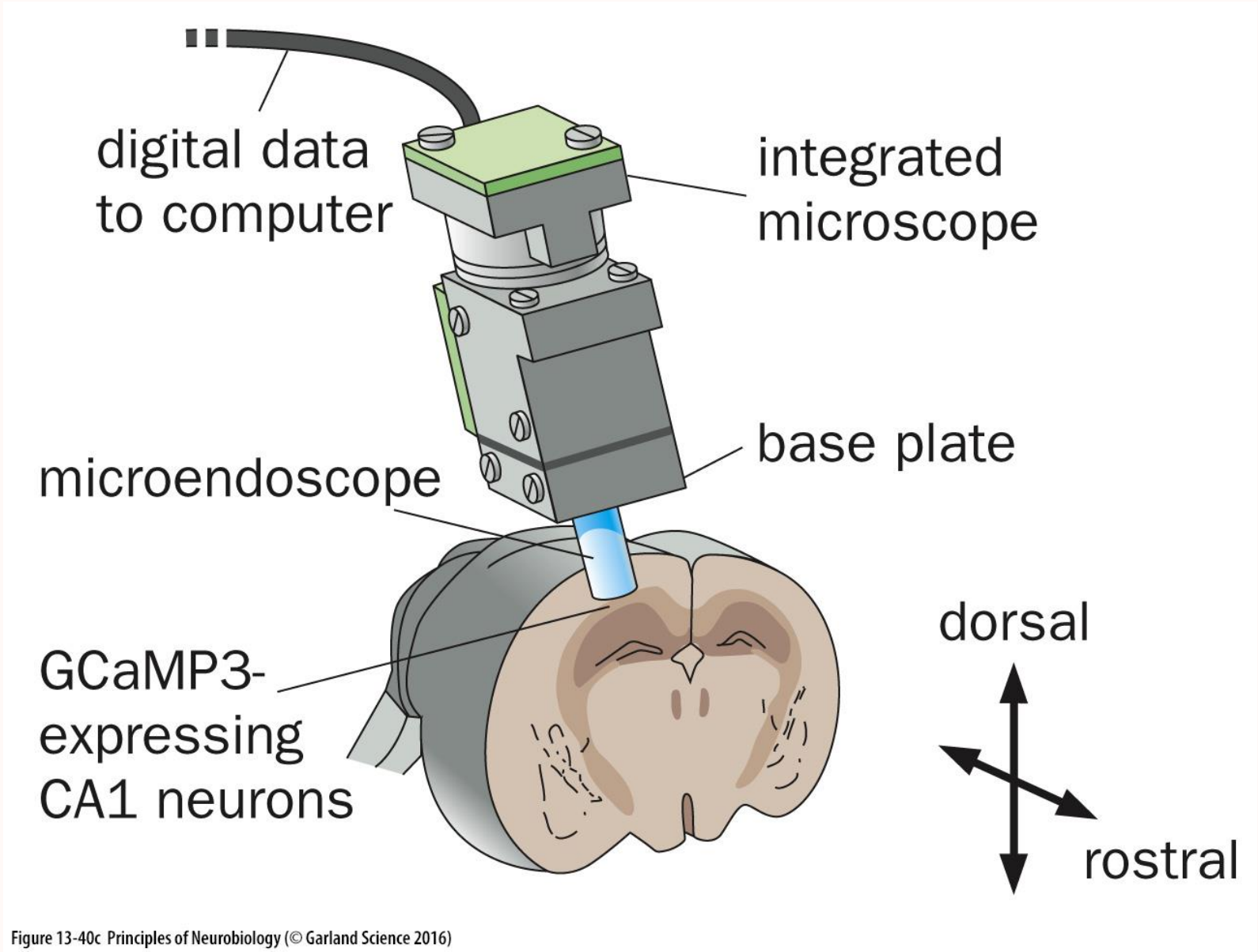

Figure 13-40c Principles of Neurobiology (© Garland Science 2016)

RECORDING AND MANIPULATING NEURONAL ACTIVITY

记录和操控神经活动

13.23 Neuronal inactivation can be used to reveal which neurons are essential for circuit function and behavior

13.23 失活神经元来揭示对于神经环路功能和行为重要的神经元

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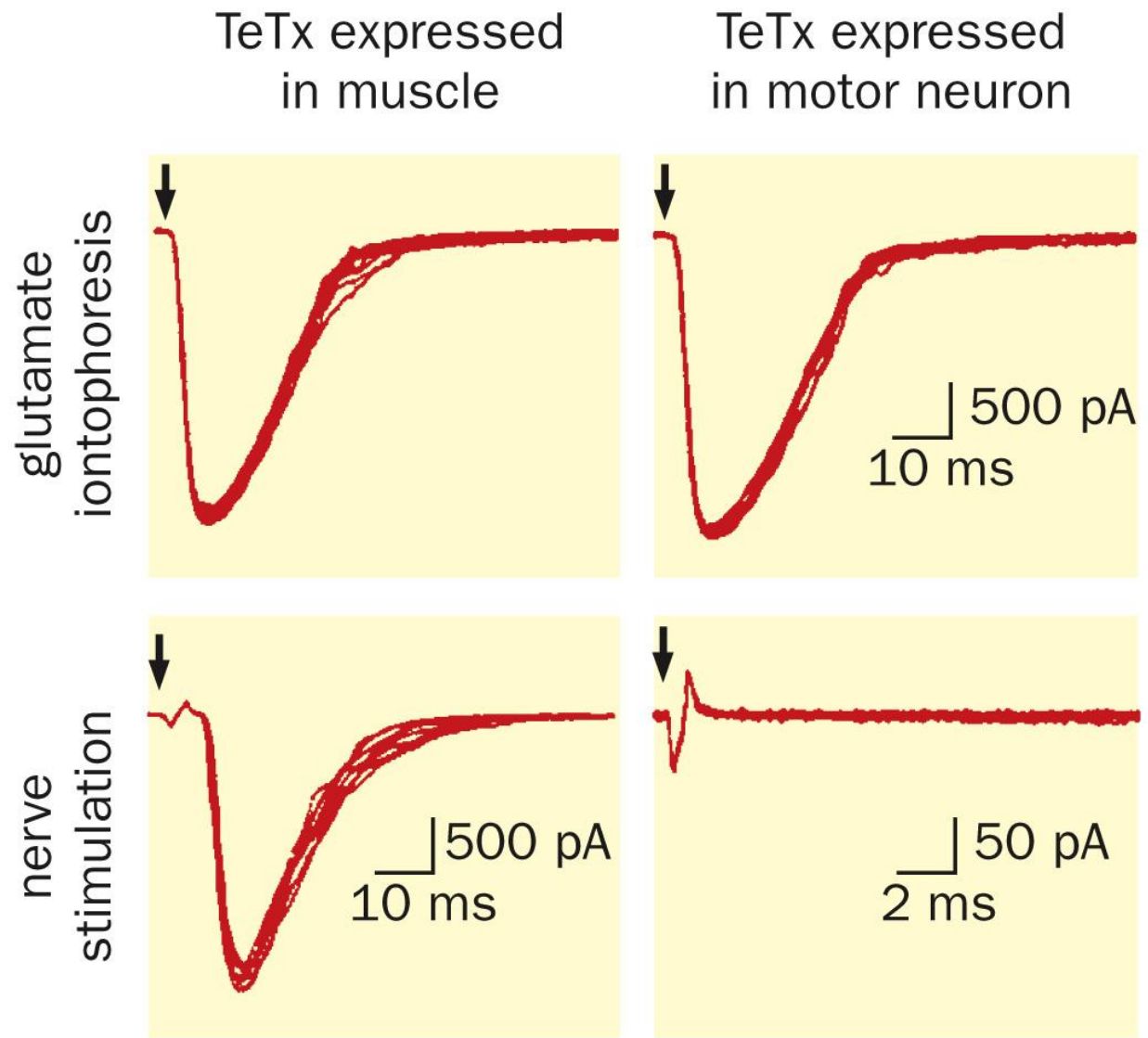

Figure 13-41 Principles of Neurobiology (© Garland Science 2016)

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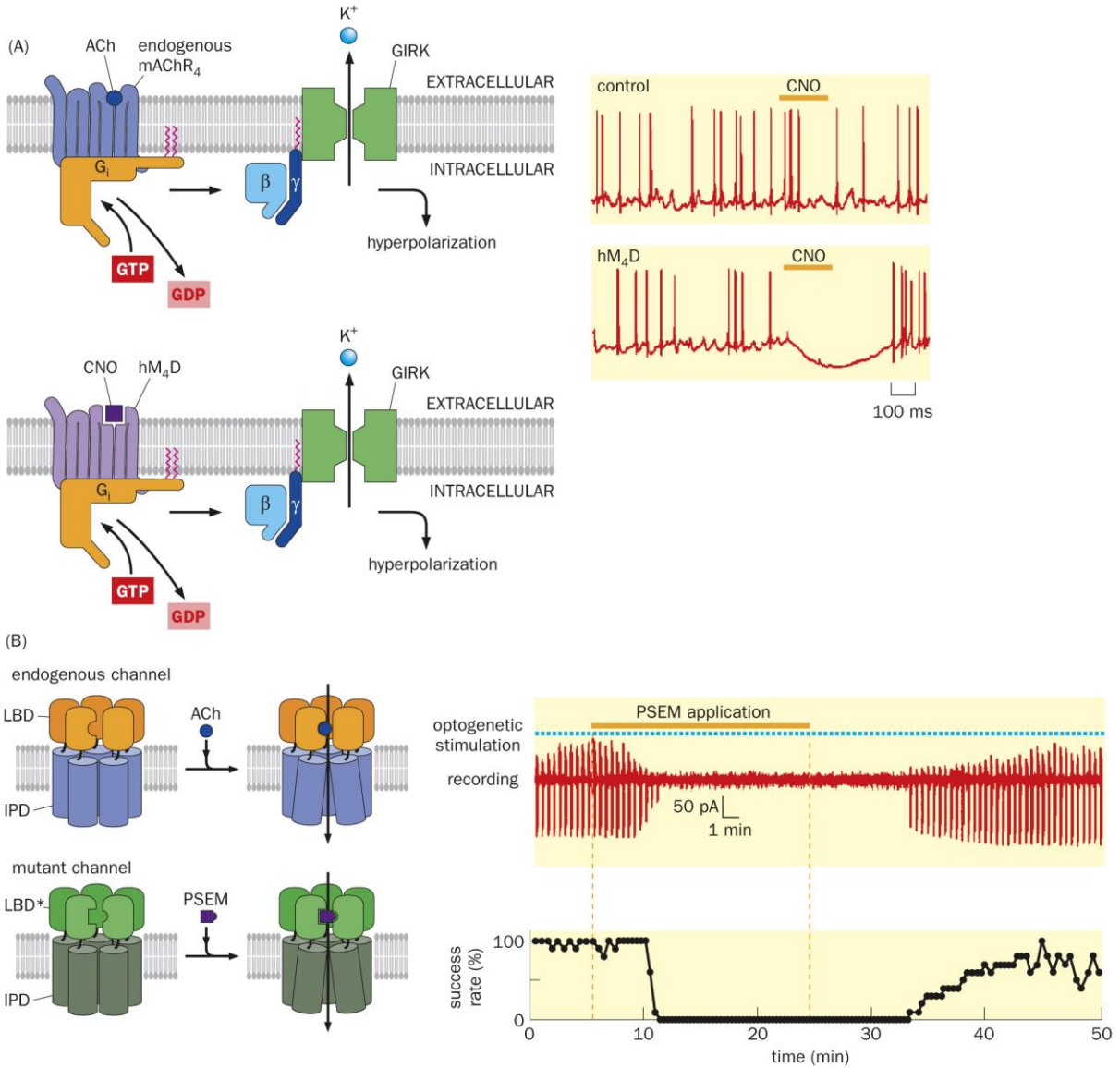

Figure 13-42 Principles of Neurobiology (© Garland Science 2016)

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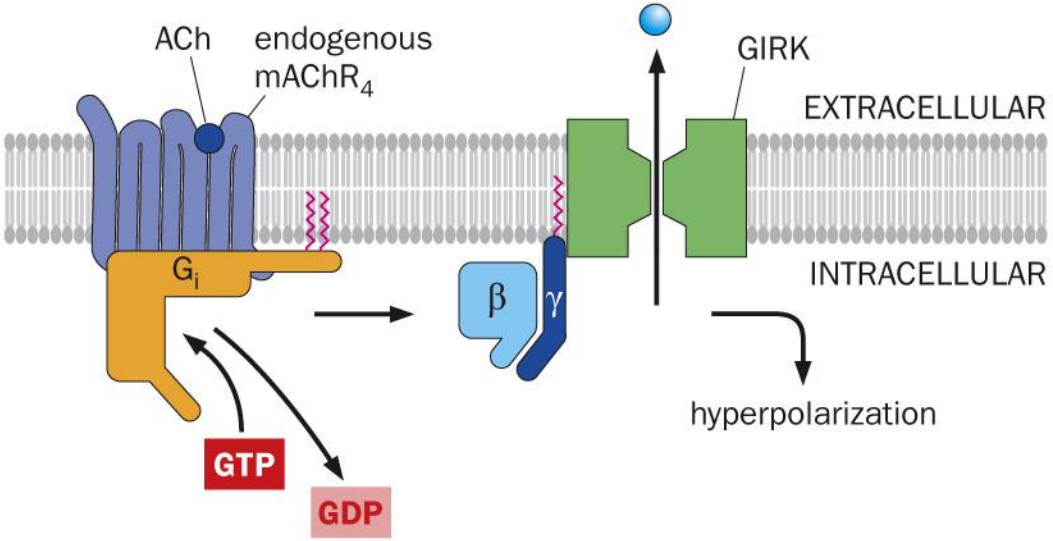

