SysCon iitb Systems & Control

Home | People | Academics | Research | Events | FAQ's | Contact Us

Welcome to Systems & Control Engineering

Room Booking Status

#103 - Class Room

#104 - Seminar Room

#301 - ARMS Lab

3D Printer Schedule

The Systems and Control group, formed in 1977, is a unique interdisciplinary program in the country that offers post-graduate education in the broad area of Systems and Control. The Ten faculty members of the group have varied research backgrounds, that includes nonlinear control, robotics, path-planning, embedded control, coordination of autonomous vehicles, multi-agent systems, game theory, information theory, combinatorics, sliding mode control and applications, fractional-order modelling and control, optimization and optimization-based control, and stochastic processes. Other faculty members of the institute with an interest in the field also participate in the activities of the group. The alumni of the group are employed in many reputed academic institutes, ISRO/DRDO and research laboratories, and corporate R & D units of the country.

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www.sc.iitb.ac.in

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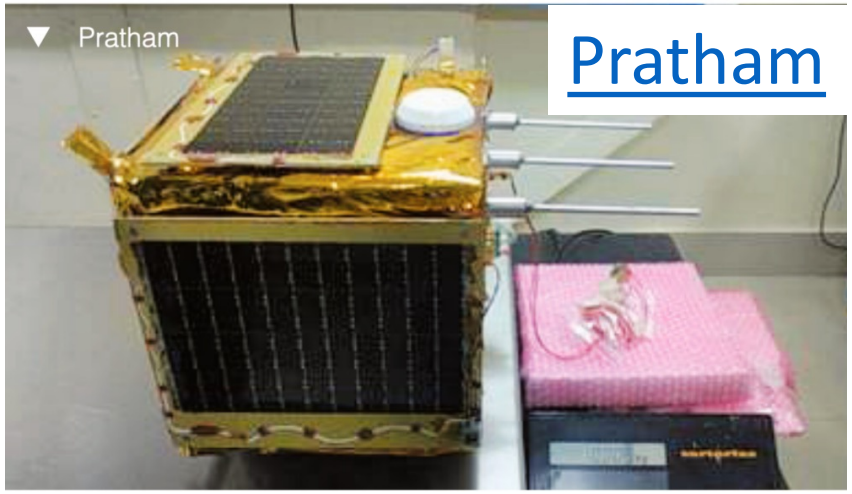
Autonomous units built by IIT Bombay students (except one!)

Matsya

Rakshak

??



Pratham

IGV

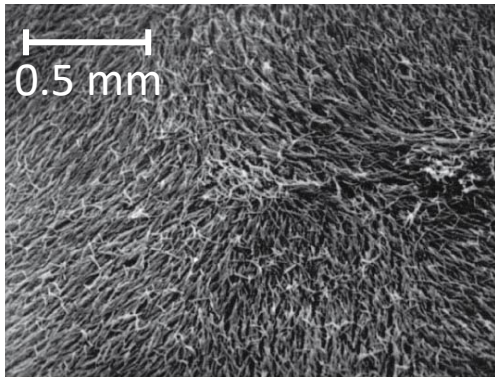
SeDriCa

Is communication important in these engineered systems?

Figure titles are hyperlinked to respective web pages.

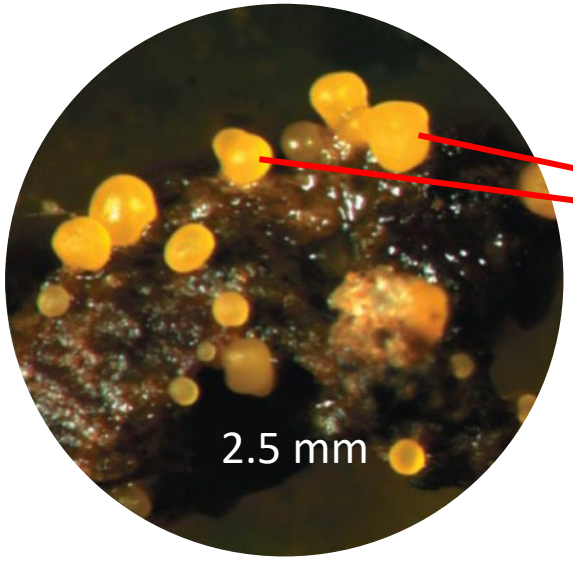
Yeast (shown in false color in an electron micrograph) is from https://www.sciencenews.org/article/yeast-life-span-calorie-restriction-may-be-wash

Signaling in unicellular organisms



Individual rod shaped cells

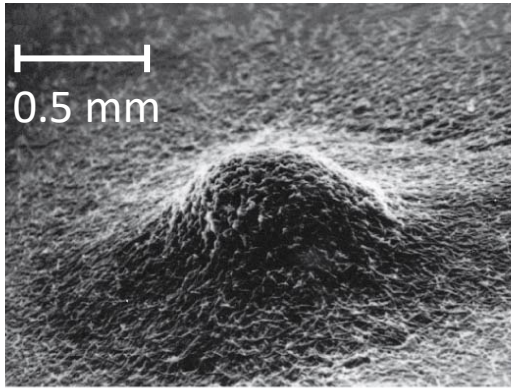
favorable conditions



Fruiting bodies (spores)

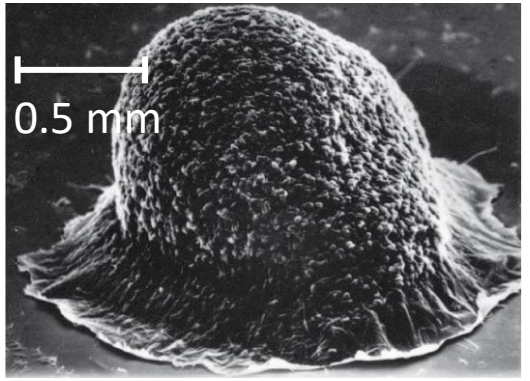
Nutrient scarcity

Starving cells send out a chemical signal



Aggregation in progress

Cells collectively form fruiting body



Spore-forming structure (fruiting body)

