Advanced Cell Biology. Lecture 32

Alexey Shipunov

Minot State University

April 13th, 2011

Outline

Outline

Outline

Questions and answers

Signaling in nerve cells

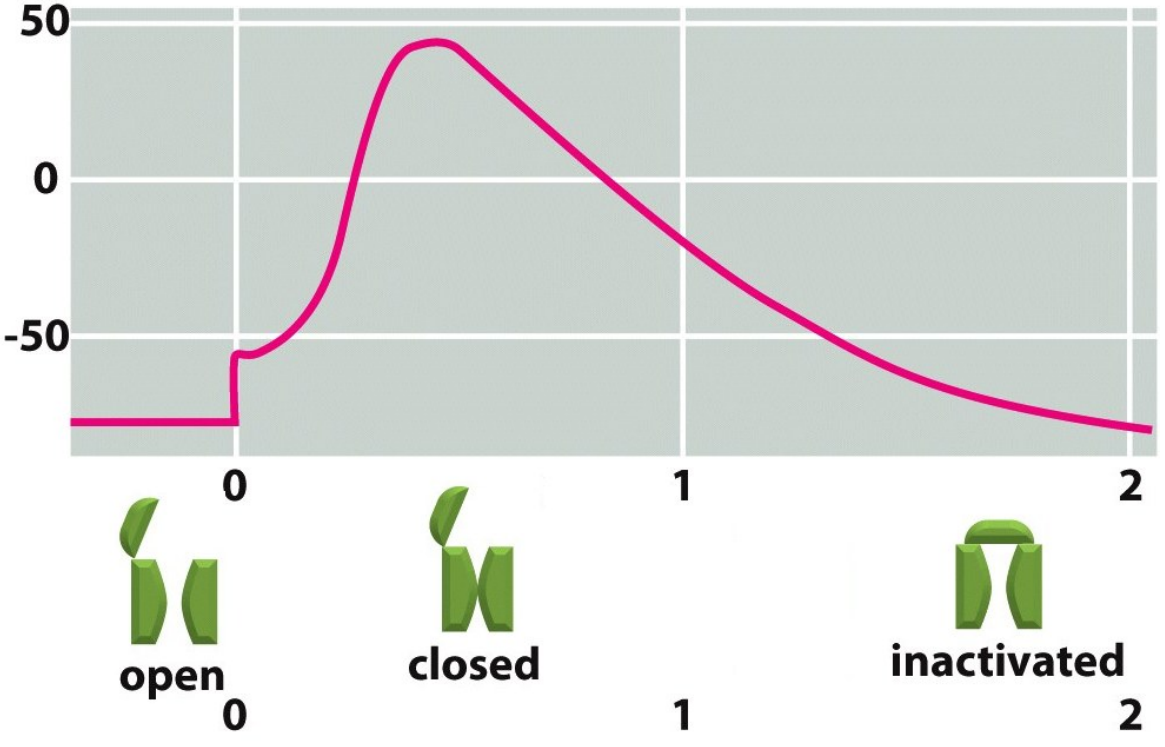
Intracellular transport

Previous final question: the answer

What is wrong in this picture?

Previous final question: the answer

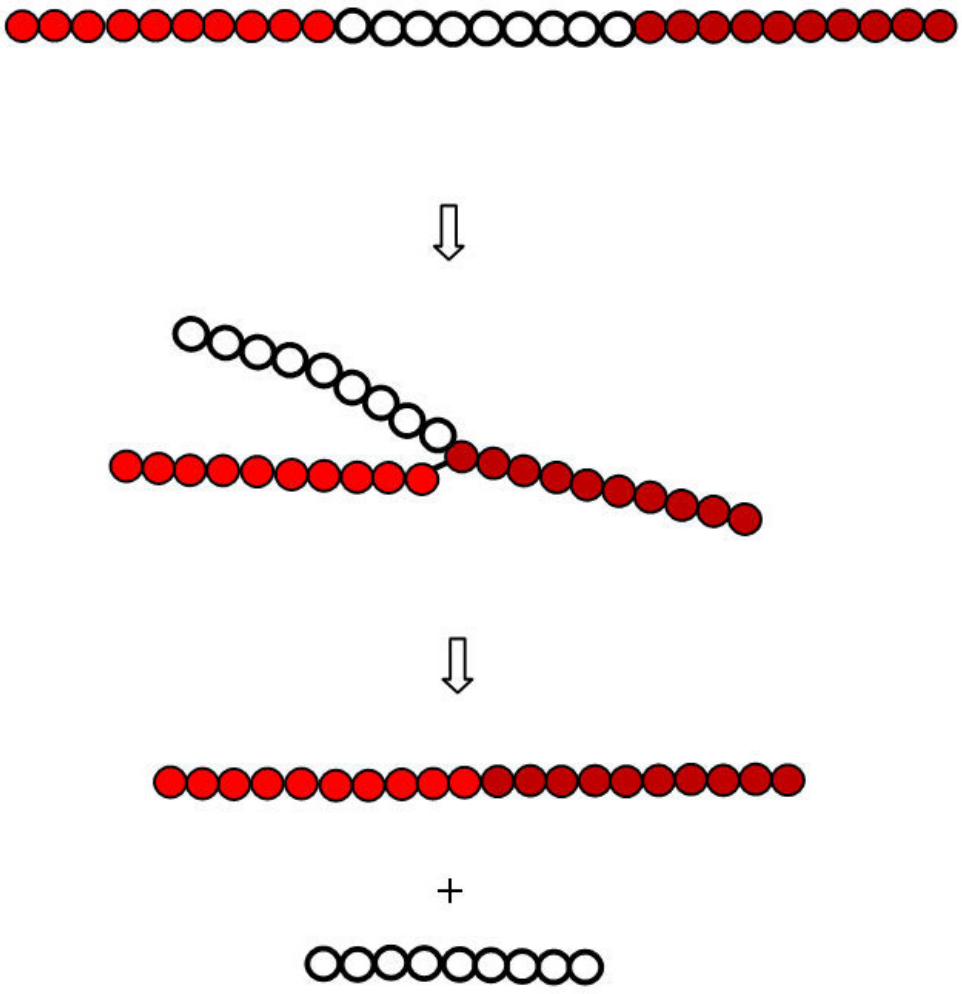
What is wrong in this picture?