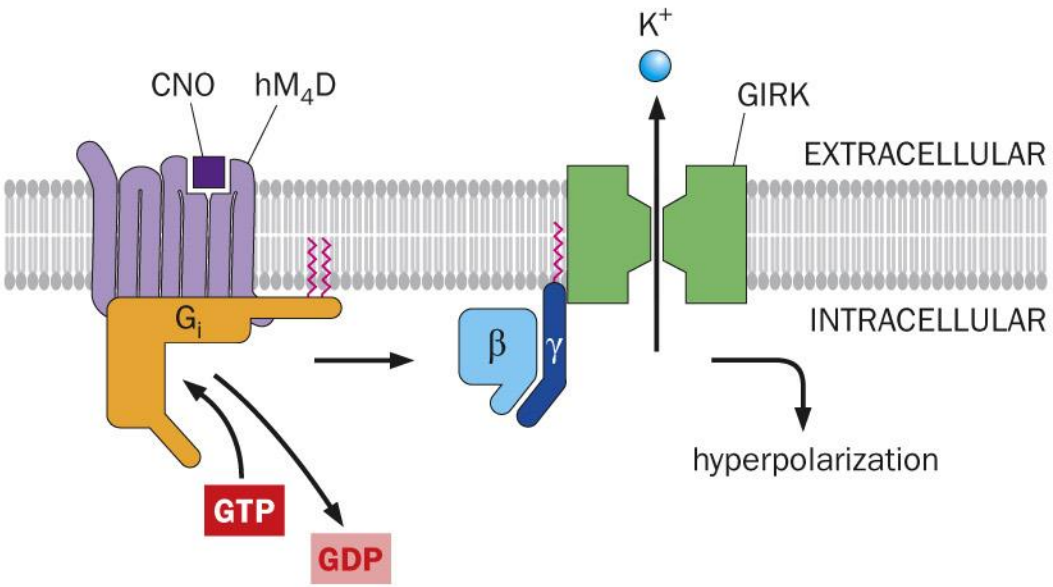

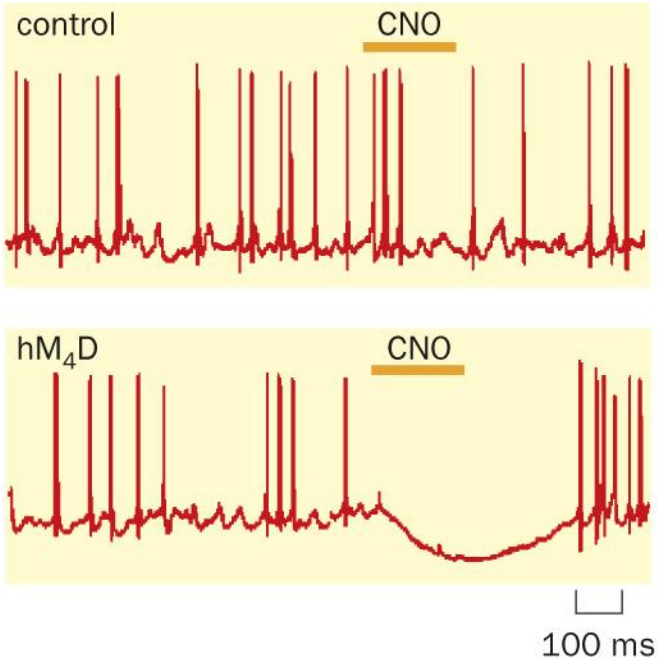

Figure 13-42a Principles of Neurobiology (© Garland Science 2016)

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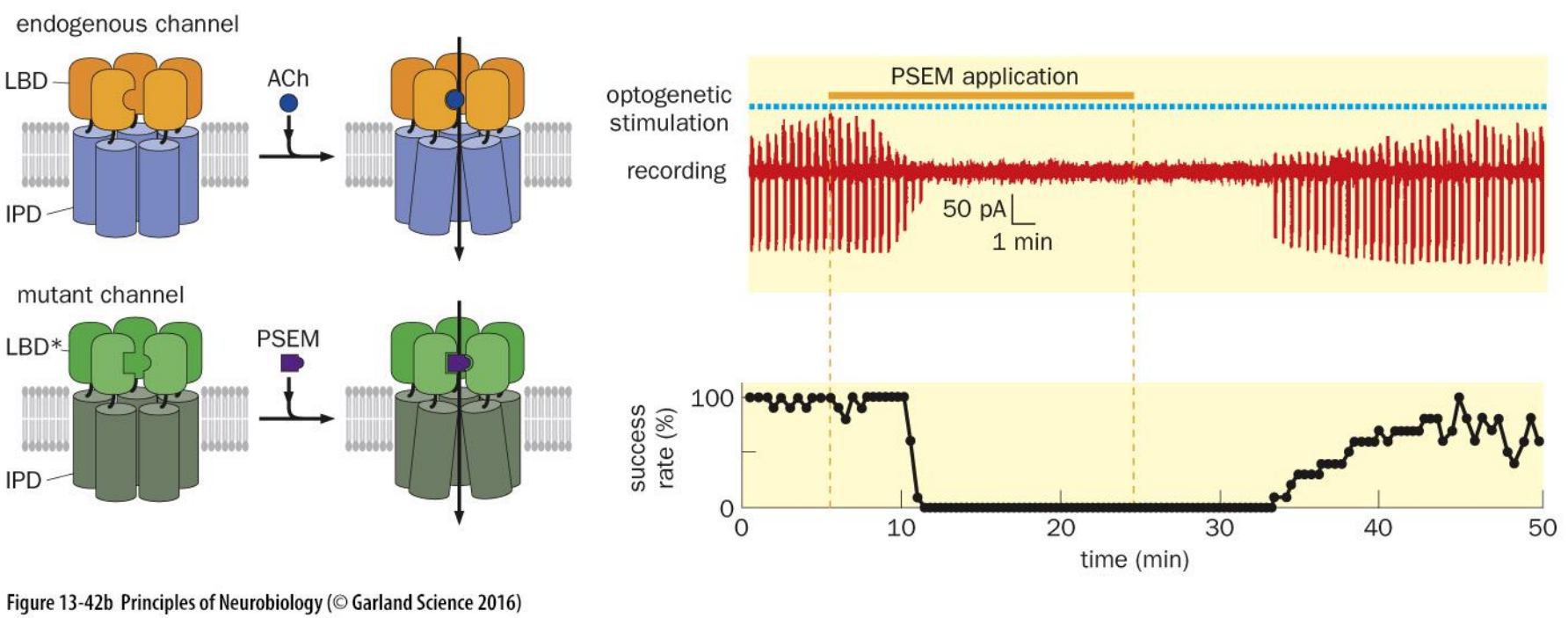

Figure 13-42b Principles of Neurobiology (© Garland Science 2016)

RECORDING AND MANIPULATING NEURONAL ACTIVITY

记录和操控神经活动

13.24 Neuronal activation can establish sufficiency of neuronal activity in circuit function and behavior

13.24 激活神经元可以产生足够的能引起神经环路功能和行的神经活动

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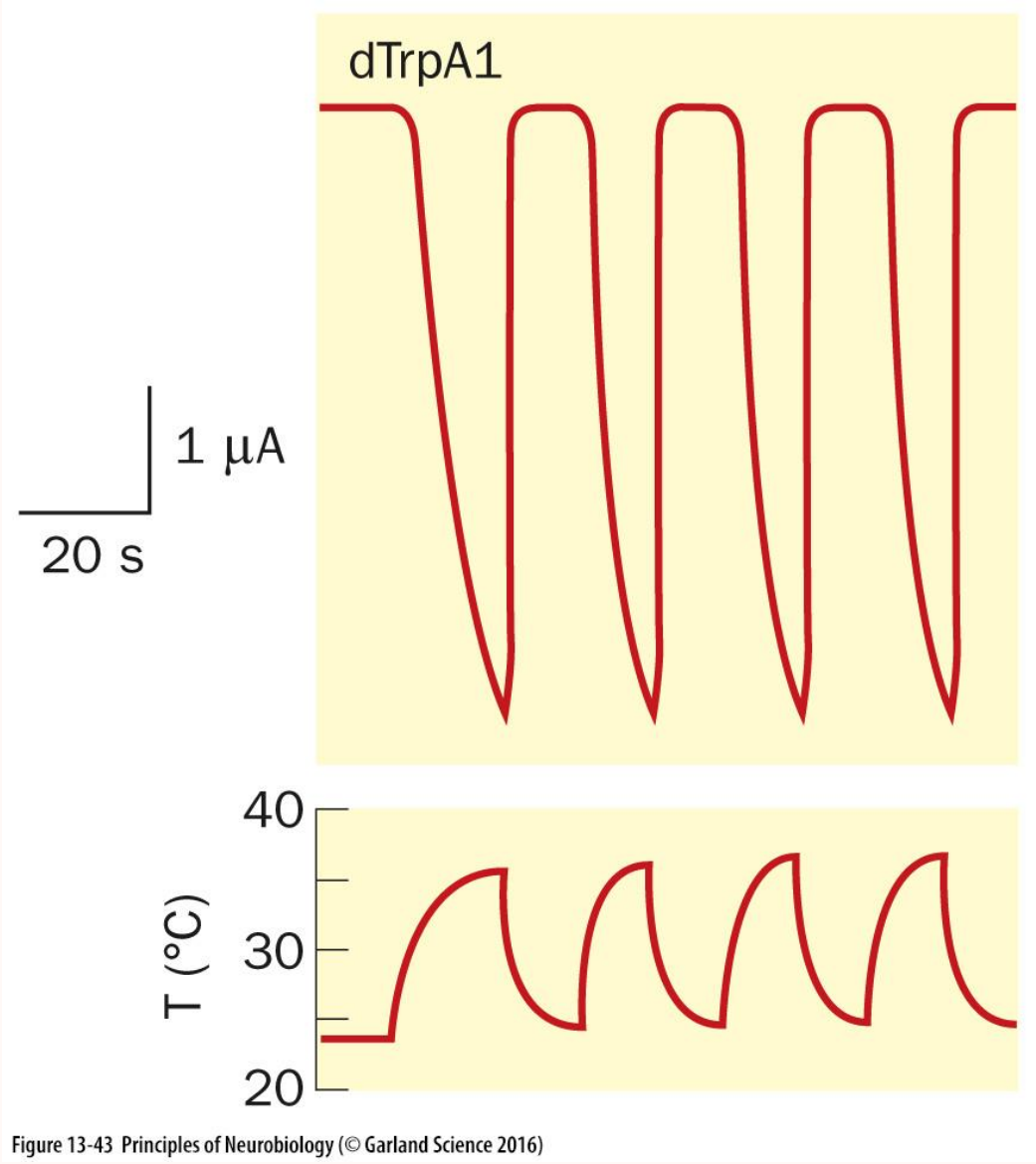

Figure 13-43 Principles of Neurobiology (© Garland Science 2016)

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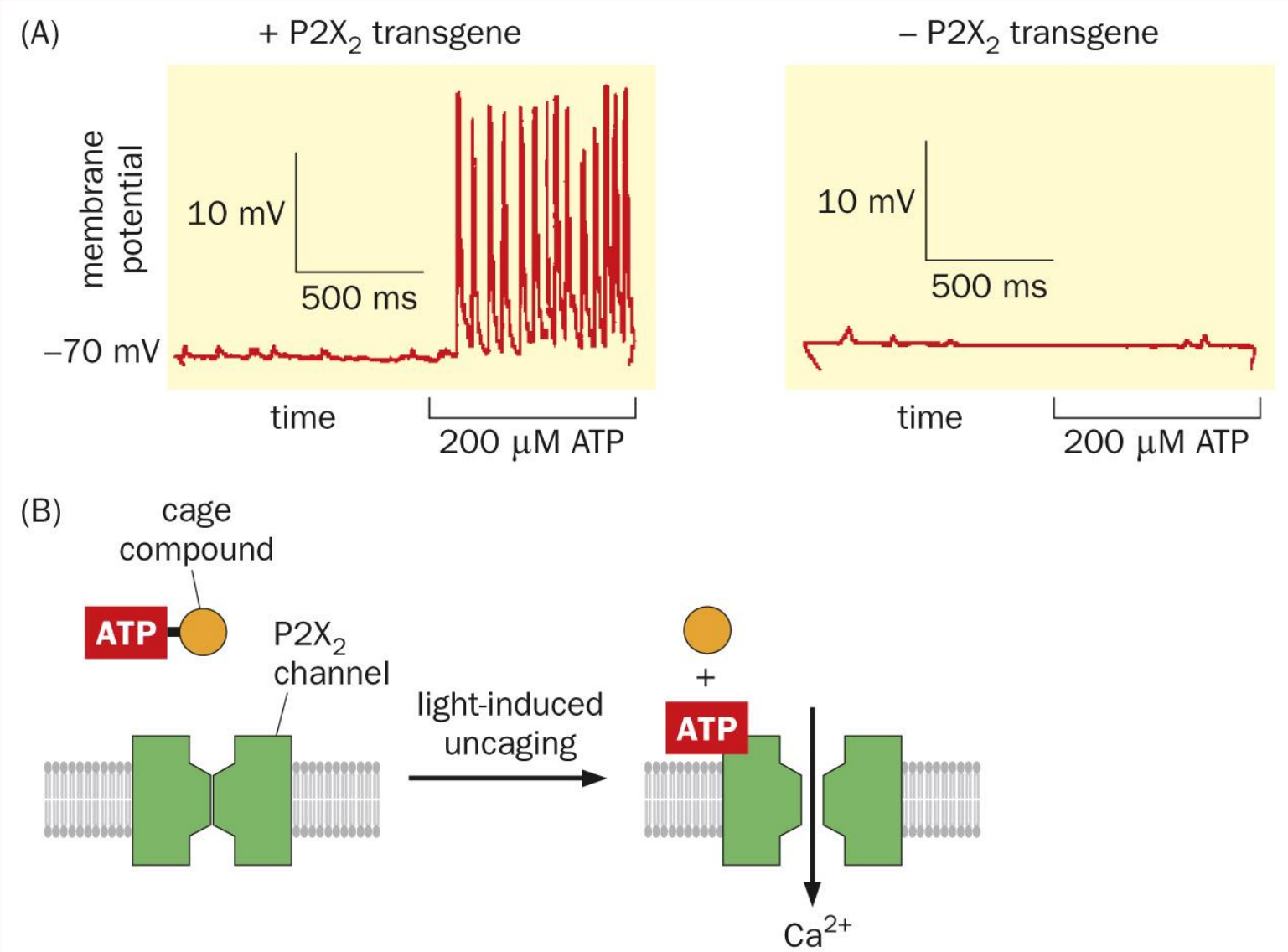

Figure 13-44 Principles of Neurobiology (© Garland Science 2016)

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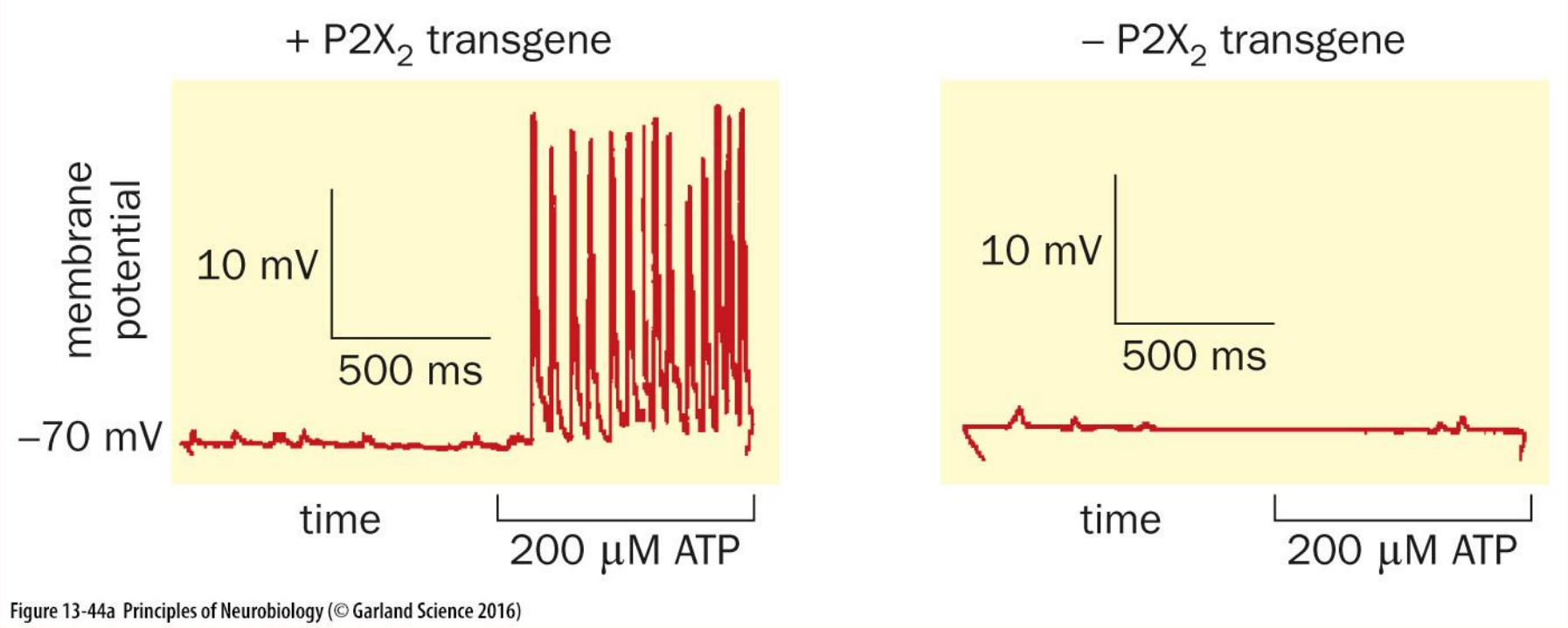