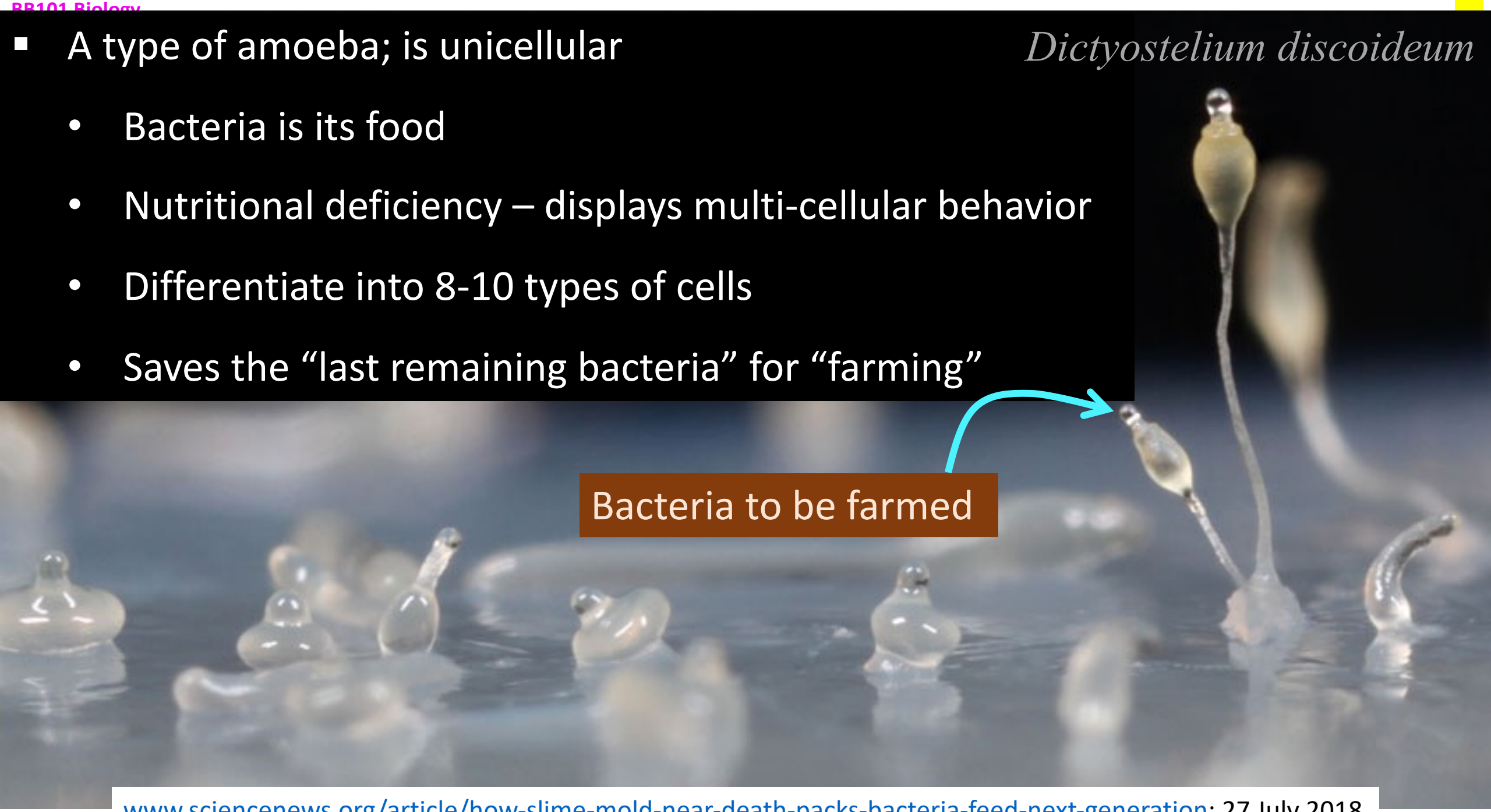
Soil-dwelling bacteria *Myxococcus xanthus*

Figure 11.3 in Campbell Biology by Reece et al., (10th edition)

- A type of amoeba; is unicellular

Dictyostelium discoideum

  - Bacteria is its food
  - Nutritional deficiency – displays multi-cellular behavior
  - Differentiate into 8-10 types of cells
  - Saves the “last remaining bacteria” for “farming”



www.sciencenews.org/article/how-slime-mold-near-death-packs-bacteria-feed-next-generation; 27 July 2018

Today's topics

- Example of cell communication: quorum sensing
- Signal transduction in eukaryotes – an overview
- G-proteins
- Signal amplification
- Signaling mechanisms in living systems

Dictionary

English

Definitions from Oxford Languages · Learn more

quorum

noun

the minimum number of members of an assembly or society that must be present at any of its meetings to make the proceedings of that meeting valid.

Quorum (pronounced as ko-rum)

- Bacteria are capable of quorum sensing!
  - Regulate gene expression depending upon cell-population density
- Quorum sensing is widespread among prokaryotes and eukaryotes
- The general mechanism is evolutionarily conserved and serves a variety of physiological purposes

Bioluminescence

- Quorum-sensing is extensively studied in the bacteria *Vibrio fischeri*
- Luminescence: emission of light by a substance that is not heated
  - Lux: unit of luminescence
- Genes involved in bioluminescence are named as lux genes
- Gene names: italics + all letters in lower case
  - Encoded proteins: normal font + first letter in upper case