Inteins: protein “introns”

- Some protein fragments may excise themselves (protein splicing)
- These fragments (inteins) may also cut DNA fragment which encodes them and move it to the different place in genome

Intein and protein splicing



Excitatory and inhibitory synapses

- Excitatory neurotransmitters (like acetylcholine, glutamate and their substitutes like ephedrine or nicotine) depolarize membrane through ligand-gated Na^+ channels
- Inhibitory neurotransmitters (like glycine or GABA) will bind to ligand-gated Cl^- channels, they open and make membrane even more polarized (hyper-polarized)
- Rich and tangled complexes of inhibition and activation receptors regulate intensity of neural signals

Excitatory and inhibitory synapses

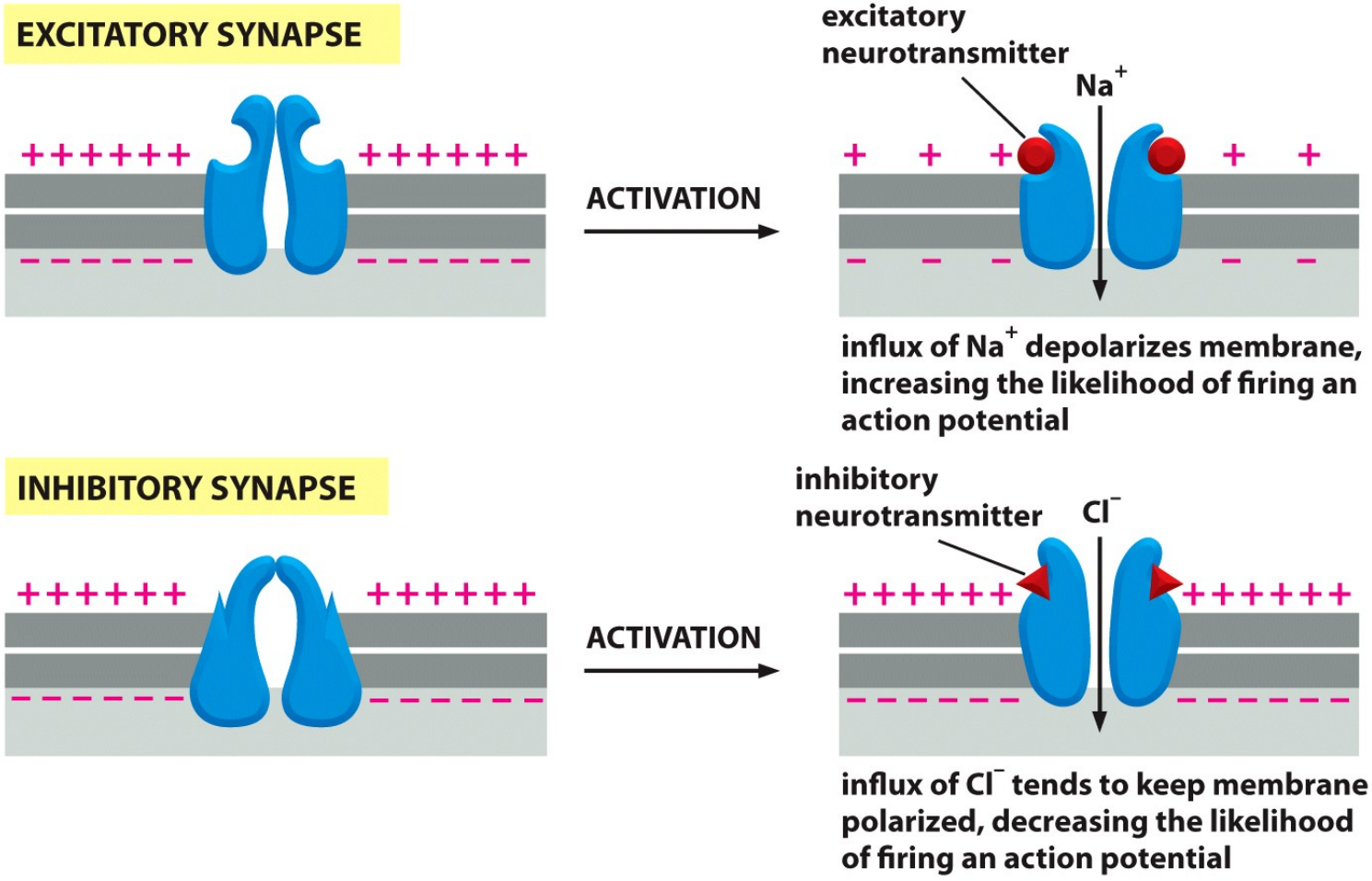


Figure 12-44 Essential Cell Biology 3/e (© Garland Science 2010)

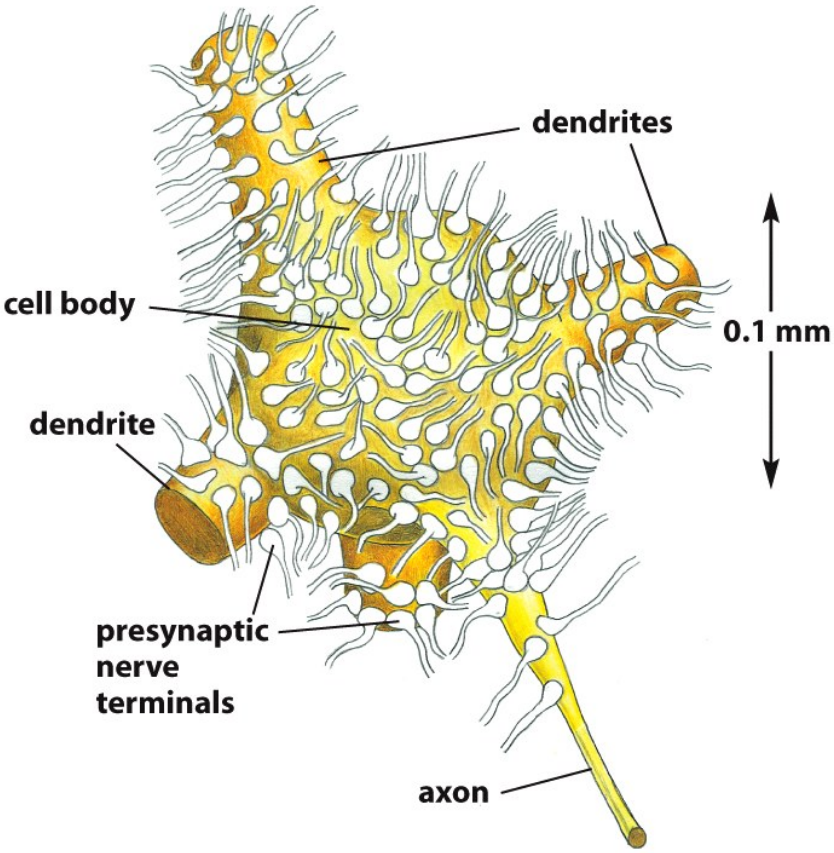
Drunkenness

- Alcohol potentiating the specific γ-2L subunit of the inhibitory GABA receptor
- Inhibits the release of activatory neurotransmitters—glutamate and acetylcholine
- Stimulate release of endorphins (which in turn activate release of dopamine), resulting in suppressing pain and euphoria

Strychnine poisoning

- Strychnine permanently attaches to glycine receptors
- As a result, signals will not be lowered with inhibition