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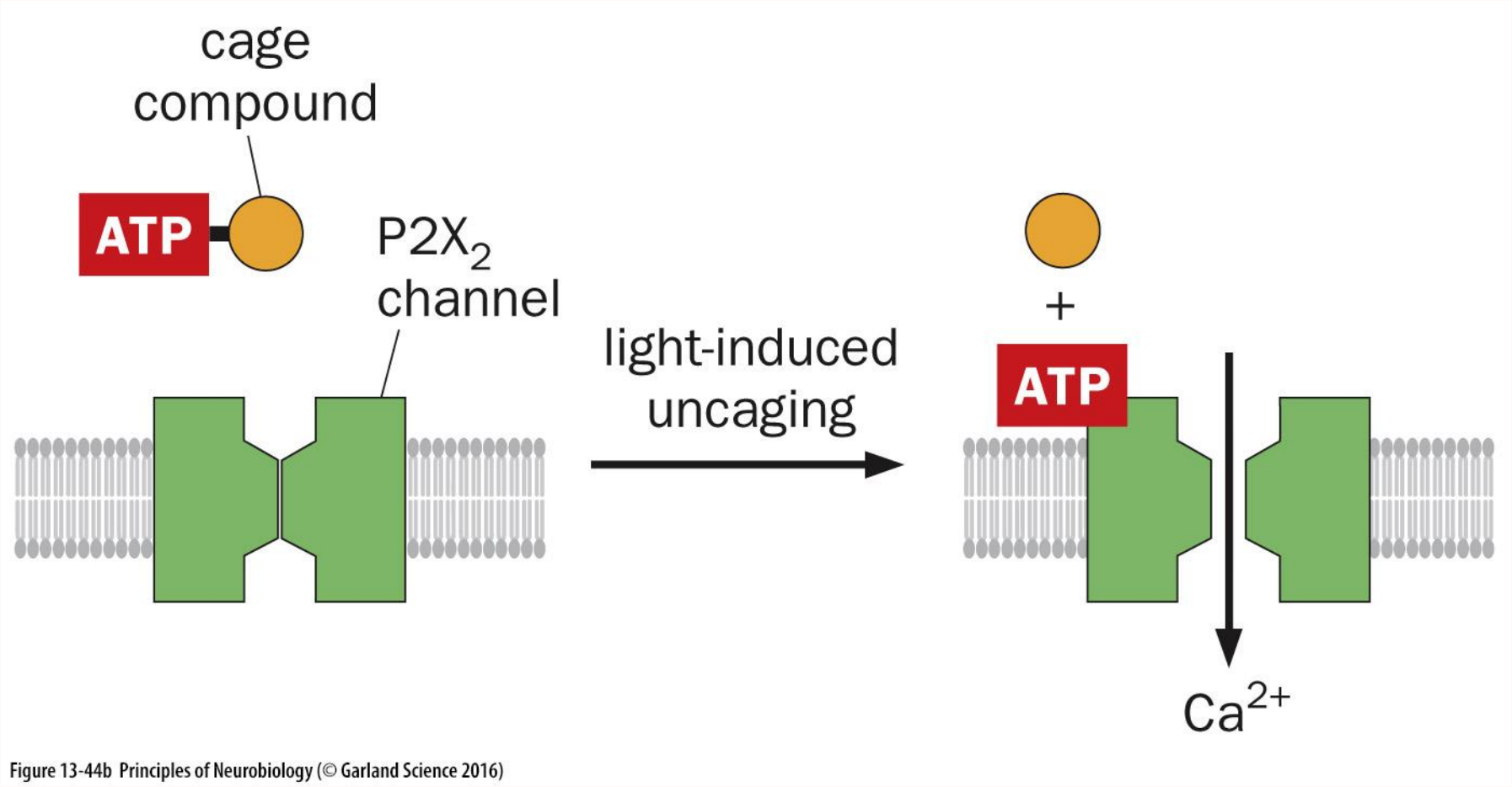

Figure 13-44b Principles of Neurobiology (© Garland Science 2016)

RECORDING AND MANIPULATING NEURONAL ACTIVITY

记录和操控神经活动

13.25 Optogenetics allows control of the activity of genetically targeted neurons with millisecond precision

13.25 光遗传学可以在毫秒级时间内控制特定遗传编码的神经元

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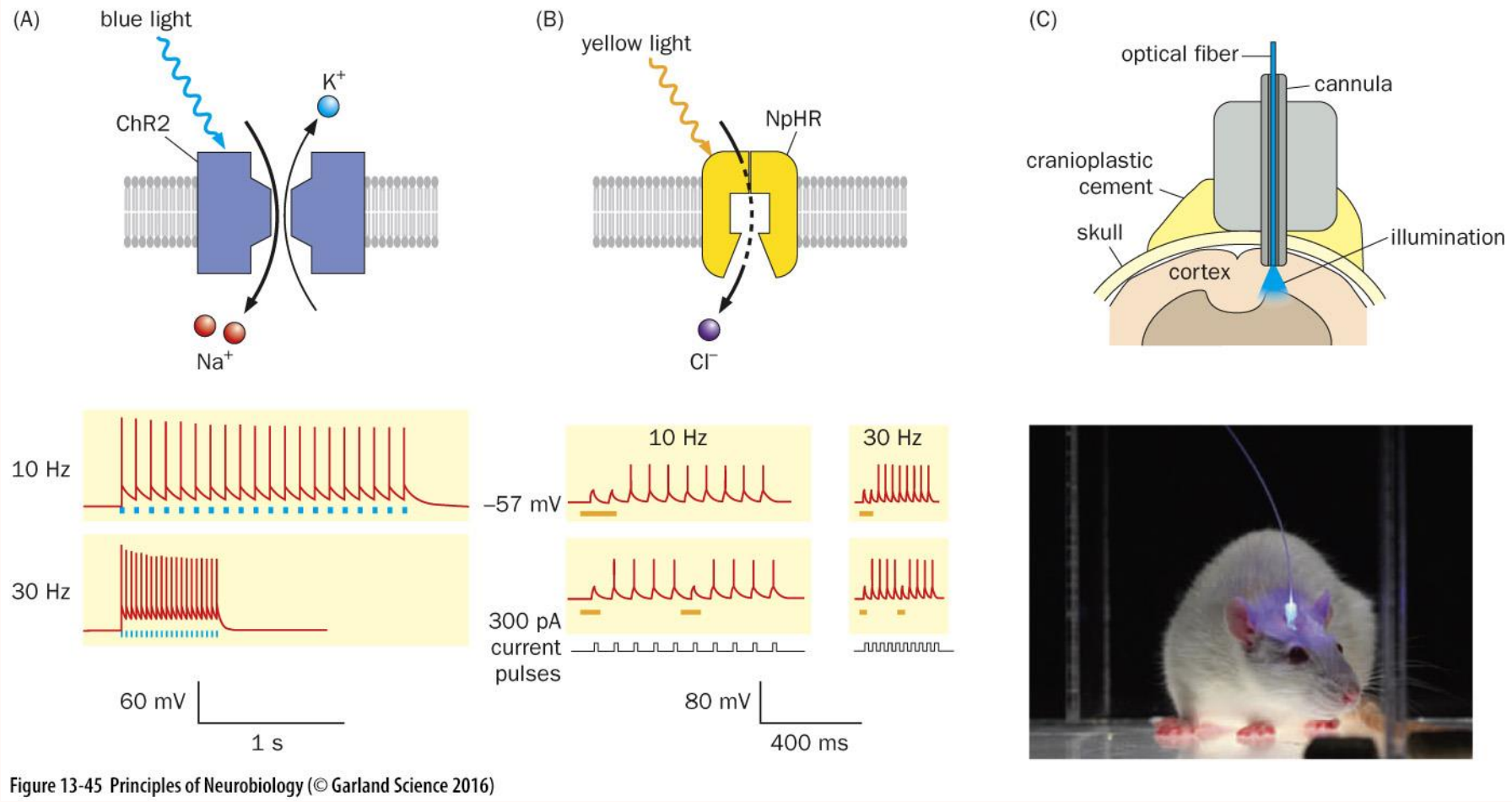

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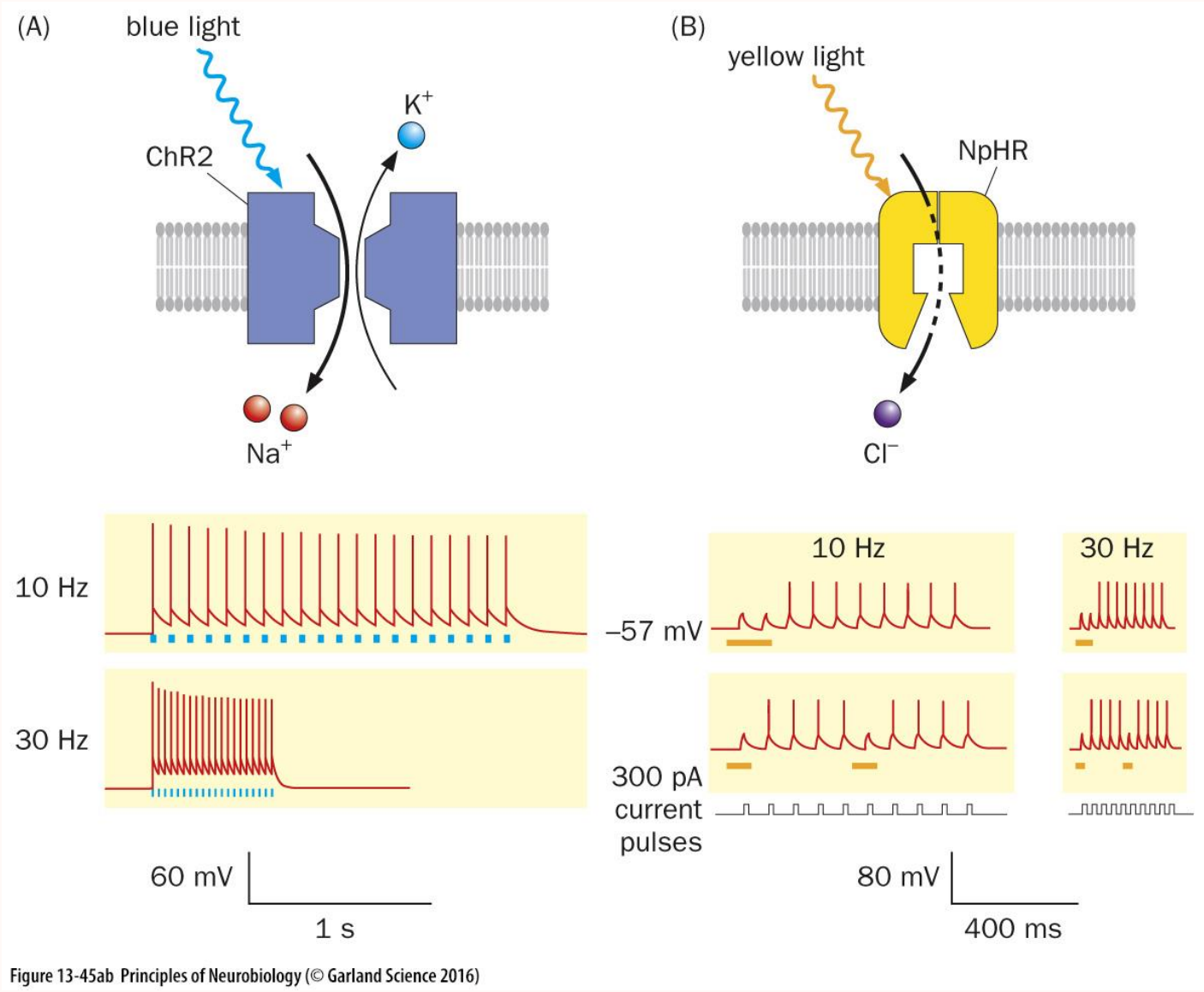

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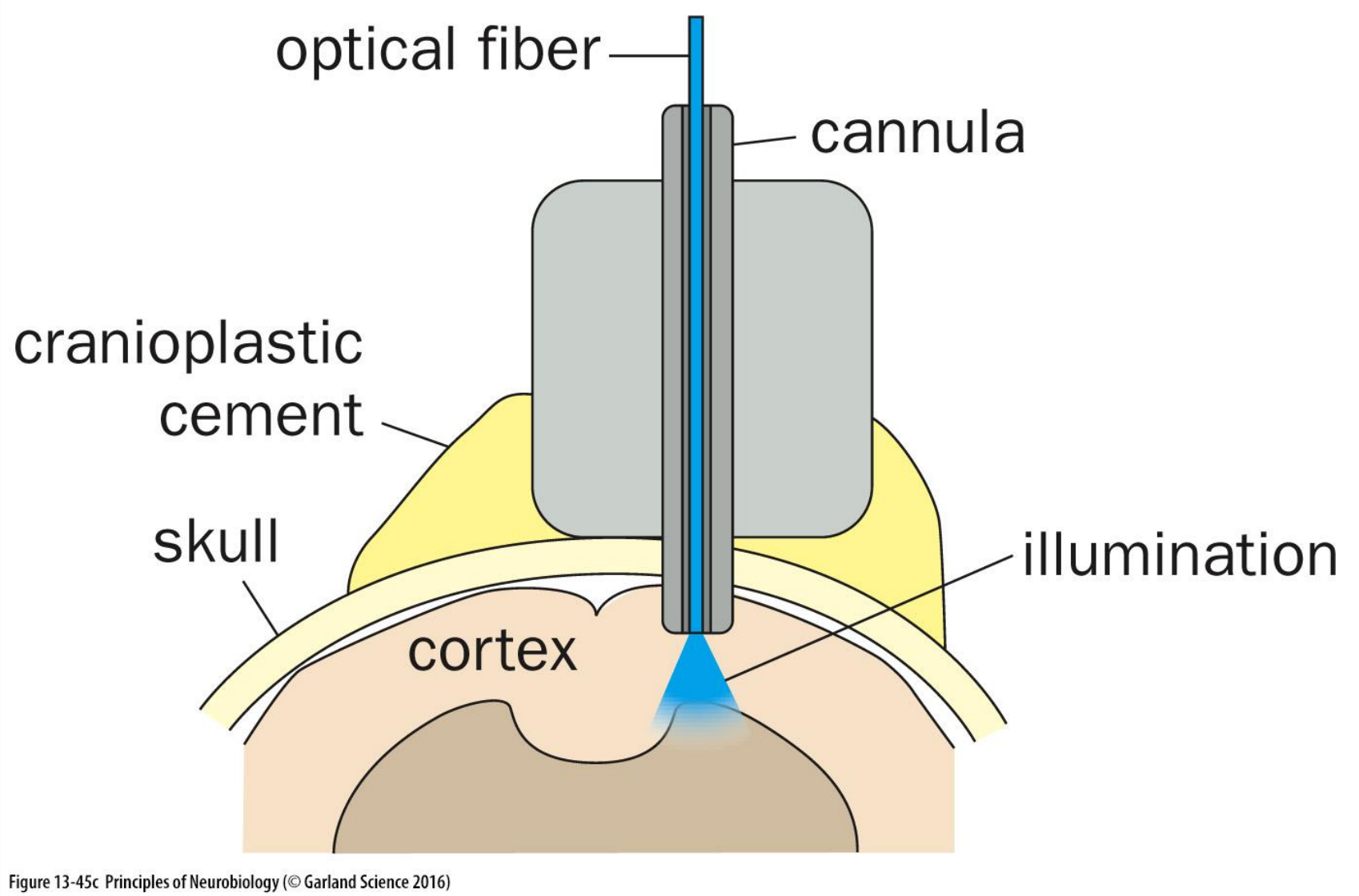