Some seawater bacteria emit light

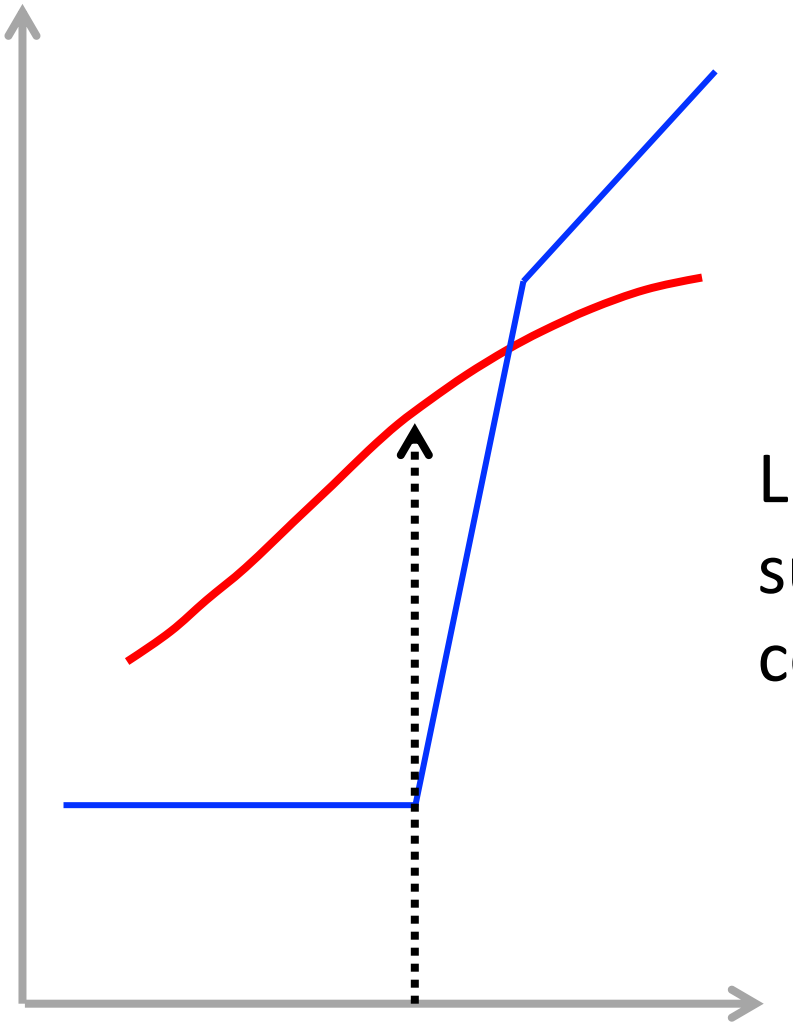
- Plating seawater samples revealed the presence of bioluminescent bacteria
  - Luminescence: emission of light by a substance that is not heated
- Abundance in sea water: <100 cells per mL
- Maximum light emission: 10^3 to 10^4 photons/sec/cell

https://jb.asm.org/content/181/9/2667.long

Luminescence: lag + sudden increase

1970s

Number of cells
or
Luminescence
(arbitrary units)



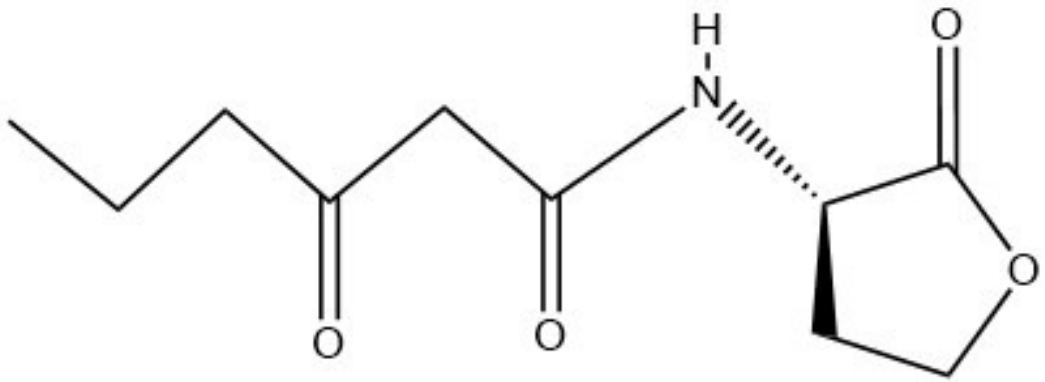
Time (arbitrary units)

Luminescence increases suddenly when the number of cells hits a certain threshold

https://jb.asm.org/content/181/9/2667.long

Sensor is a small molecule

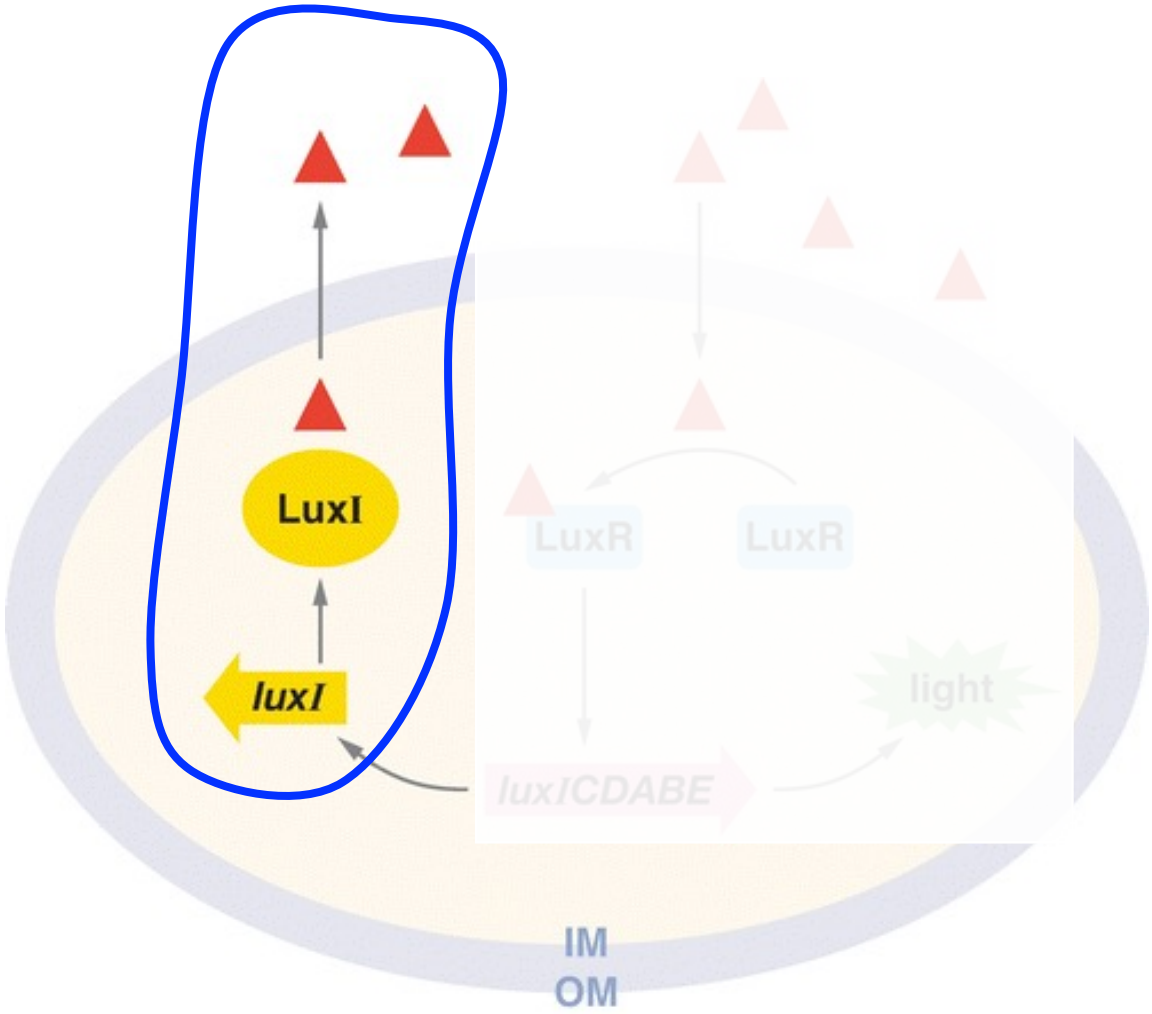
LuxI is the enzyme responsible for the synthesis of “auto-inducer” (AI)