Synaptic complex



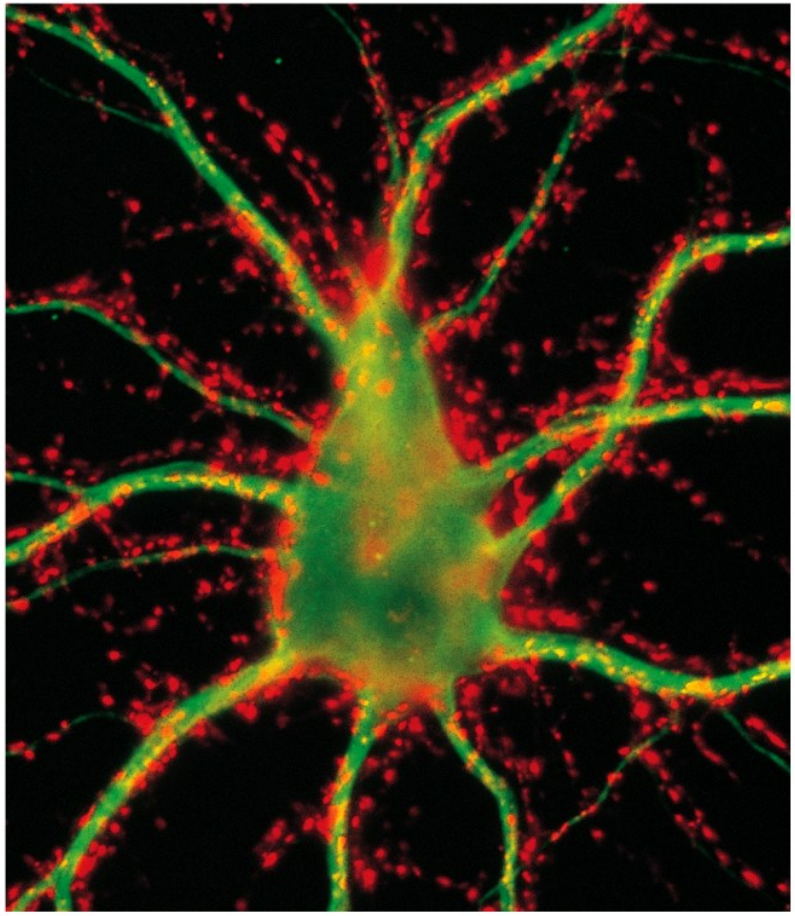


Figure 12-45 Essential Cell Biology 3/e (© Garland Science 2010)

Diversity of ion channels

TABLE 12–3 SOME EXAMPLES OF ION CHANNELS

ION CHANNEL	TYPICAL LOCATION	FUNCTION
K^+ leak channel	plasma membrane of most animal cells	maintenance of resting membrane potential
Voltage-gated Na^+ channel	plasma membrane of nerve cell axon	generation of action potentials
Voltage-gated K^+ channel	plasma membrane of nerve cell axon	return of membrane to resting potential after initiation of an action potential
Voltage-gated Ca^{2+} channel	plasma membrane of nerve terminal	stimulation of neurotransmitter release
Acetylcholine receptor (acetylcholine-gated Na^+ and Ca^{2+} channel)	plasma membrane of muscle cell (at neuromuscular junction)	excitatory synaptic signaling
Glutamate receptors (glutamate-gated Na^+ and Ca^{2+} channels)	plasma membrane of many neurons (at synapses)	excitatory synaptic signaling
GABA receptor (GABA-gated Cl^- channel)	plasma membrane of many neurons (at synapses)	inhibitory synaptic signaling
Glycine receptor (glycine-gated Cl^- channel	plasma membrane of many neurons (at synapses)	inhibitory synaptic signaling
Stress-activated cation channel	auditory hair cell in inner ear	detection of sound vibrations

Membrane-enclosed organelles

- Why eukaryotes need them?
- Cytosol (54% of cell volume), nucleus (12), mitochondria (22), chloroplasts, ER (12), GA (3), lysosomes, endosomes, peroxisomes and small vesicles

Origin of membrane organelles

- Endogenous (e.g., invagination of plasma membrane)
- Symbiotic

Protein sorting: mechanisms of import

- Nuclear pores
- Across membranes
- By vesicles

Signal sequences

- Small sequences of amino acids which indicate where to put this protein
- This works almost exactly like destination block in TCP/IP package!
- Cell enzymes may insert and remove signal sequences