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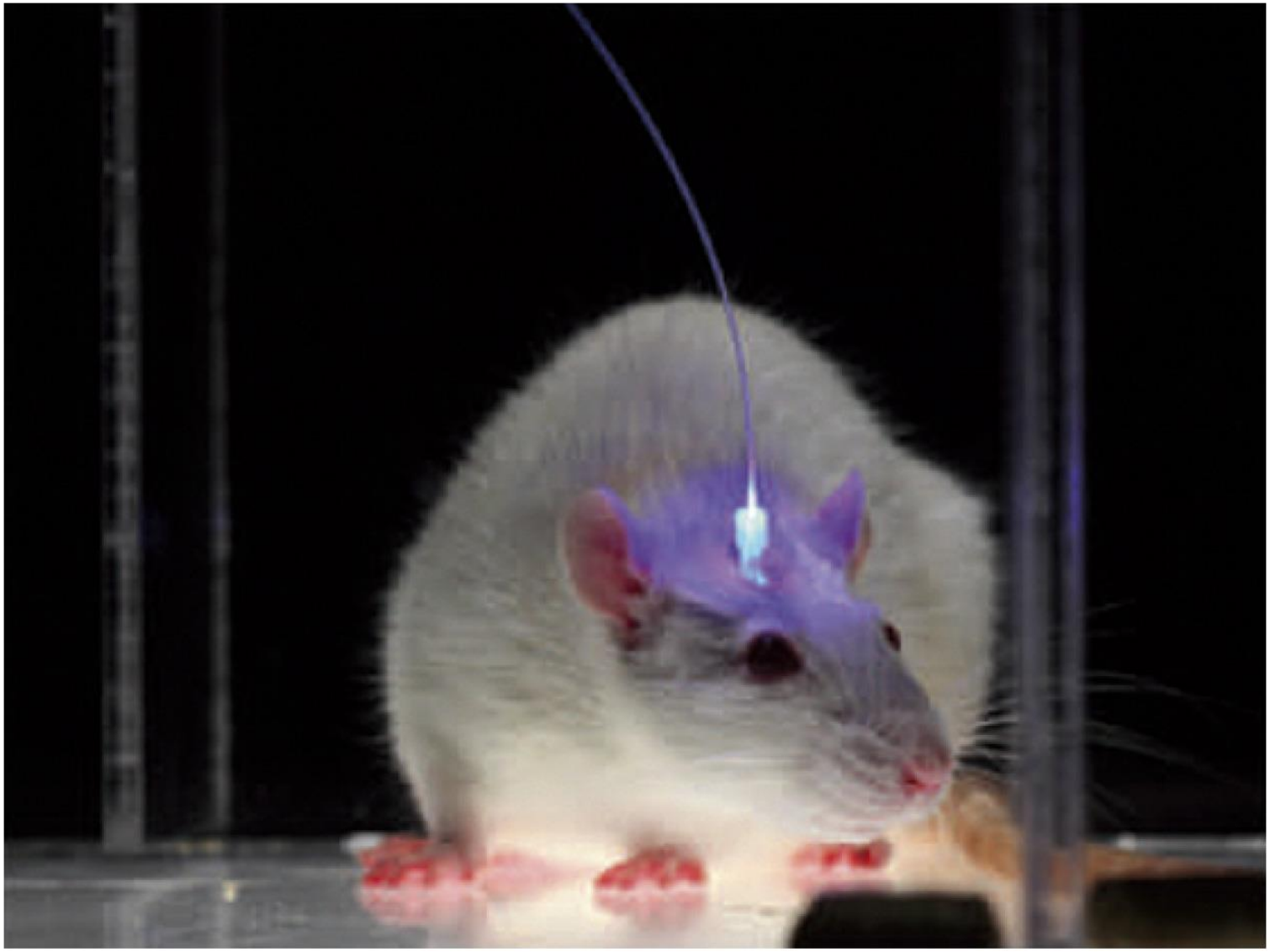

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RECORDING AND MANIPULATING NEURONAL ACTIVITY

记录和操控神经活动

13.26 Synaptic connections can be mapped by physiological and optogenetic methods

13.26 利用生理学和光遗传学方法了解突触间连接

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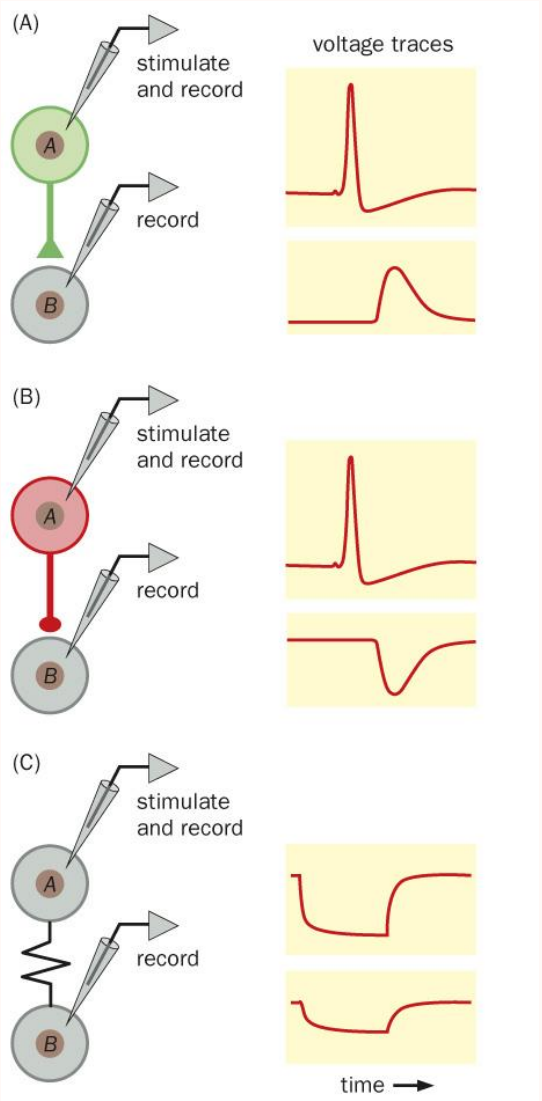

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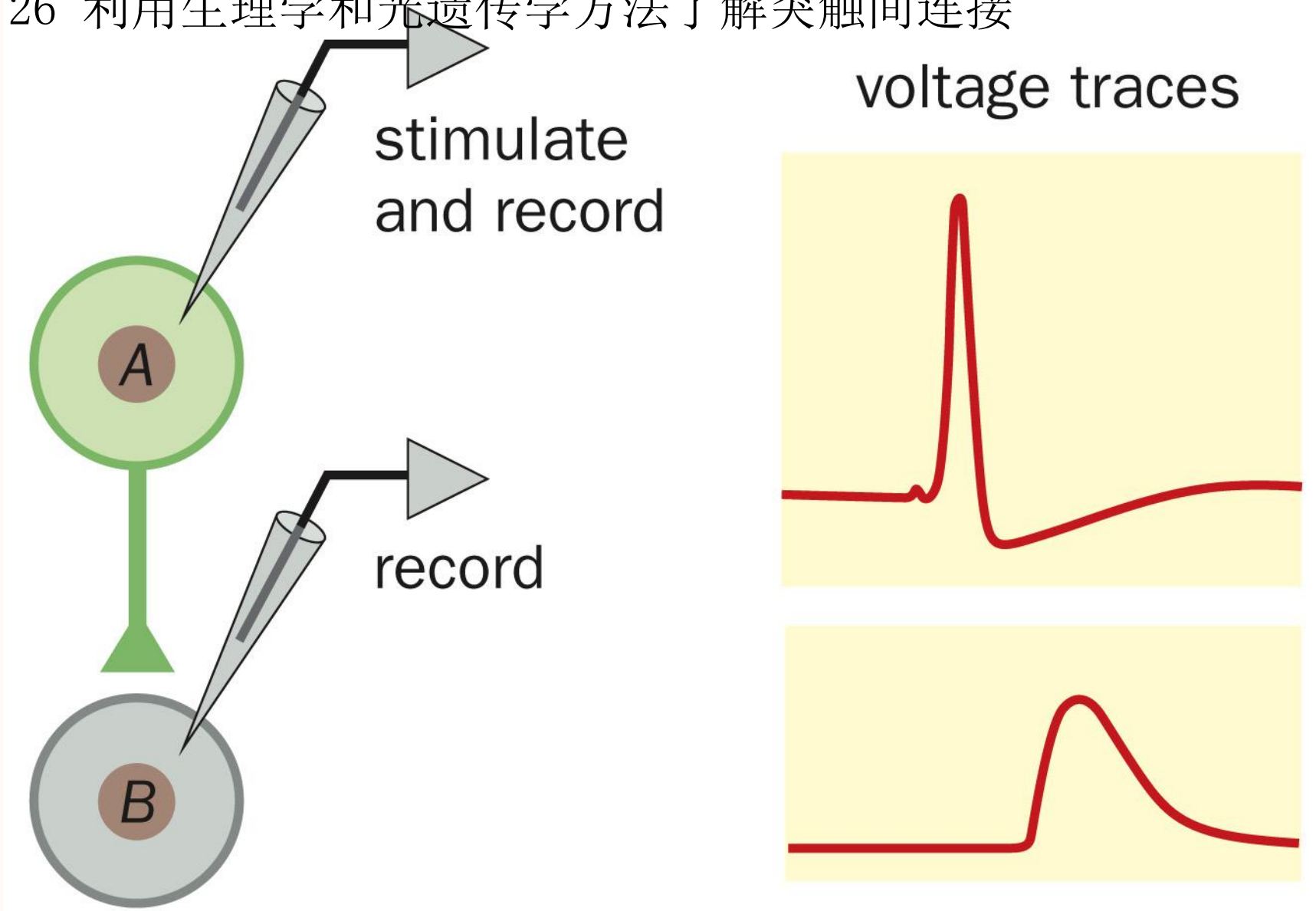

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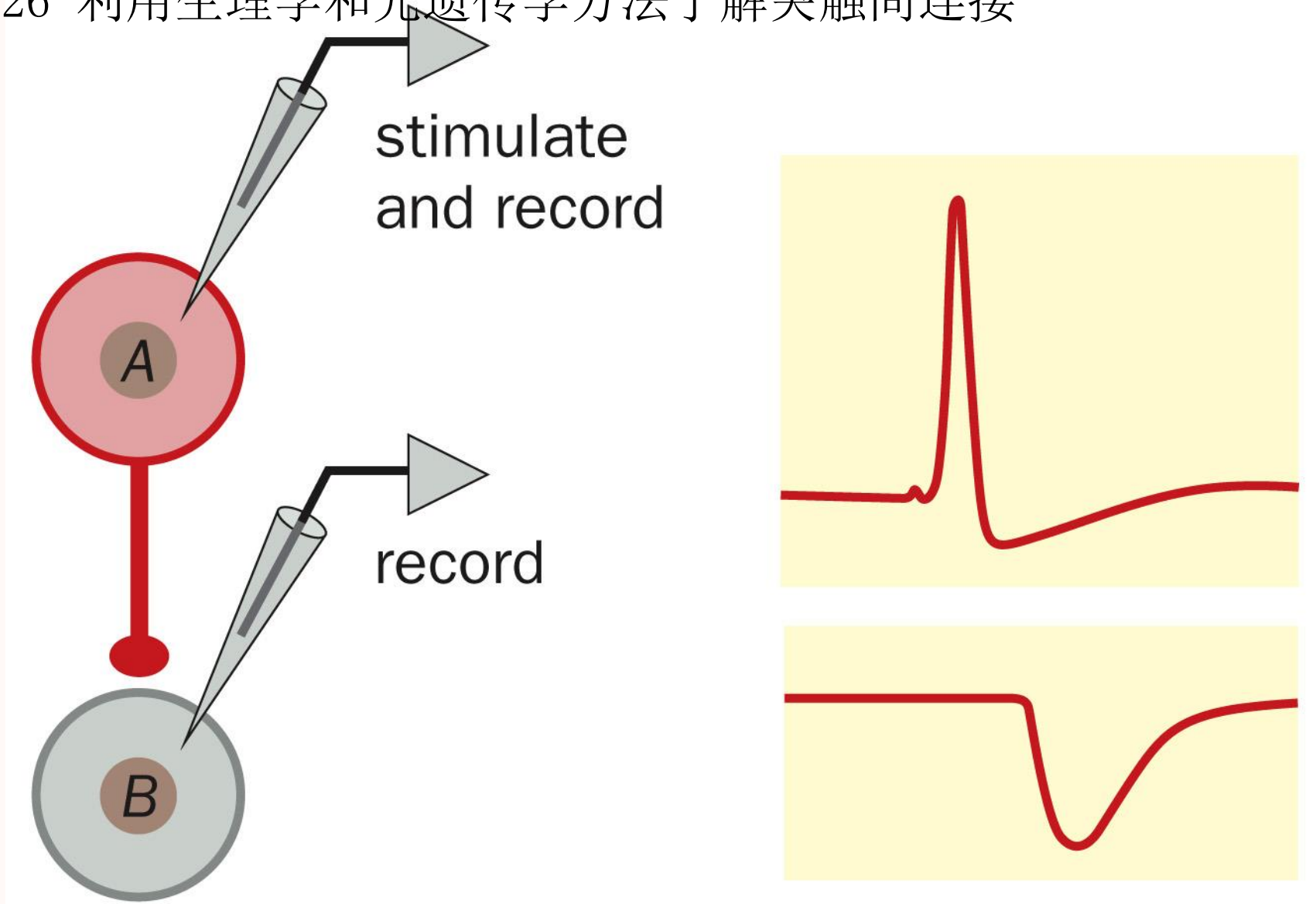

Figure 13-46b Principles of Neurobiology (© Garland Science 2016)