3-Oxo hexanoyl homoserine lactone

▲ Denoted by red triangle in the schematic

Quorum sensing in *Vibrio fischeri*



- luxI gene is expressed at a basal level
  - Basal level means some kind of "default" level of expression
  - How much is basal level??
- Individual bacterial cells produce some amount of the auto-inducer
  - Auto-inducer "moves" out of the cell

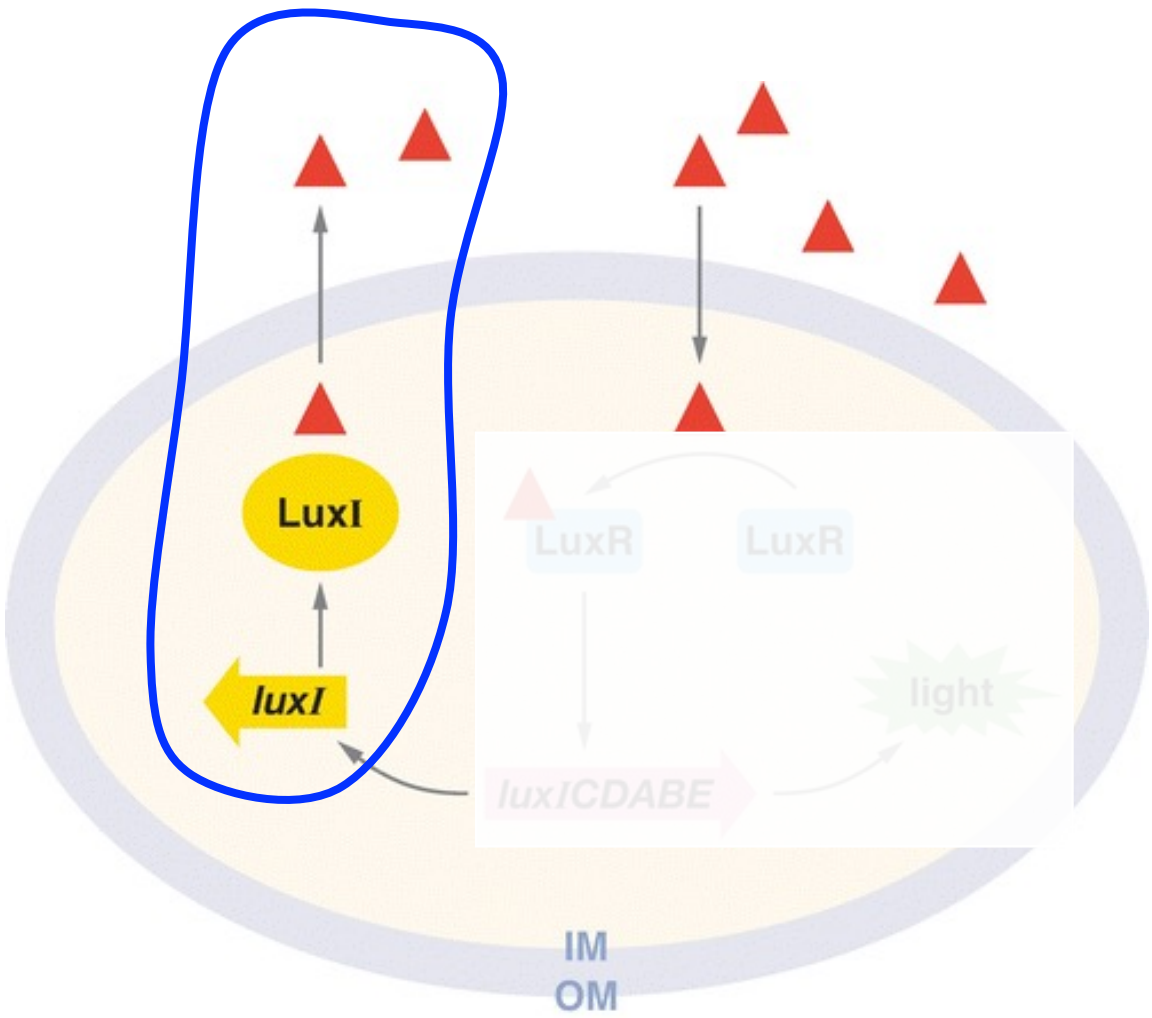
moves = in general, can be passive diffusion or active transport

IM: inner membrane
OM: outer membrane

▲ Auto-inducer

Annu. Rev. Cell Dev. Biol. (2005) 21:319

Quorum sensing in *Vibrio fischeri*



- $[\mathrm{AI}]_{extracellular}$ reaches a threshold level when the quorum is reached
  - Reaching quorum means attaining a certain density of bacteria per unit area
- Auto-inducer "moves" back into the cell when the threshold concentration is met