Signal sequences

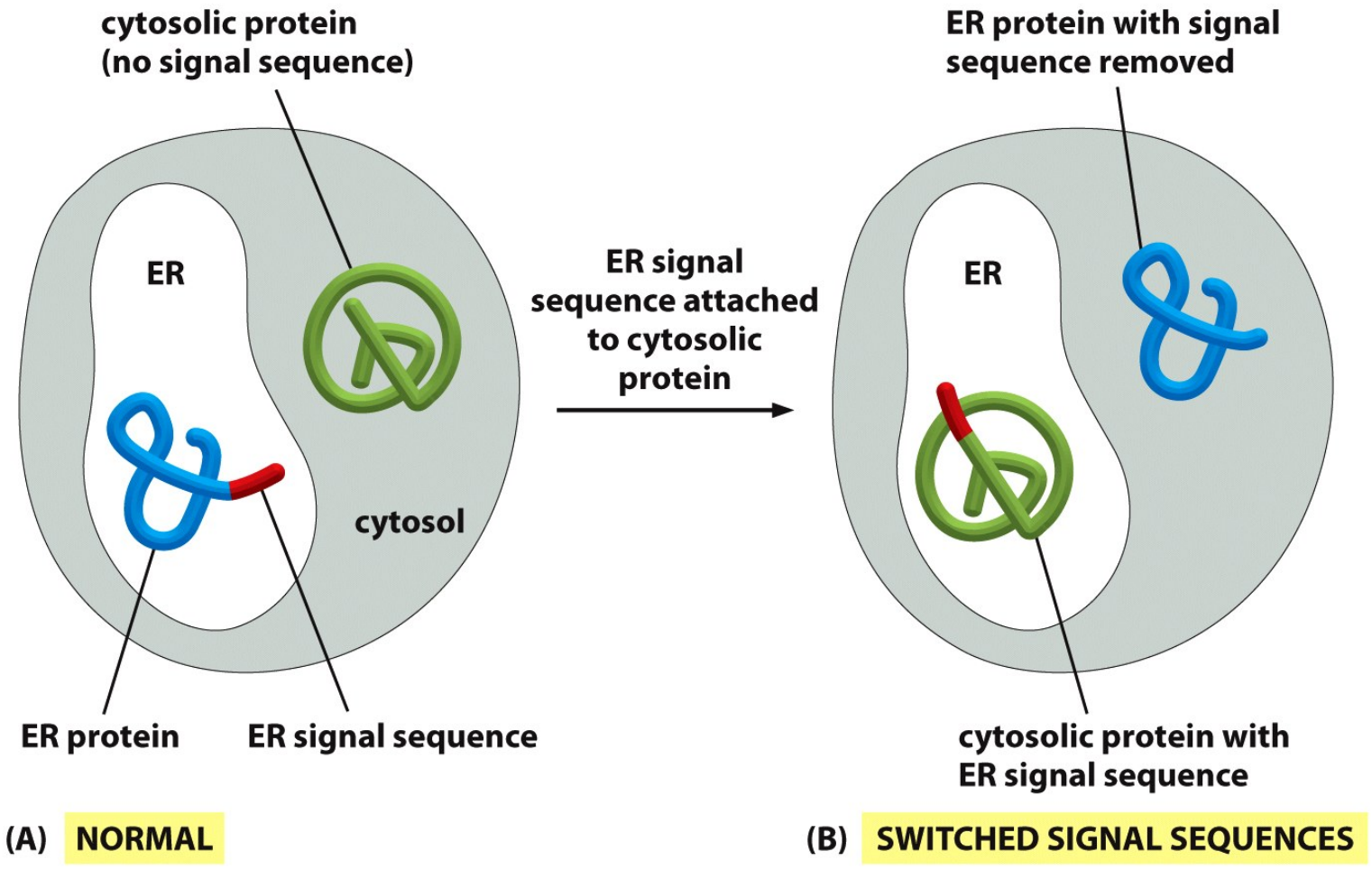


Figure 15-6 Essential Cell Biology 3/e (© Garland Science 2010)