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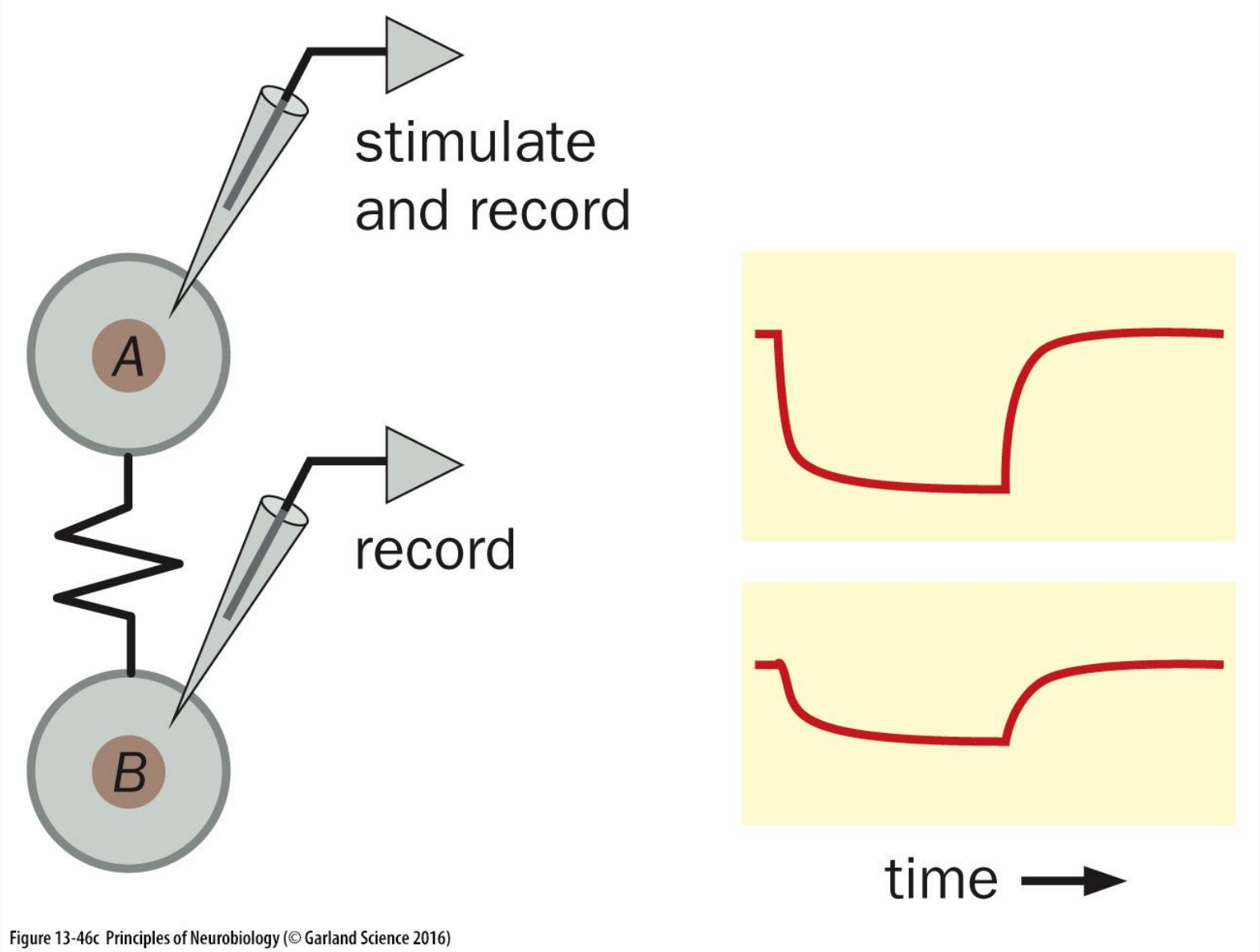

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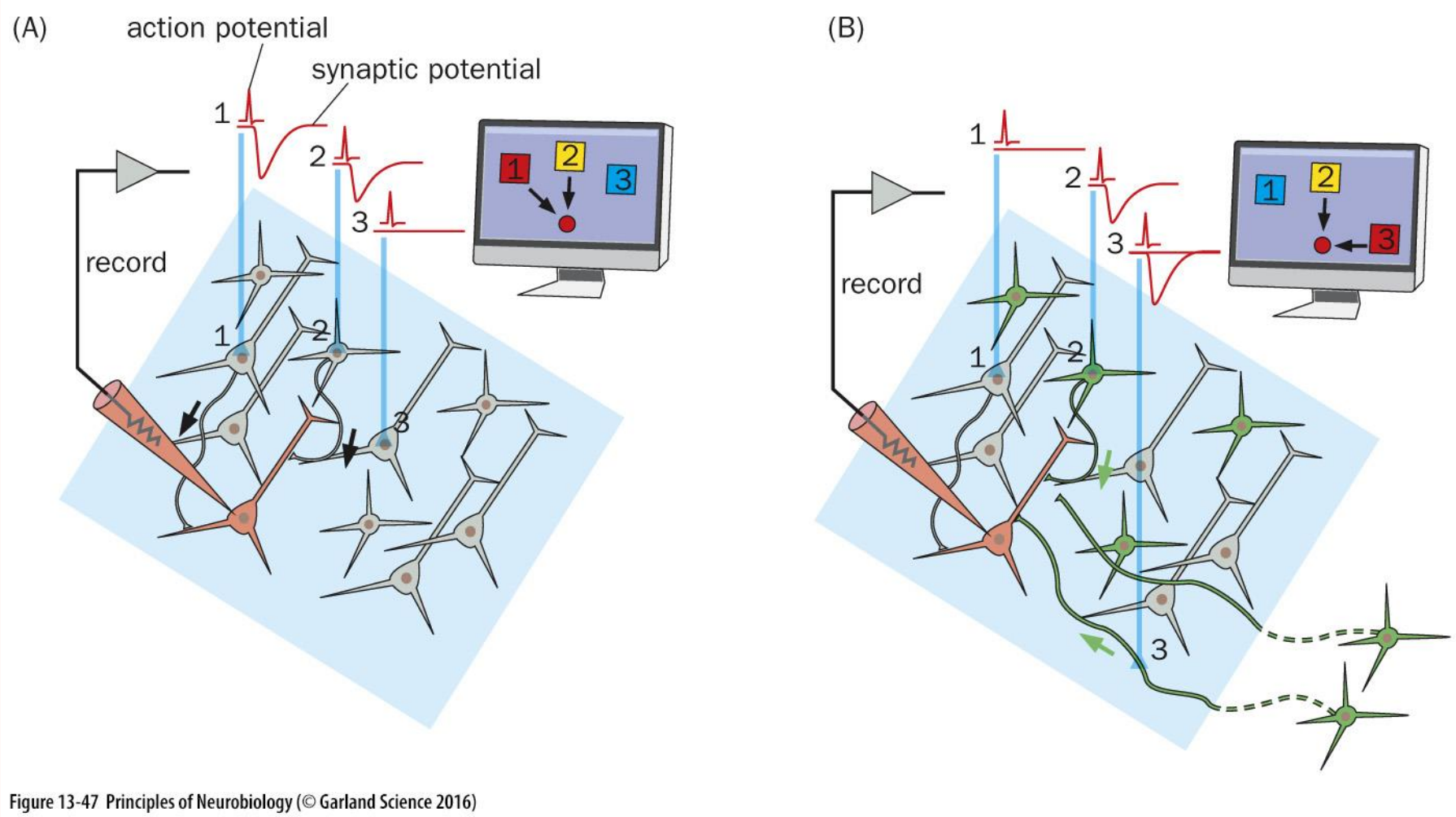

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BEHAVIORAL ANALYSES

行为分析

13.27 Studying animal behavior in natural environments can reveal behavioral repertoires and their adaptive value

13.28 Studying behaviors in highly controlled conditions facilitates investigation of their neural basis

13.29 Behavioral assays can be used to evaluate the functions of genes and neurons and to model human brain disorders

13.27 研究自然环境下动物的行为可以揭示行为能力和适应能力

13.28 研究人为控制环境下的动物的行为有利于揭示神经基础

13.29 行为学实验可以被用来评估基因和神经元的功能，模拟人类脑功能紊乱

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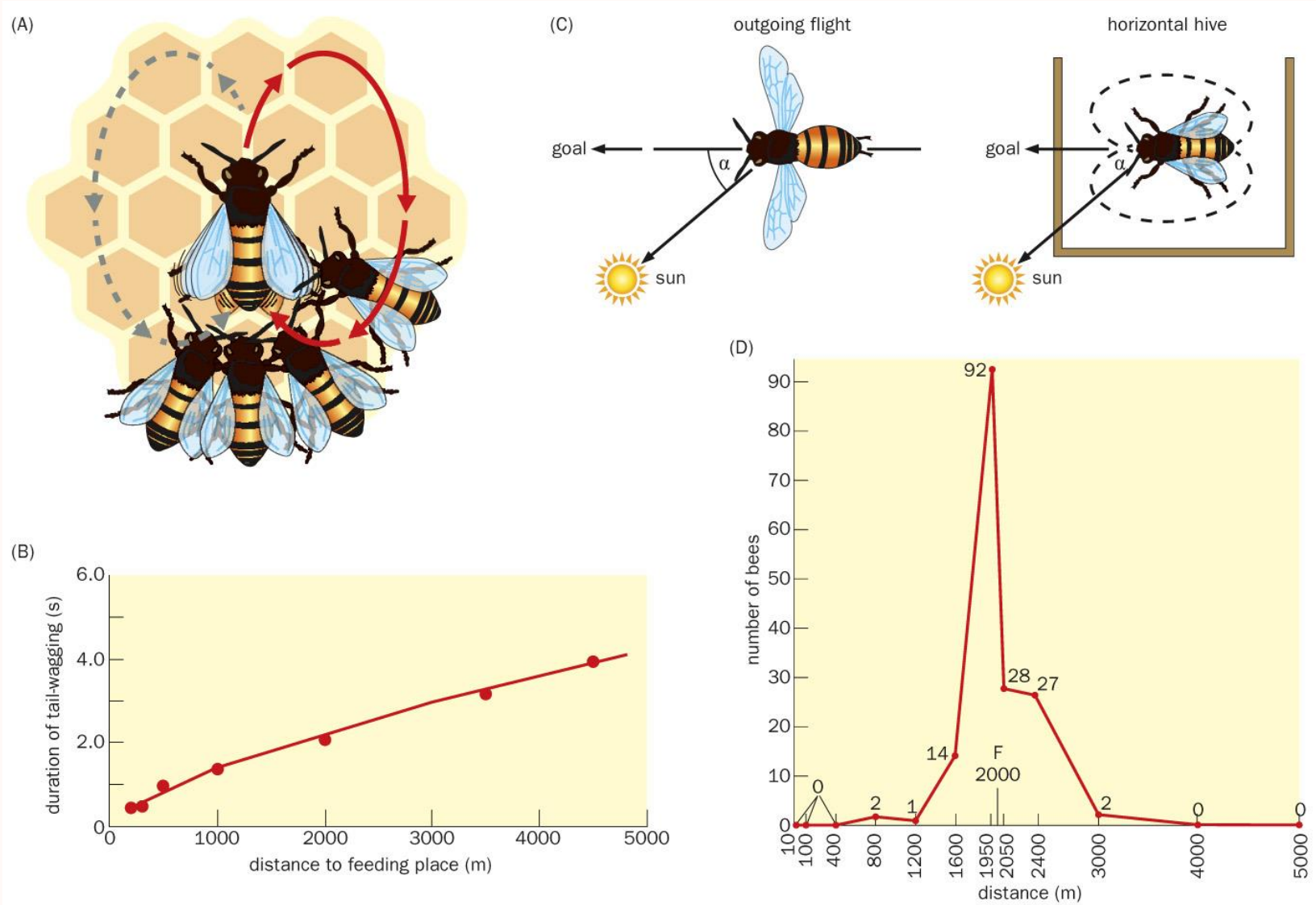

Figure 13-48 Principles of Neurobiology (© Garland Science 2016)

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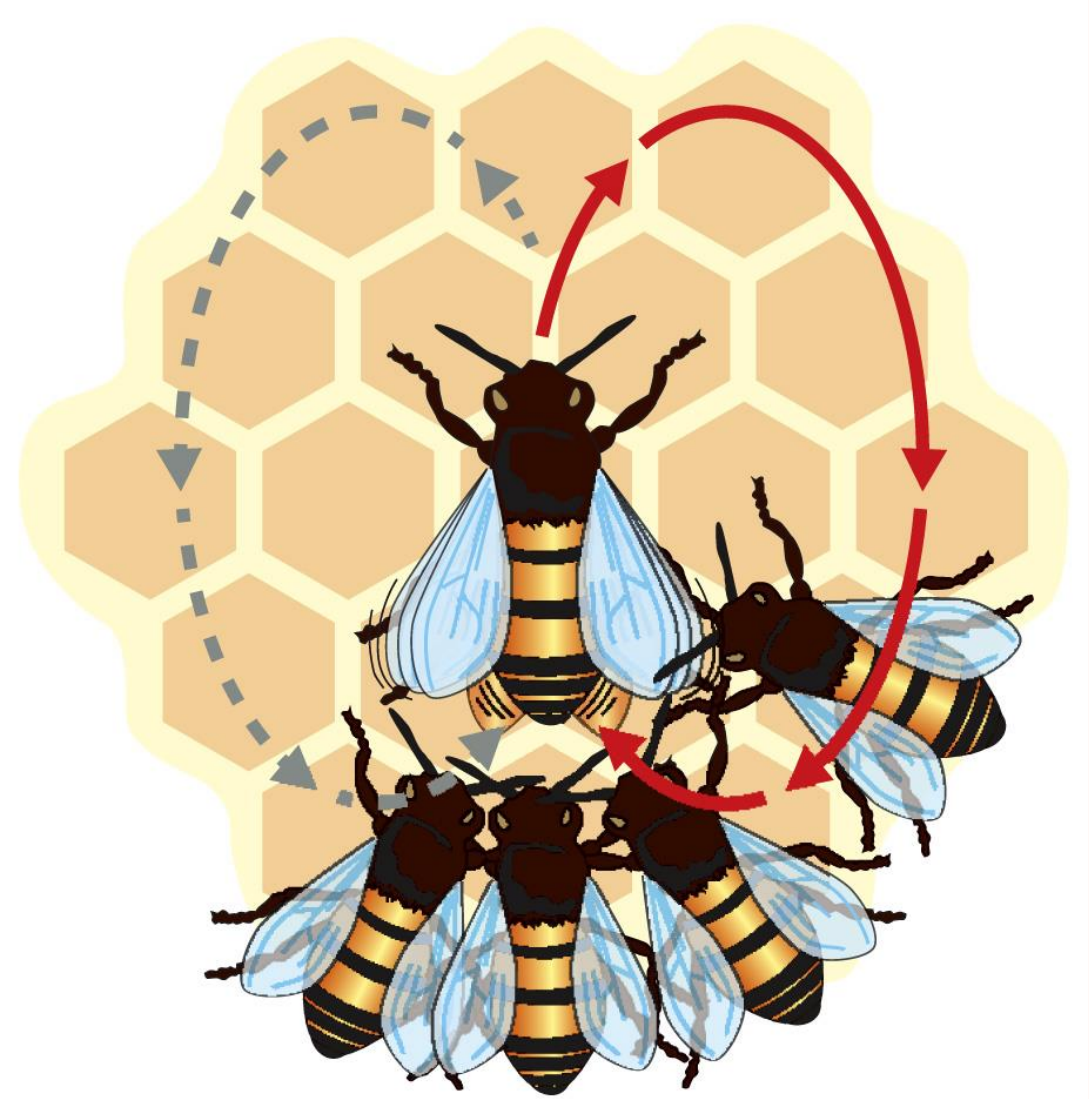