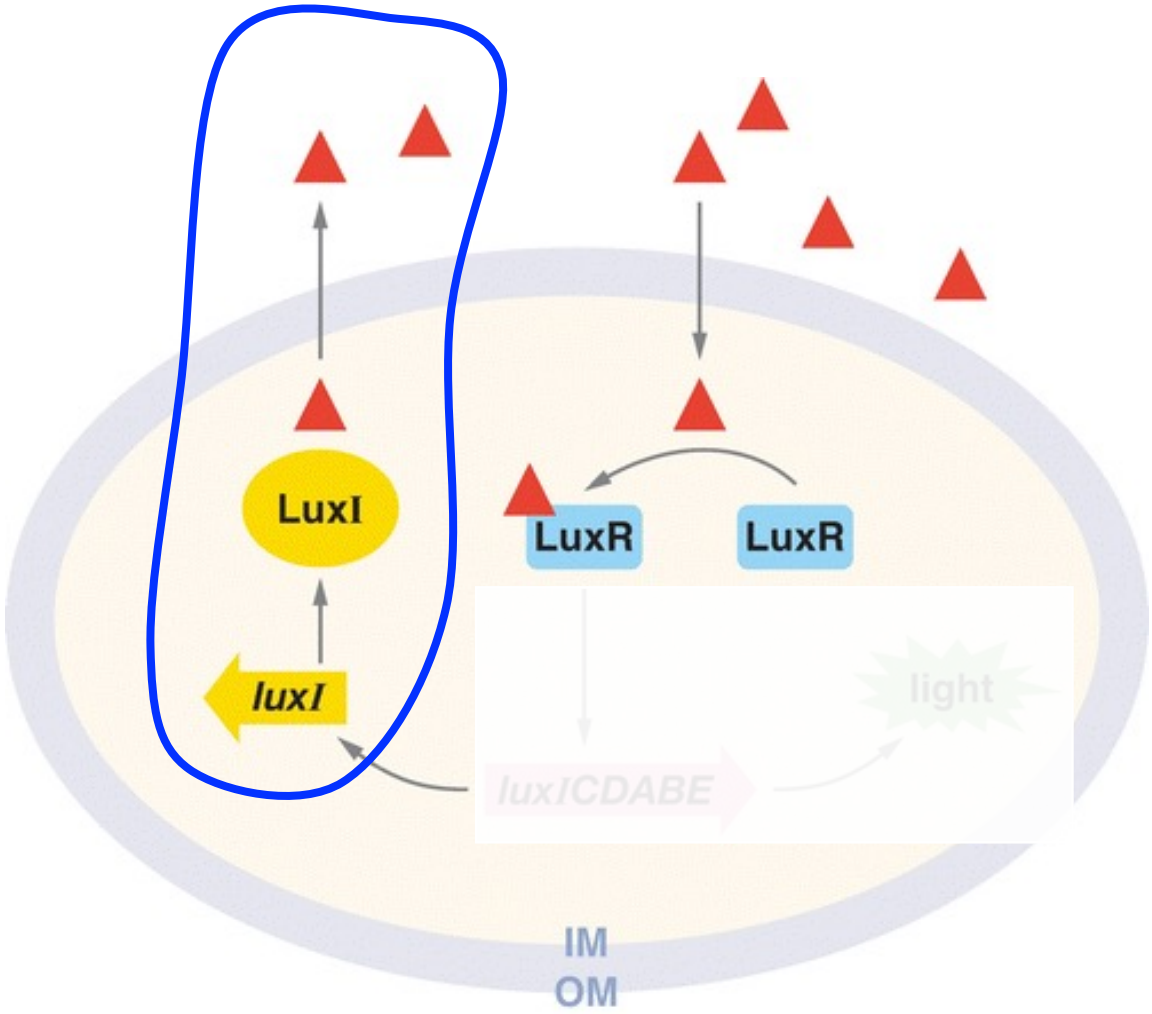
IM: inner membrane
OM: outer membrane

▲ Auto-inducer

moves = in general, can be passive diffusion or active transport

Annu. Rev. Cell Dev. Biol. (2005) 21:319

Quorum sensing in *Vibrio fischeri*



IM: inner membrane
OM: outer membrane

Auto-inducer

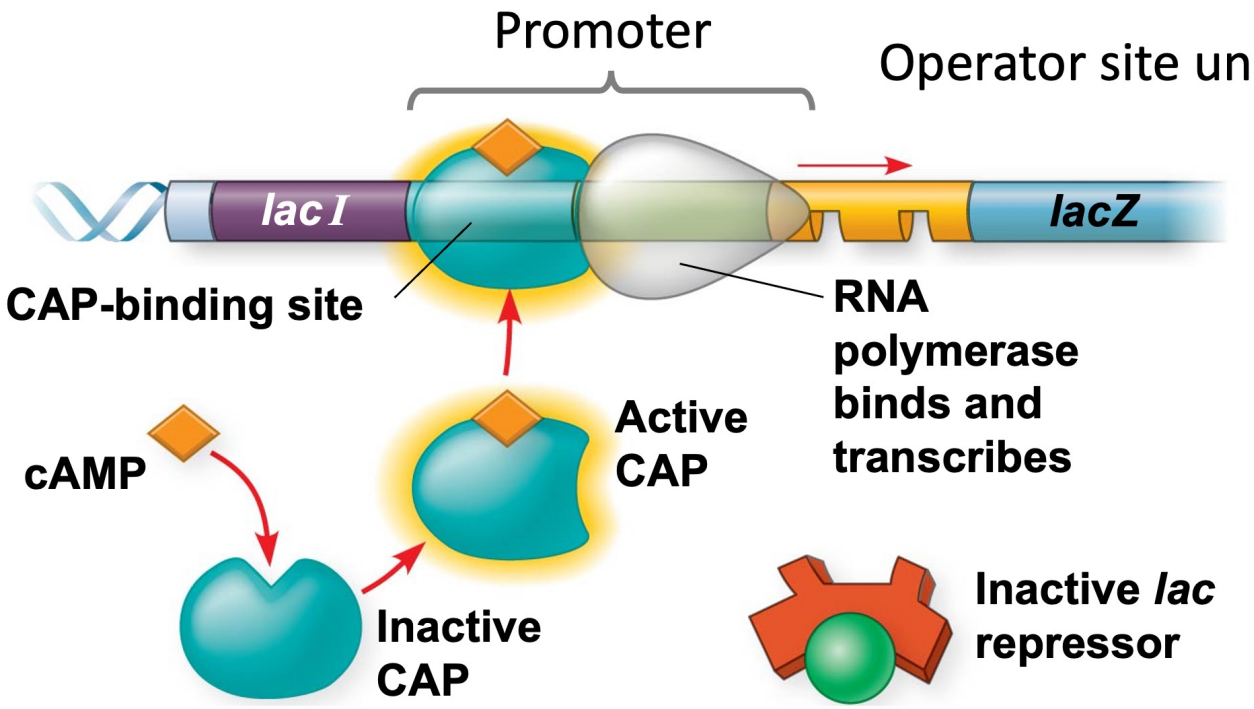
- LuxR is a protein
  - It is intracellular
  - It acts as a receptor for the auto-inducer

https://www.firstpost.com/tech/science/chandrayaan-2-can-isro-get-the-silent-possibly-broken-vikram-lander-on-the-moon-to-talk-7320881.html