Different signal sequences

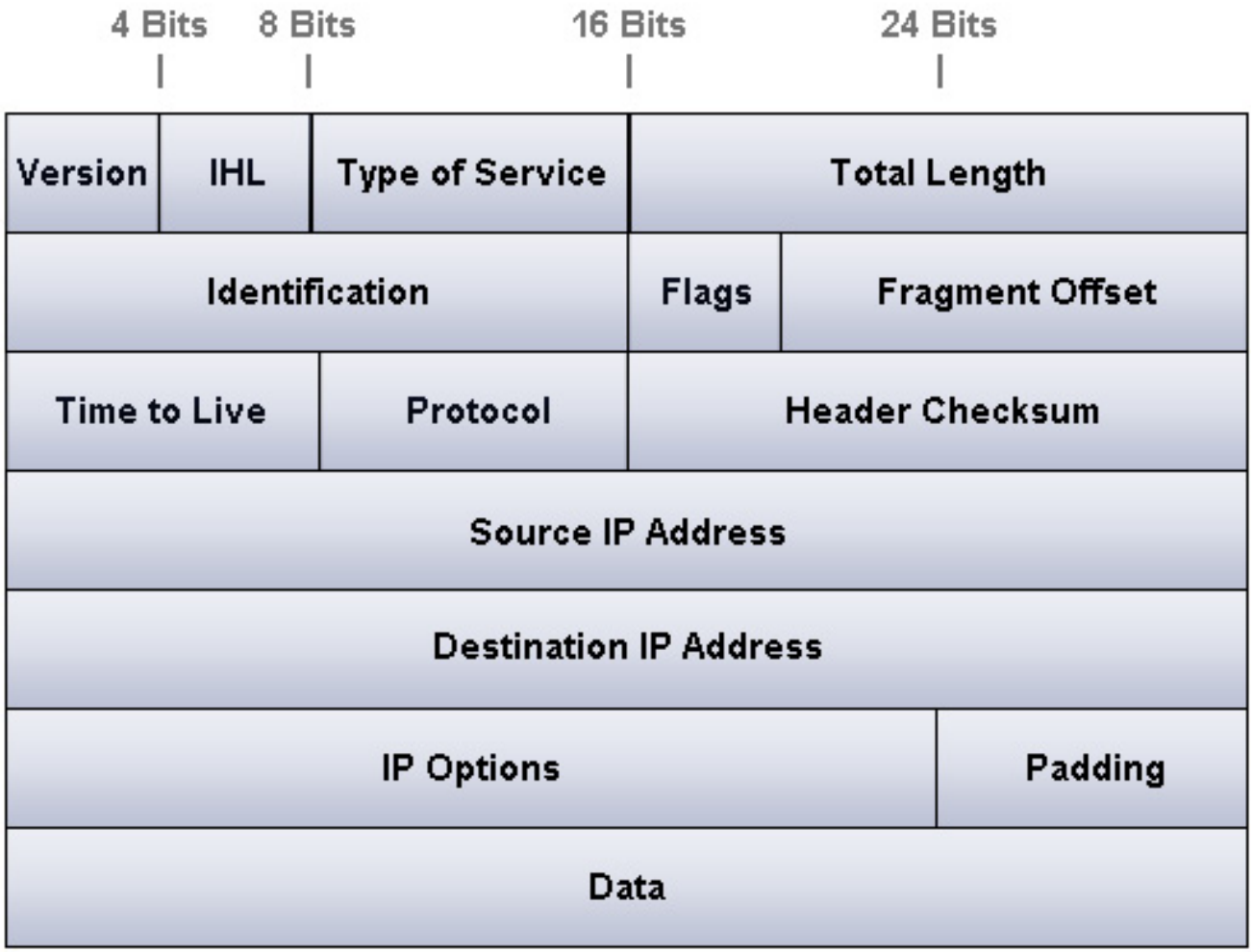
TABLE 15–3 SOME TYPICAL SIGNAL SEQUENCES