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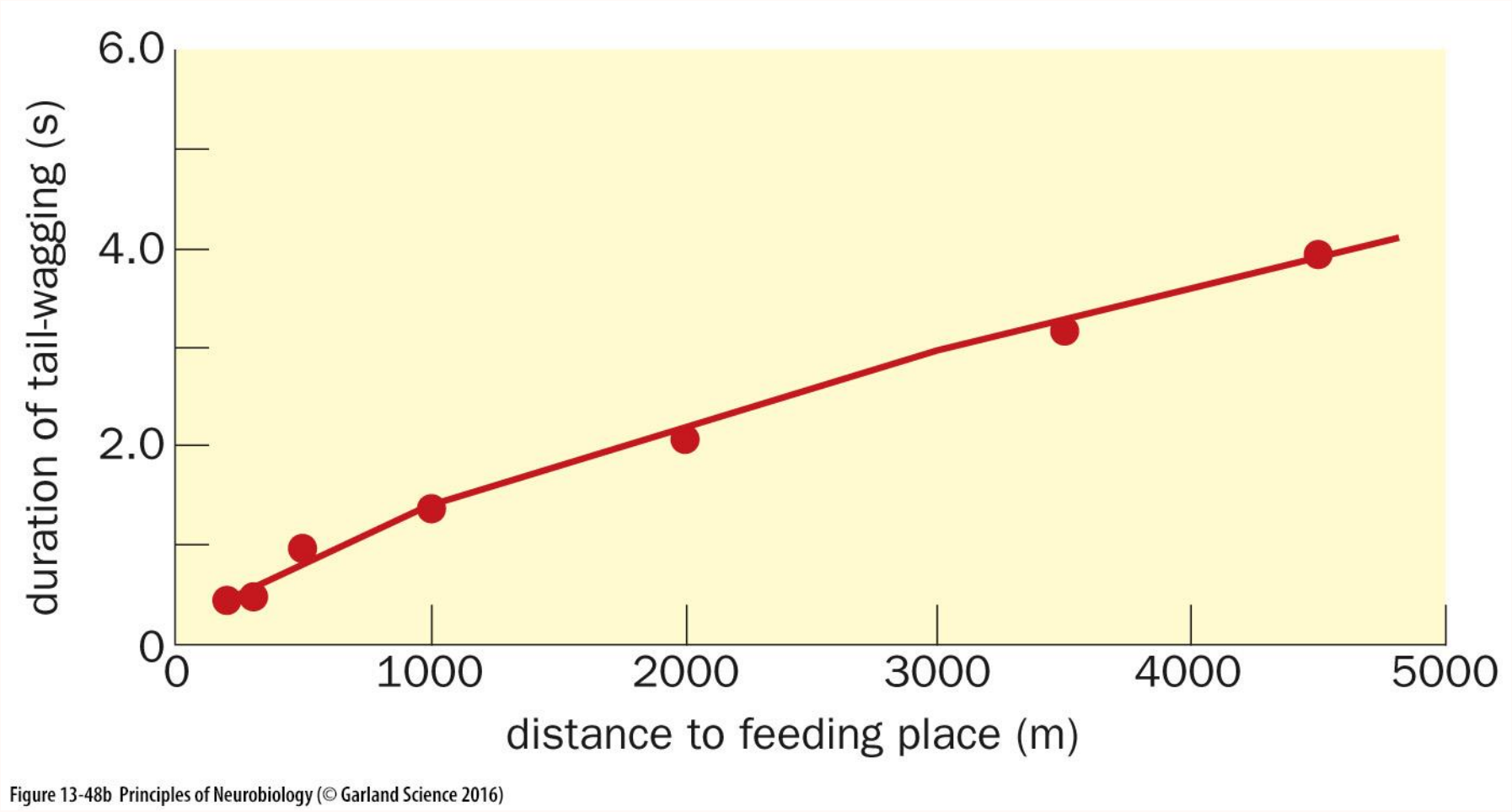

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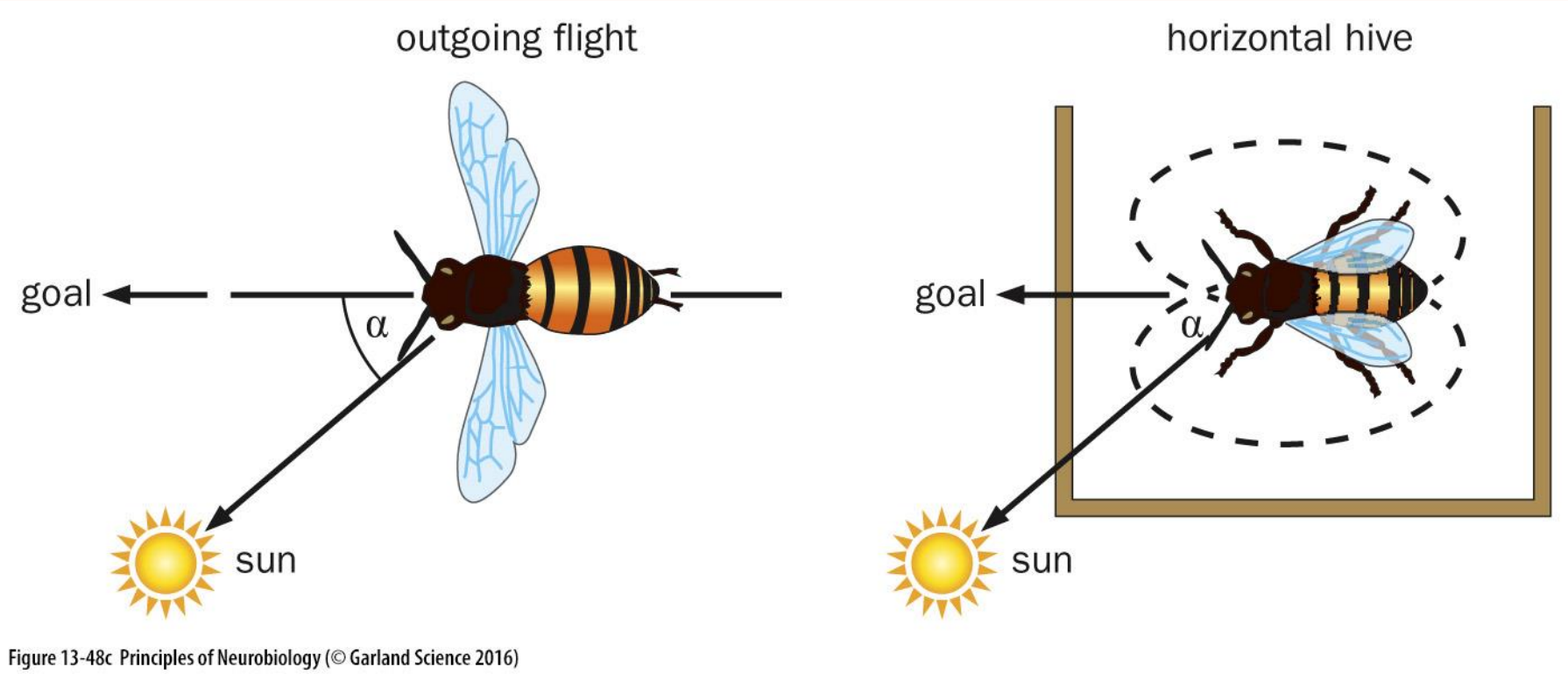

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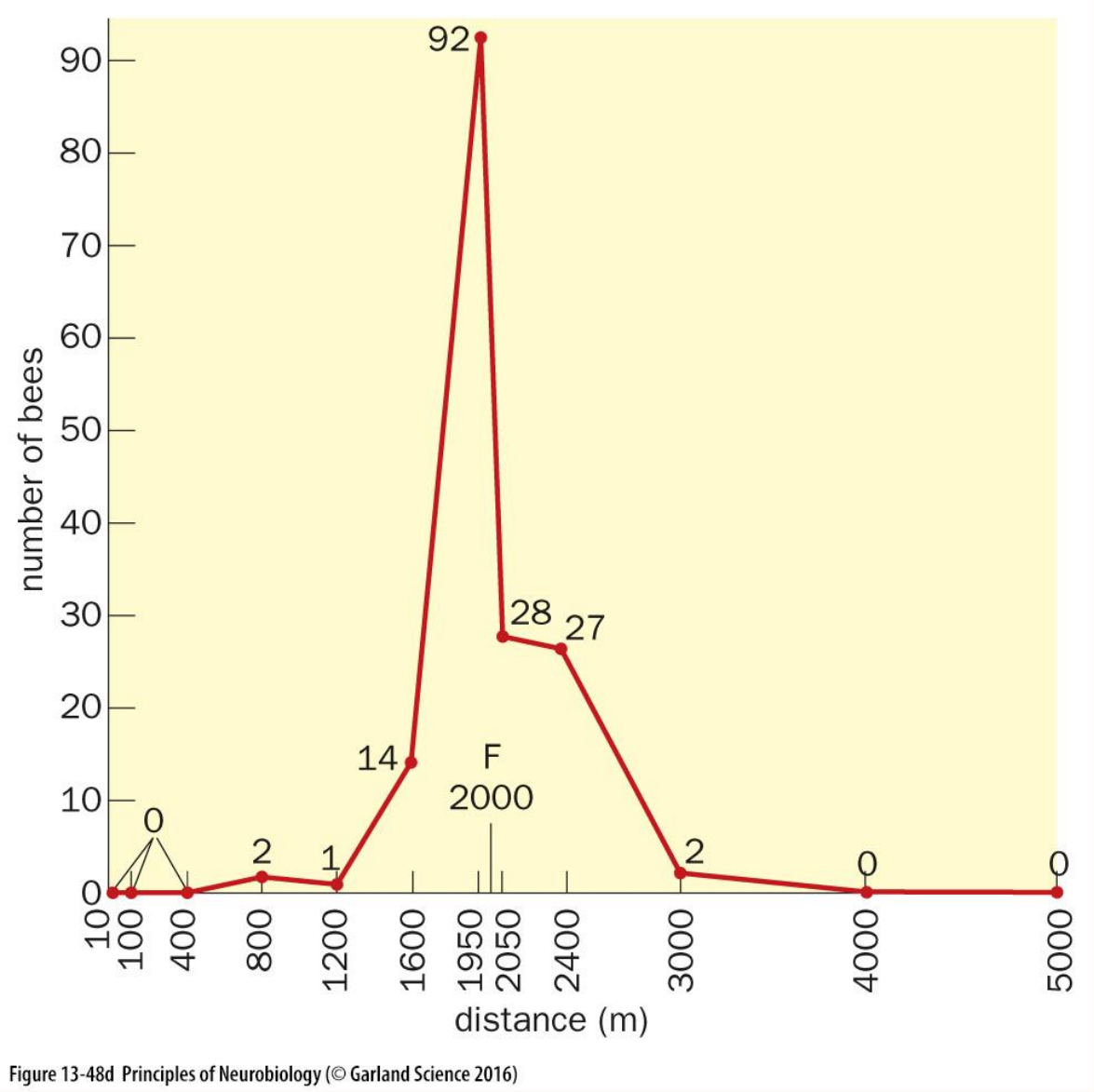

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BEHAVIORAL ANALYSES

行为分析

13.28 Studying behaviors in highly controlled conditions facilitates investigation of their neural basis

13.28 研究人为控制环境下的动物的行为有利于揭示神经基础

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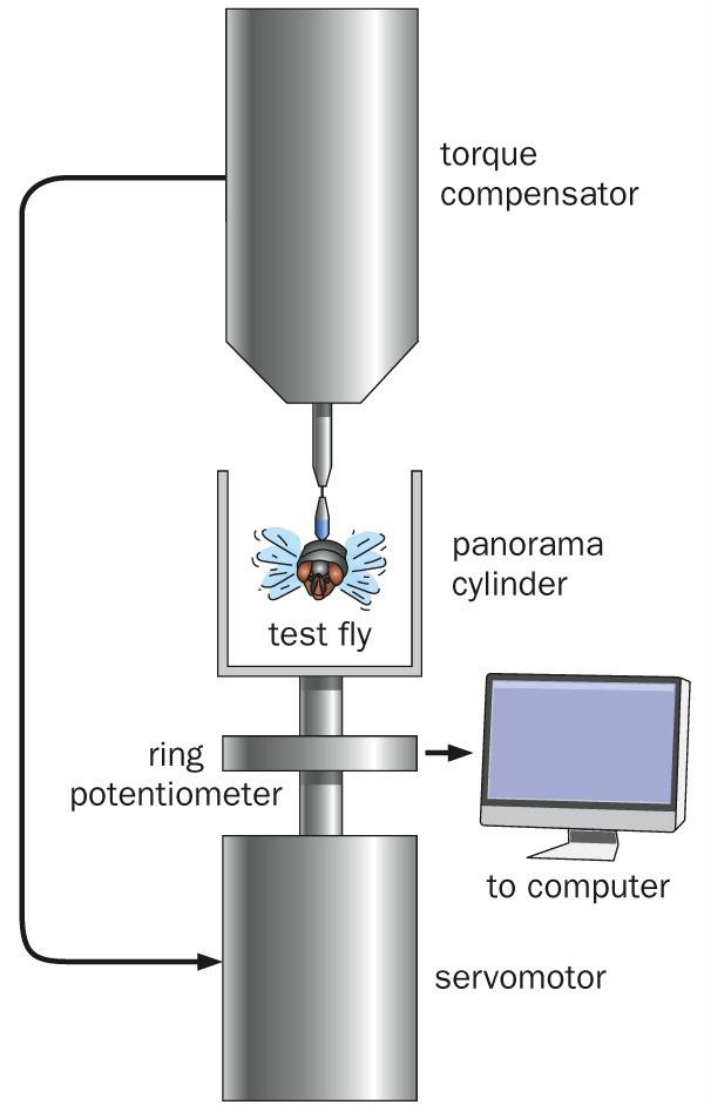