Annu. Rev. Cell Dev. Biol. (2005) 21:319

Slide from Lecture 6

Lactose present, but glucose is NOT present



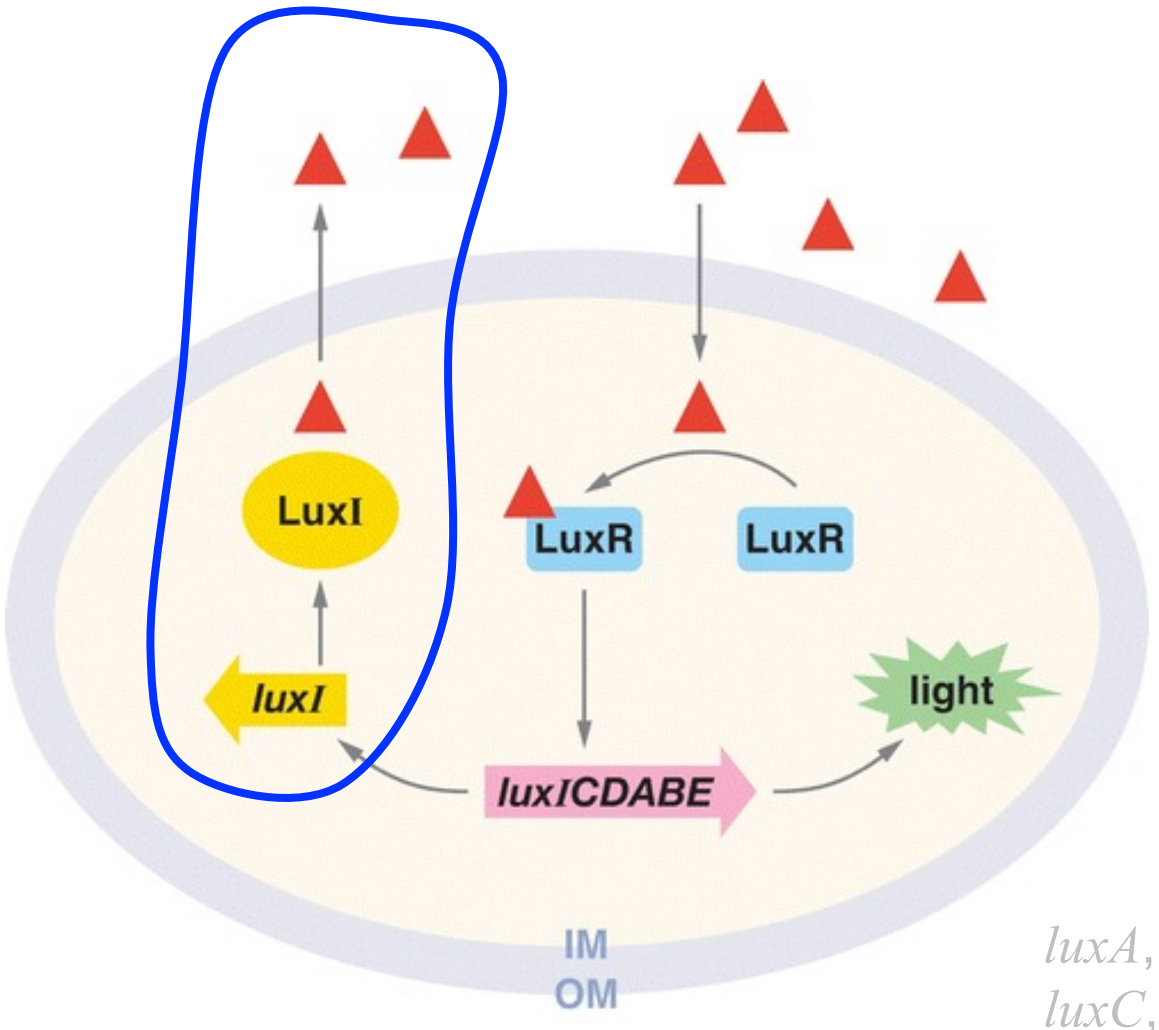
lac operon genes: transcribed

No glucose → cAMP accumulates

Lactose present
Repressor inactive

Figure 18.5 in Campbell Biology by Reece et al., (10th edition)

Quorum sensing in *Vibrio fischeri*



- Auto-inducer binds to LuxR
- (LuxR + auto-inducer) complex turns on the expression of genes in the lux operon
- Various proteins encoded by the lux operon collectively act to produce light

luxA, *luxB*: α, β subunits of luciferase
luxC, *luxD*, *luxE*: synthesis + recycling of luciferase substrate

IM: inner membrane
OM: outer membrane

▲ Auto-inducer

Annu. Rev. Cell Dev. Biol. (2005) 21:319

The "why" and "how" of bioluminescence

- Bioluminescence in *Vibrio fischeri*
- How is light produced?
  - Auto-inducer + *lux* operon
  - Quorum sensing
- Why does *Vibrio fischeri* produce light?
  - Hmmm...