FUNCTION OF SIGNAL	EXAMPLE OF SIGNAL SEQUENCE
Import into ER	$^{+}H_3N$-Met-Met-Ser-Phe-Val-Ser-Leu-Leu-Leu-Val-Gly-Ile-Leu-Phe-Trp-Ala-Thr-Glu-Ala-Glu-Gln-Leu-Thr-Lys-Cys-Glu-Val-Phe-Gln-
Retention in lumen of ER	-Lys-Asp-Glu-Leu-COO^{-}
Import into mitochondria	$^{+}H_3N$-Met-Leu-Ser-Leu-Arg-Gln-Ser-Ile-Arg-Phe-Phe-Lys-Pro-Ala-Thr-Arg-Thr-Leu-Cys-Ser-Ser-Arg-Tyr-Leu-Leu-
Import into nucleus	-Pro-Pro-Lys-Lys-Lys-Arg-Lys-Val-
Import into peroxisomes	-Ser-Lys-Leu-

Positively charged amino acids are shown in *red*, and negatively charged amino acids in *blue*. An extended block of hydrophobic amino acids is shown in *green*. $^{+}H_3N$ indicates the N-terminus of a protein; COO^{-} indicates the C-terminus. The ER retention signal is commonly referred to by its single-letter amino acid abbreviation, KDEL.

Table 15-3 Essential Cell Biology 3/e (© Garland Science 2010)

TCP/IP package header



Nuclear import

- Nucleus needs many proteins which are synthesized in cytoplasm
- Inner nuclear membrane binds chromosome-binding proteins and also nuclear lamina
- Outer membrane is normally continuous with ER

Nuclear pore

- Large, complicated structure of ≈30 proteins
- Some formed passages for small molecules, some participate in floating structures, some form a central channel with meshwork in the middle
- Cytoplasmic fibrils and nuclear basket fibrils are proteins located around the entrance of pore