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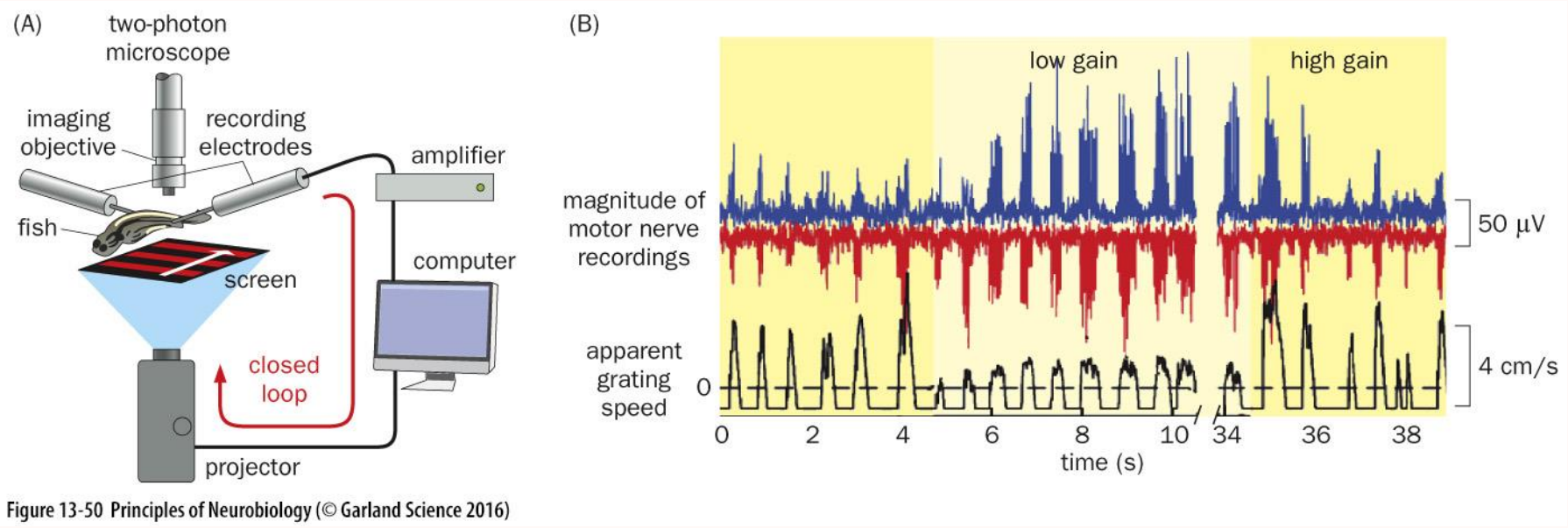

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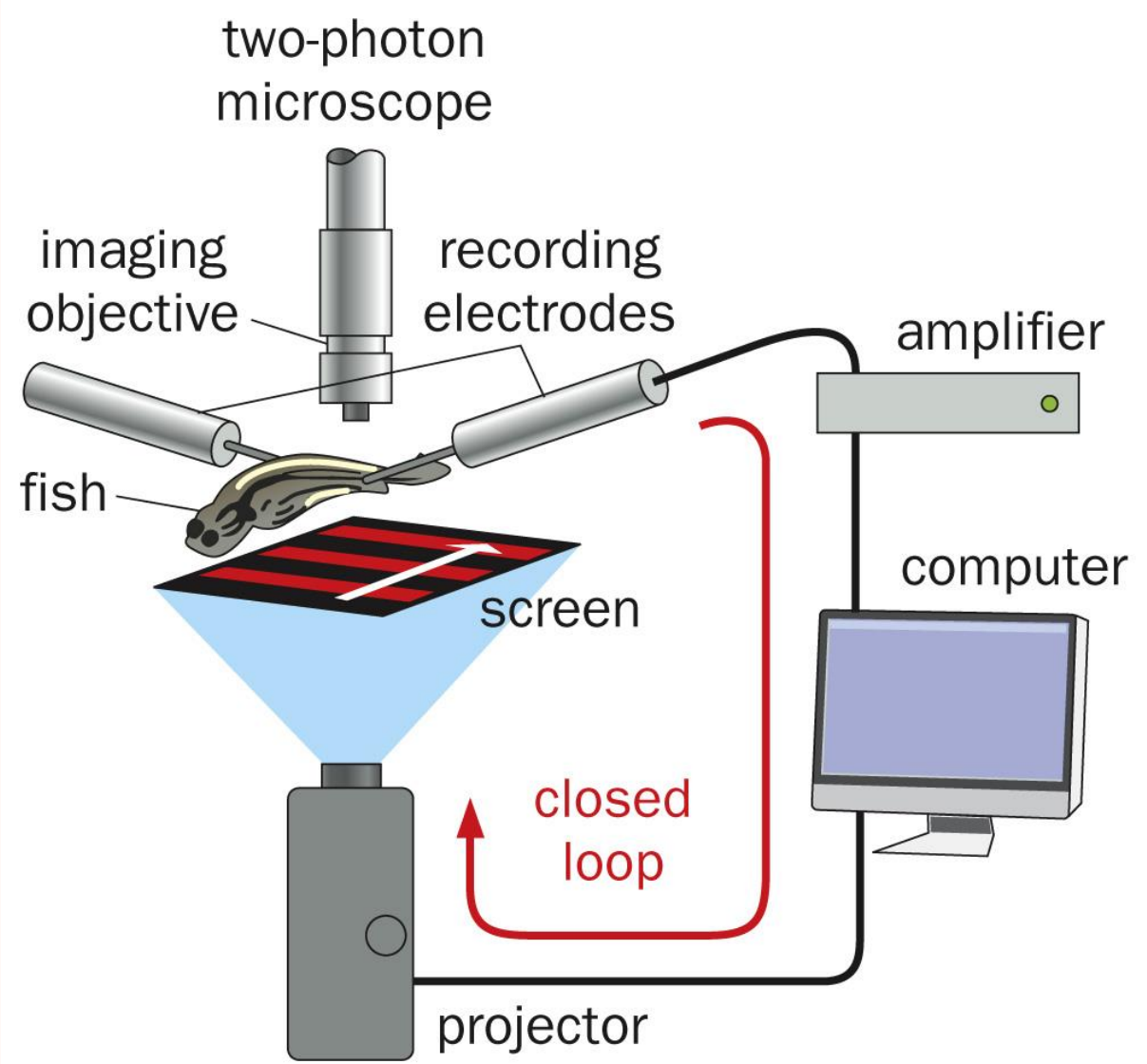

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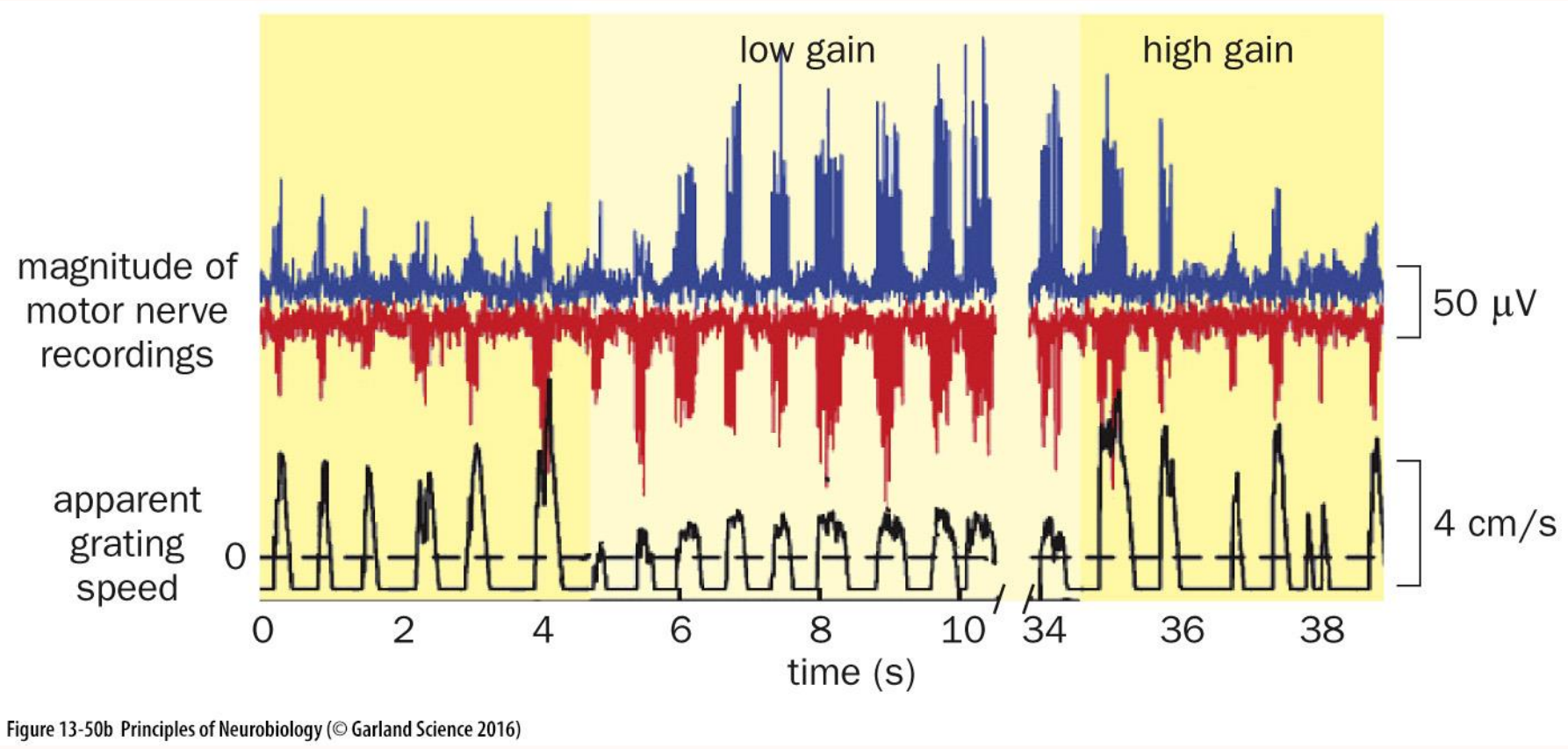

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BEHAVIORAL ANALYSES

行为分析

13.29 Behavioral assays can be used to evaluate the functions of genes and neurons and to model human brain disorders

13.29 行为学实验可以被用来评估基因和神经元的功能，模拟人类脑功能紊乱

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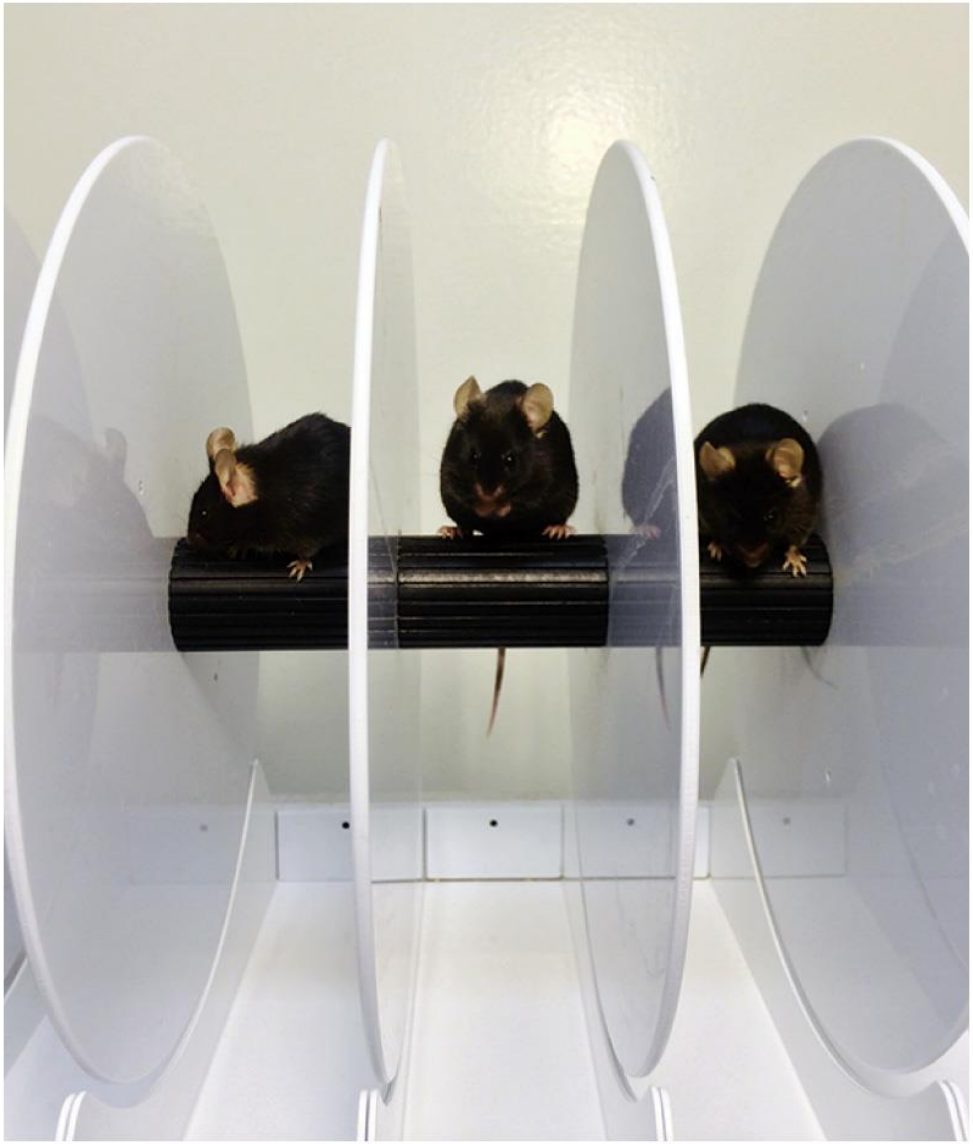

Figure 13-51 Principles of Neurobiology (© Garland Science 2016)

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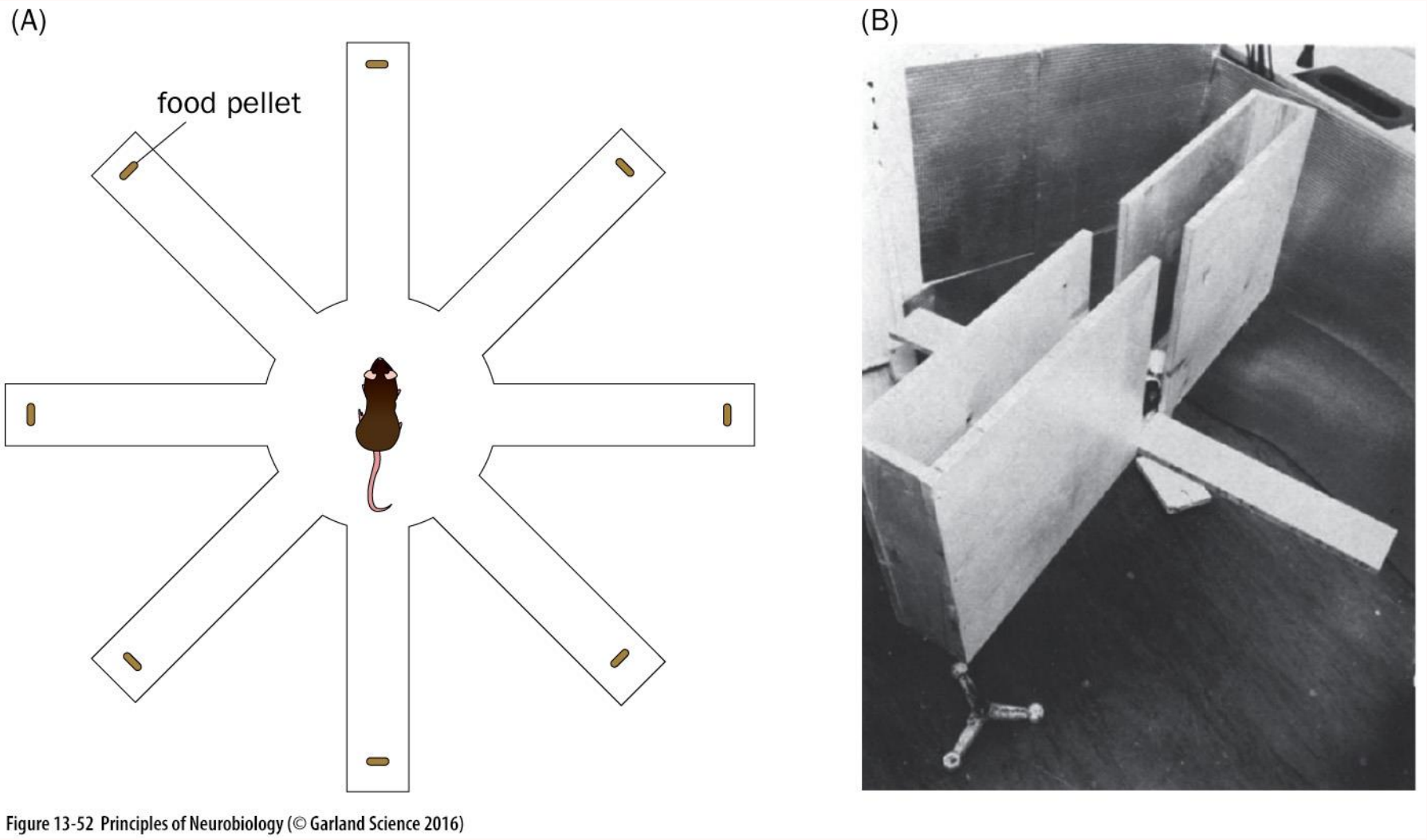