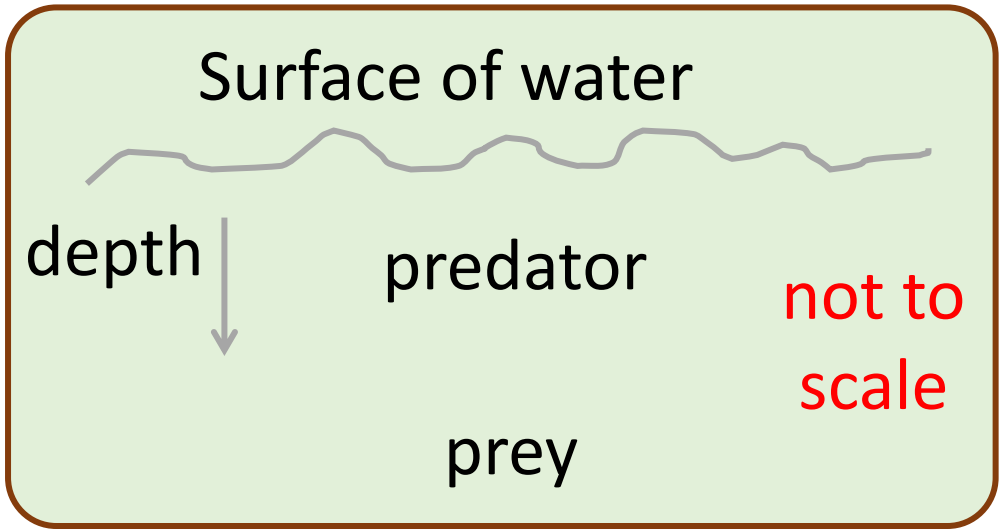
Bacteria – squid mutualism

Hawaiian bob-tailed squid

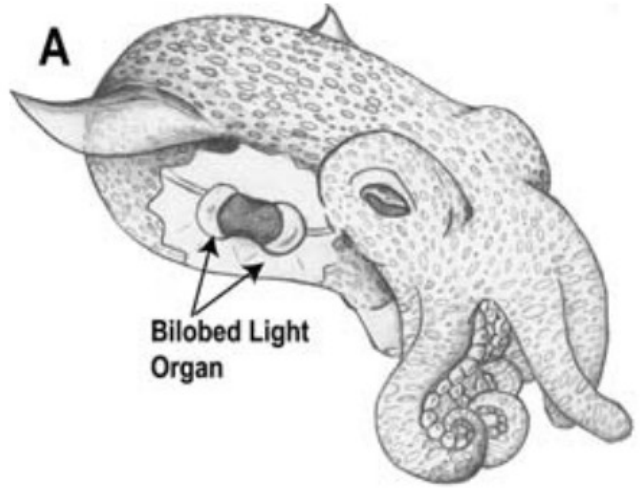
Both species benefit from each other in mutualism

https://multimediaquest.com/watch/L71RyeRA2YL

Counter-illumination by Hawaiian bob-tailed squid



- This squid predates during night
  - Prey is “below” the predator
- Prey is unable to perceive the presence of a predator
  - Because the predator uses counter-illumination
  - Matching light intensity to that of background light (moonlight / starlight)



Marine Biology (2004) 144:1151

Counter-illumination by Hawaiian bob-tailed squid

- Luminescence by symbiont *Vibrio fischeri*
- Bioluminescence also controls circadian rhythms of the squid
- What do the bacteria get out of this symbiosis?
  - Nutrients from the light organ – seems to be a reasonable explanation

Purpose of luminescence in *Vibrio fischeri*

- Luminescence is an energy-consuming process
  - Generation of light
  - Biosynthesis of the relevant proteins / associated molecules
- Inference:
  - Luminescence ought to be beneficial
  - Why retain this phenotype if there is no advantage for growth and/or survival?
- No luminescence in seawater
  - Guess why?
  - Quorum sensing! Reaches adequate density when inside the squid

J. Molec. Microbiol. Biotechnol. (1999) 1:5

Finding a purpose while reverse engineering

http://timesofindia.indiatimes.com/india/air-india-to-add-7-international-destinations-this-year/articleshow/58915099.cms

https://i.stack.imgur.com/K6DPI.jpg

Today's topics

- Example of cell communication: quorum sensing
- Signal transduction in eukaryotes – an overview
- G-proteins
- Signal amplification
- Signaling mechanisms in living systems

Signal transduction

transduce (*verb*): to convert energy or message into another form

A chemical outside a cell…

triggers a response inside the cell

Signal transduction

transduce (*verb*): to convert energy or message into another form

A chemical outside a cell…

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Quorum sensing…

illustrates the concept of cell-cell communication and intra-cellular signal transduction

Signal transduction

transduce (*verb*): to convert energy or message into another form

A chemical outside a cell…
triggers a response inside the cell

Quorum sensing…
illustrates the concept of cell-cell communication and intra-cellular signal transduction

Communication among microbes…
insight into cell communication in multicellular organisms

Fight or flight

Figure 9.1 of Biology. A global approach

Cellular messaging

- Based on visual and other sensory inputs,

  adrenal glands secrete hormones...

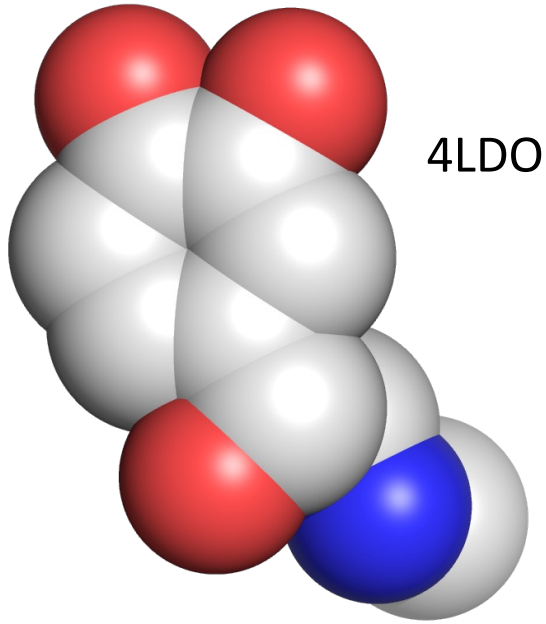
  which trigger metabolic responses

- When a prey is being hunted by a predator…
  - Muscles perform at the highest level – to run faster
  - Heart beats faster – carry more oxygen to muscles
  - Breathing is accelearted – need more oxygen
- Cells communicate with each other, coordinate with each other

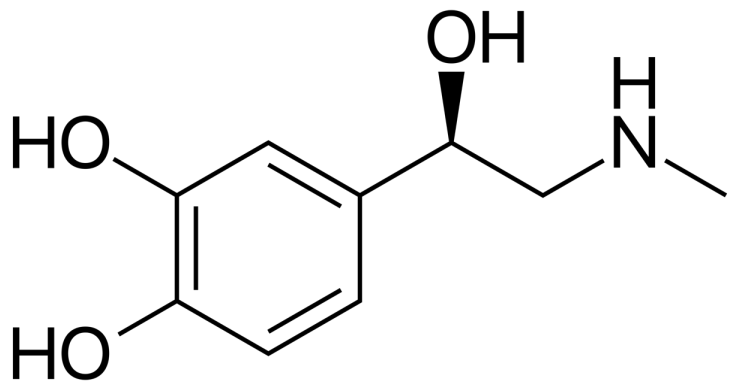
How do cells talk to each other?

How does adrenaline mobilize energy?

- Fight or flight is usually associated with adrenaline
- Adrenaline rush – “quick” release of adrenaline into the blood stream
- Adrenaline is a small molecule
  - It is a hormone produced by adrenal glands
  - Target: muscle and heart



4LDO.pdb



How does adrenaline mobilize energy?