Nuclear pore

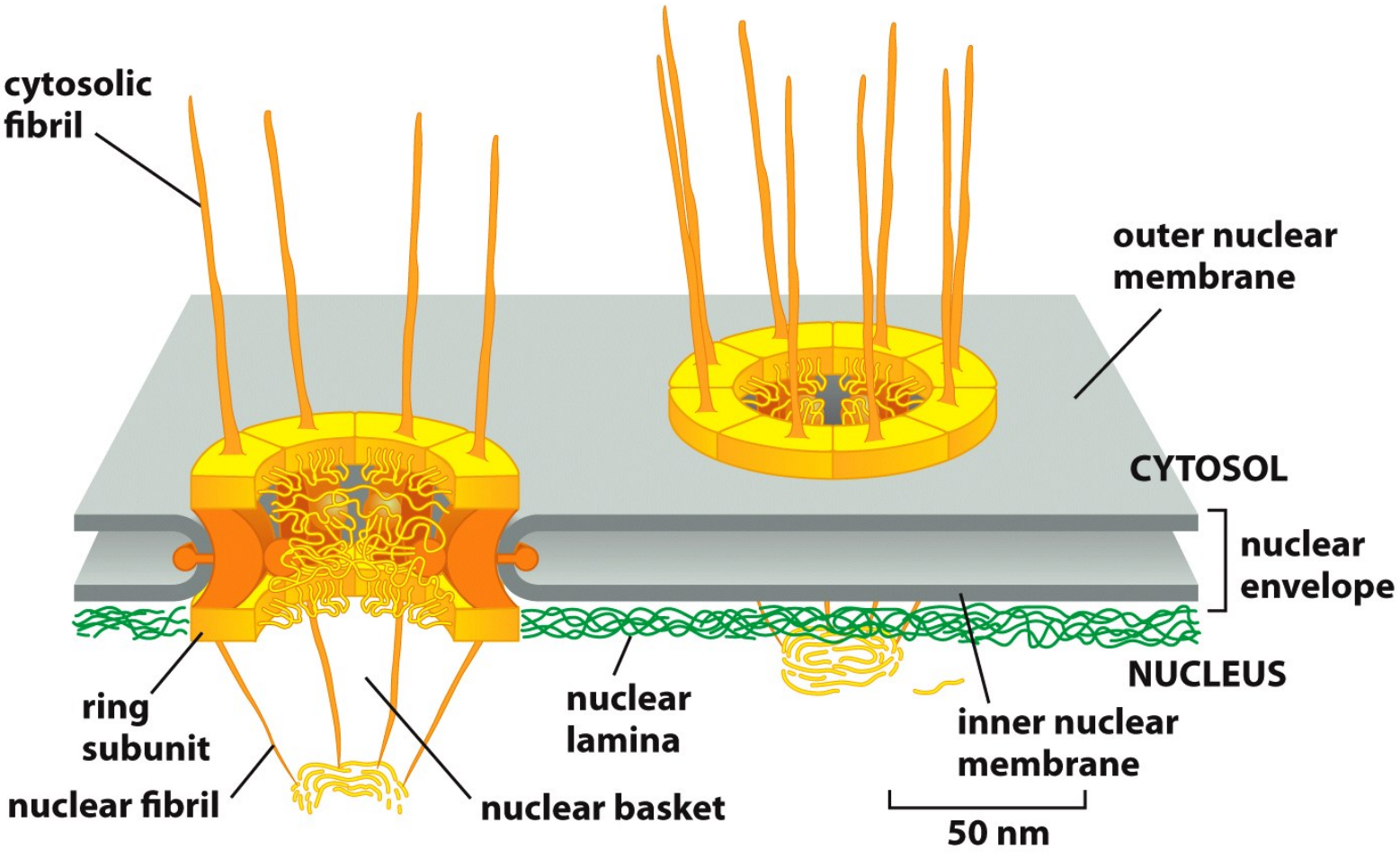


Figure 15-8a Essential Cell Biology 3/e (© Garland Science 2010)

Nuclear transport cycle

- Cargo proteins bind with nuclear transport receptor proteins and go through pore
- Then Ran-GTP protein binds to transport receptor protein, replaces cargo and complex go back to outer cytoplasm
- GTP hydrolyzes to GDP and phosphate, Ran-GDP dissociates, energy used for binding new cargo protein

Nuclear transport: general view

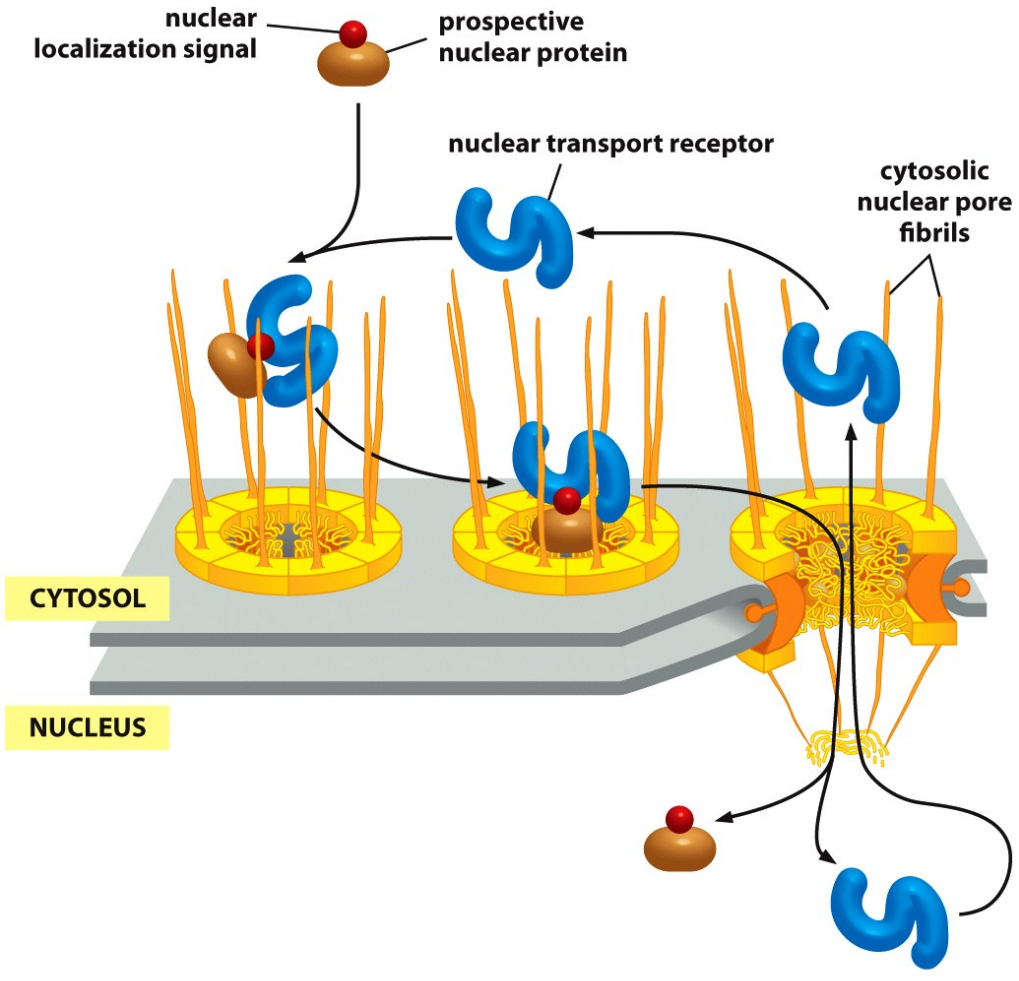


Figure 15-9 Essential Cell Biology 3/e (© Garland Science 2010)