Figure 13-52 Principles of Neurobiology (© Garland Science 2016)

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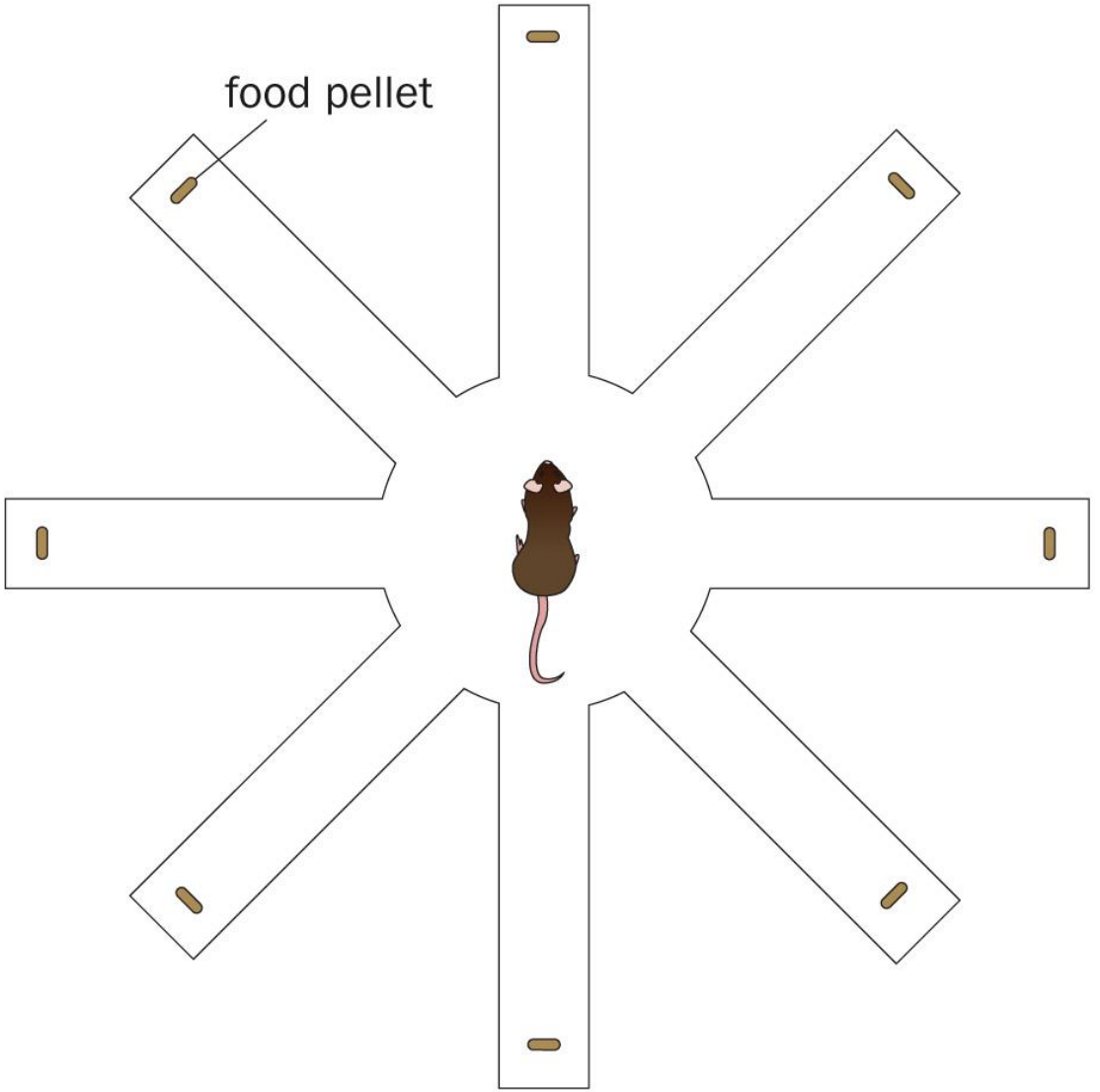

Figure 13-52a Principles of Neurobiology (© Garland Science 2016)

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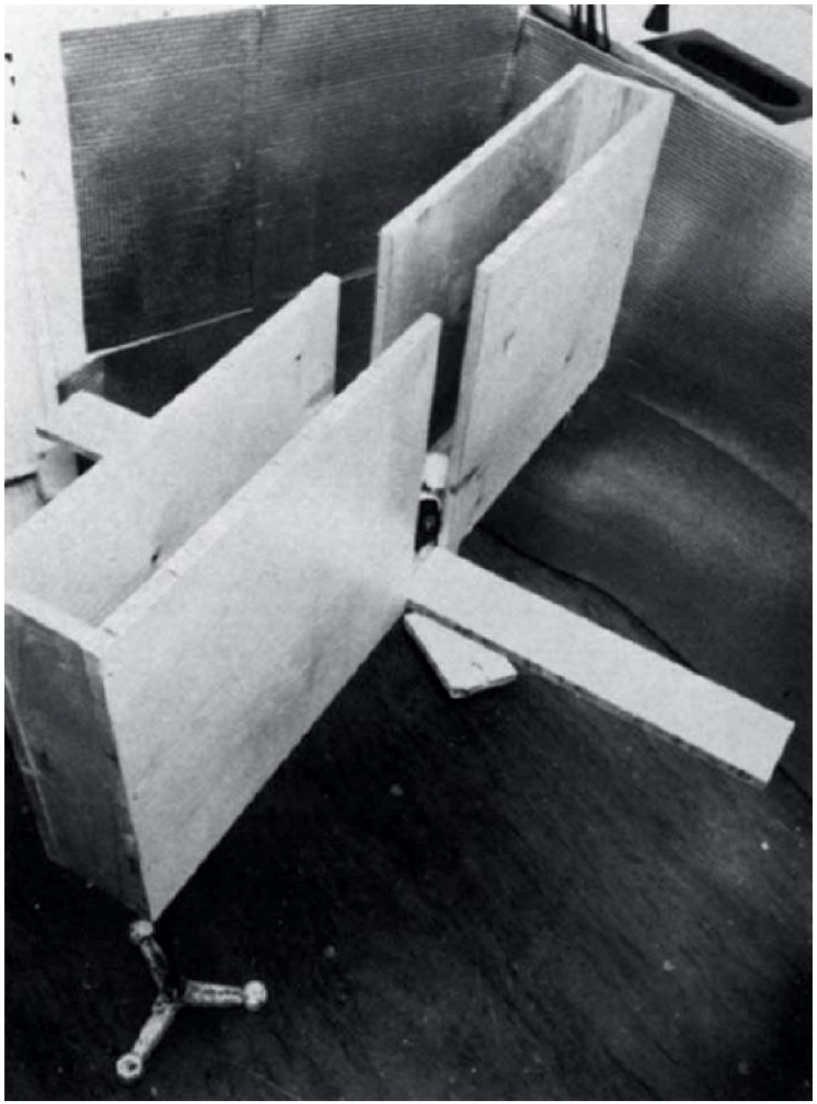

Figure 13-52b Principles of Neurobiology (© Garland Science 2016)

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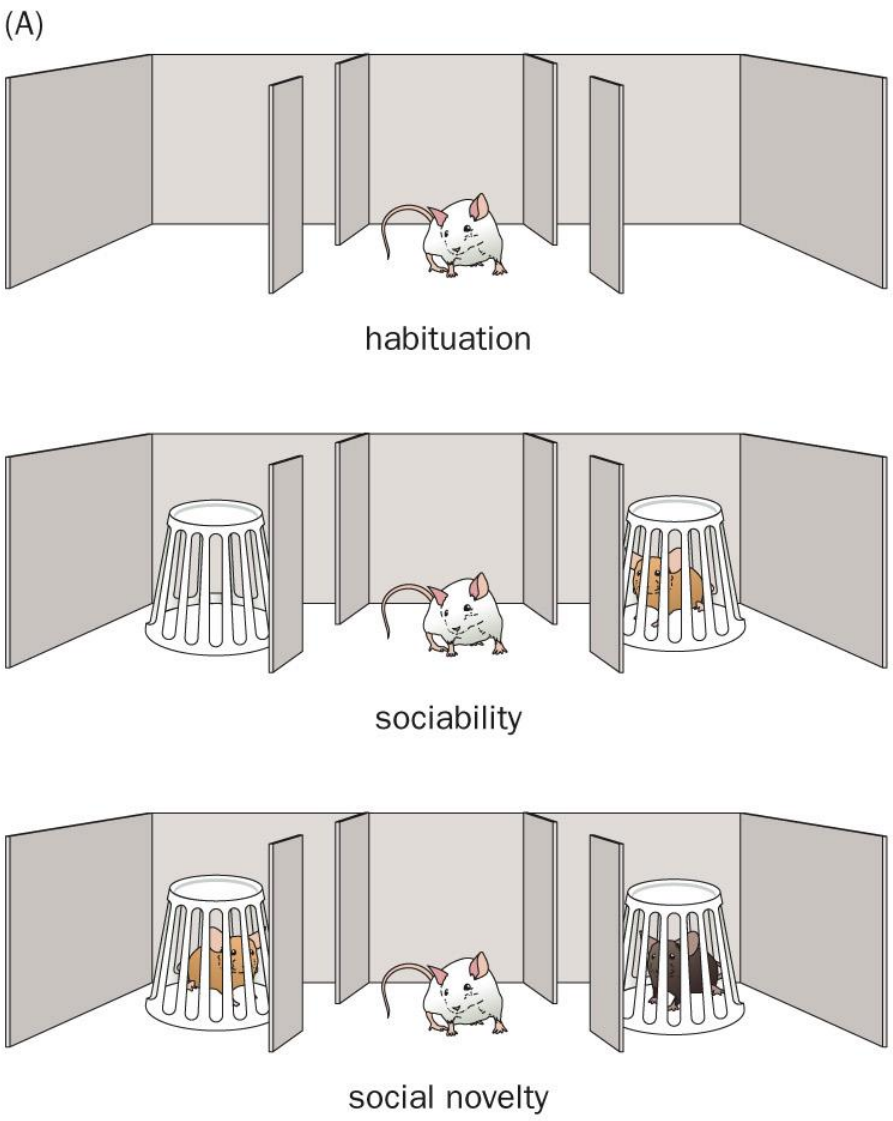

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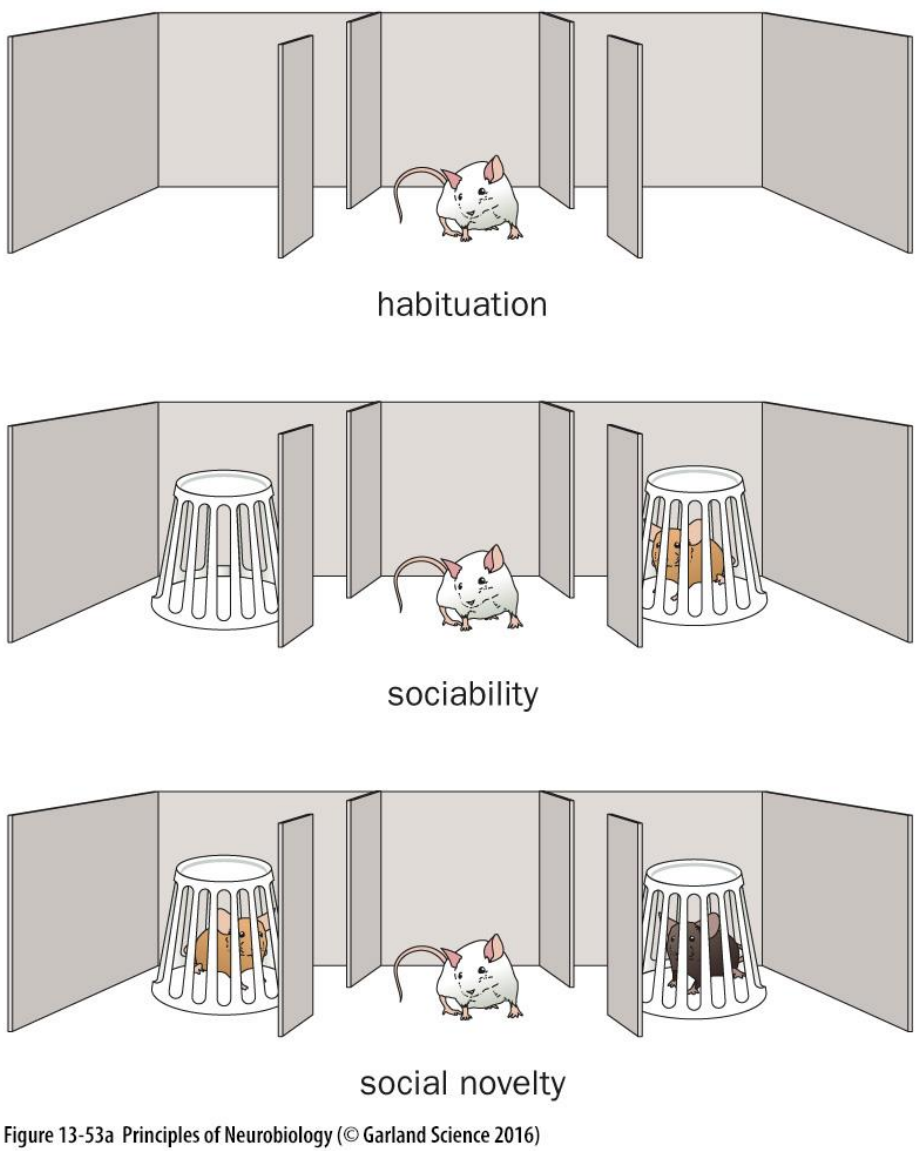

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