Nuclear transport cycle: detailed view

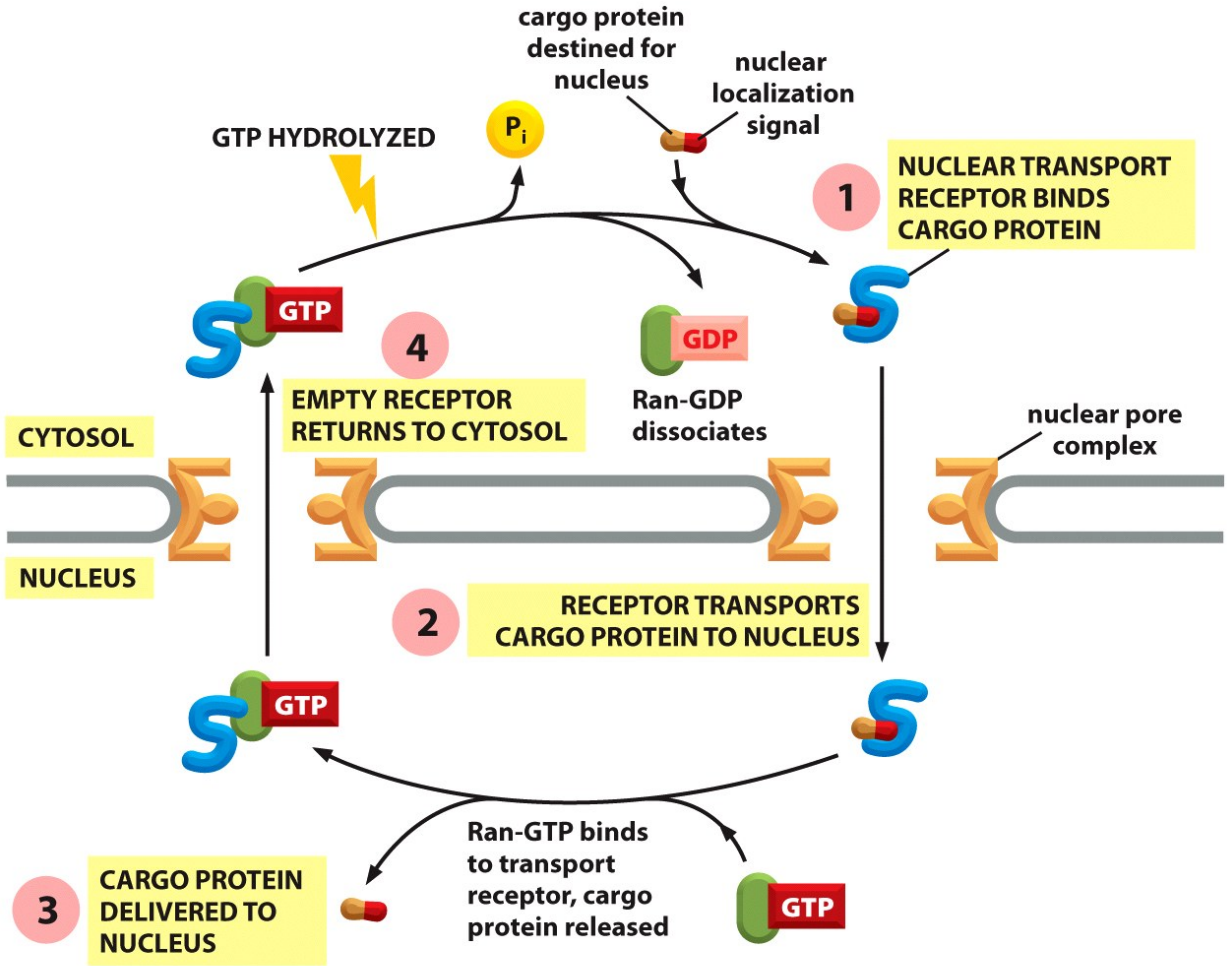


Figure 15-10 Essential Cell Biology 3/e (© Garland Science 2010)

Minot State UNIVERSITY

Final question (1 point)

Final question (1 point)

What will happen to cytosol protein, if it has no signal sequence?

Summary

- Effects of drugs and narcotics are often due to complex interaction with different synapses in different synaptic complexes
- Membrane organelles have two different origins
- Moved protein bears signal sequence which corresponds with destination
- Nuclear pore transport is a cyclic process involving Ran-GTP and nuclear transport receptor

For Further Reading

A. Shipunov.
Advanced Cell Biology [Electronic resource].
2011—onwards.
Mode of access: `http://ashipunov.info/shipunov/school/biol_250`.

B. Alberts et al.
Essential Cell Biology. 3rd edition.
Garland Science, 2009.
Chapter 15: 495–505.