Earl W. Sutherland
Nobel prize (1971)

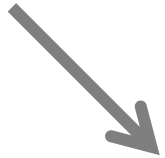
https://www.nasonline.org/publications/biographical-memoirs/memoir-pdfs/sutherland-earl.pdf

Signal transduction: three main stages

a knock on the door

Reception

Discriminator



message received at the door

Transduction

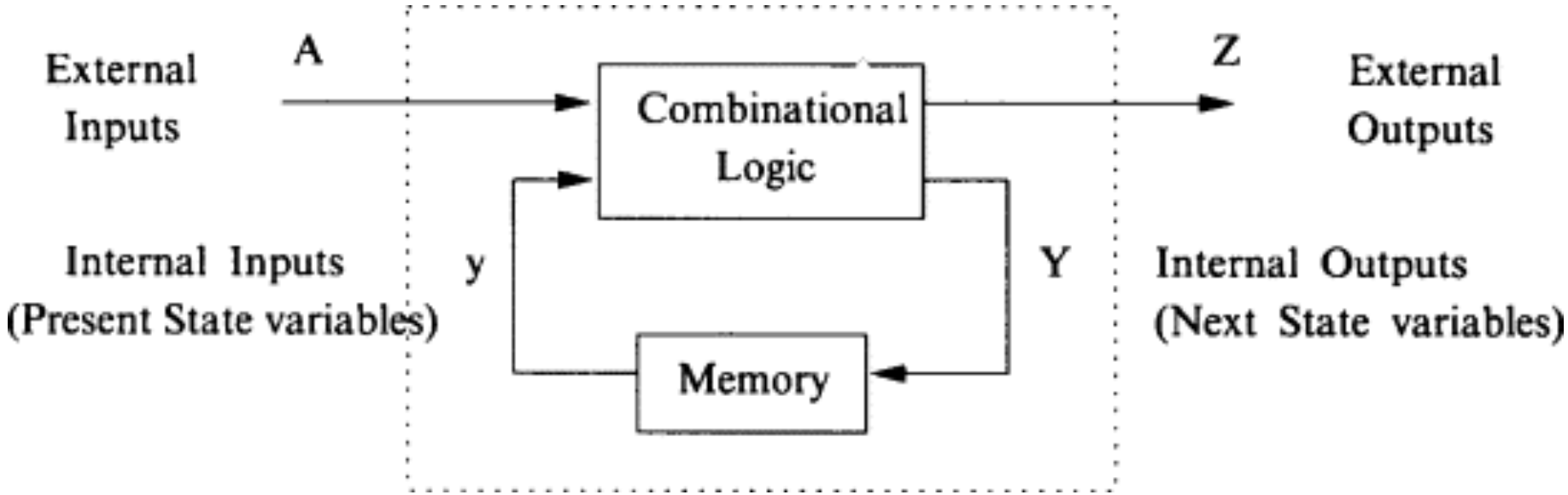
Transducer

Response

Amplifier

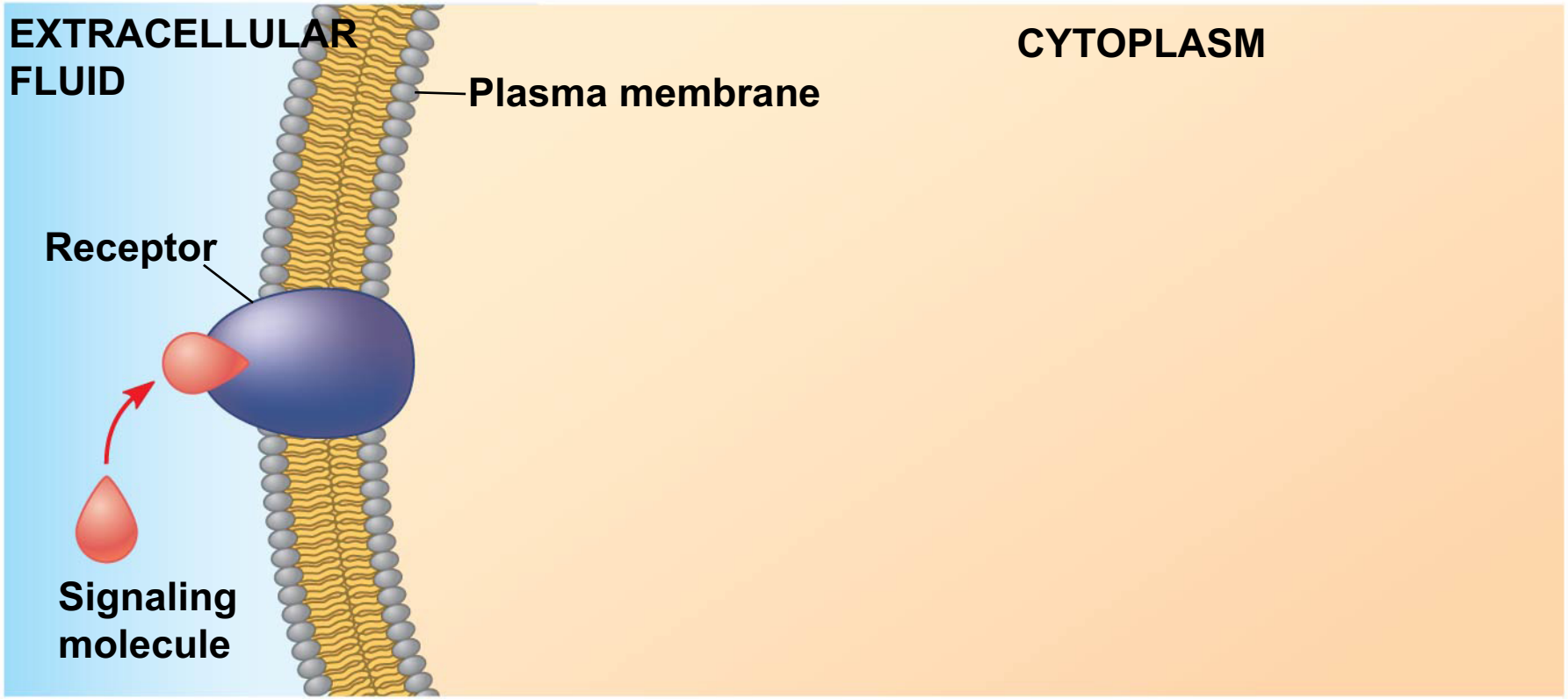
message conveyed inside
and an action is triggered

A digital circuit



https://www.sciencedirect.com/topics/engineering/combinatorial-circuits

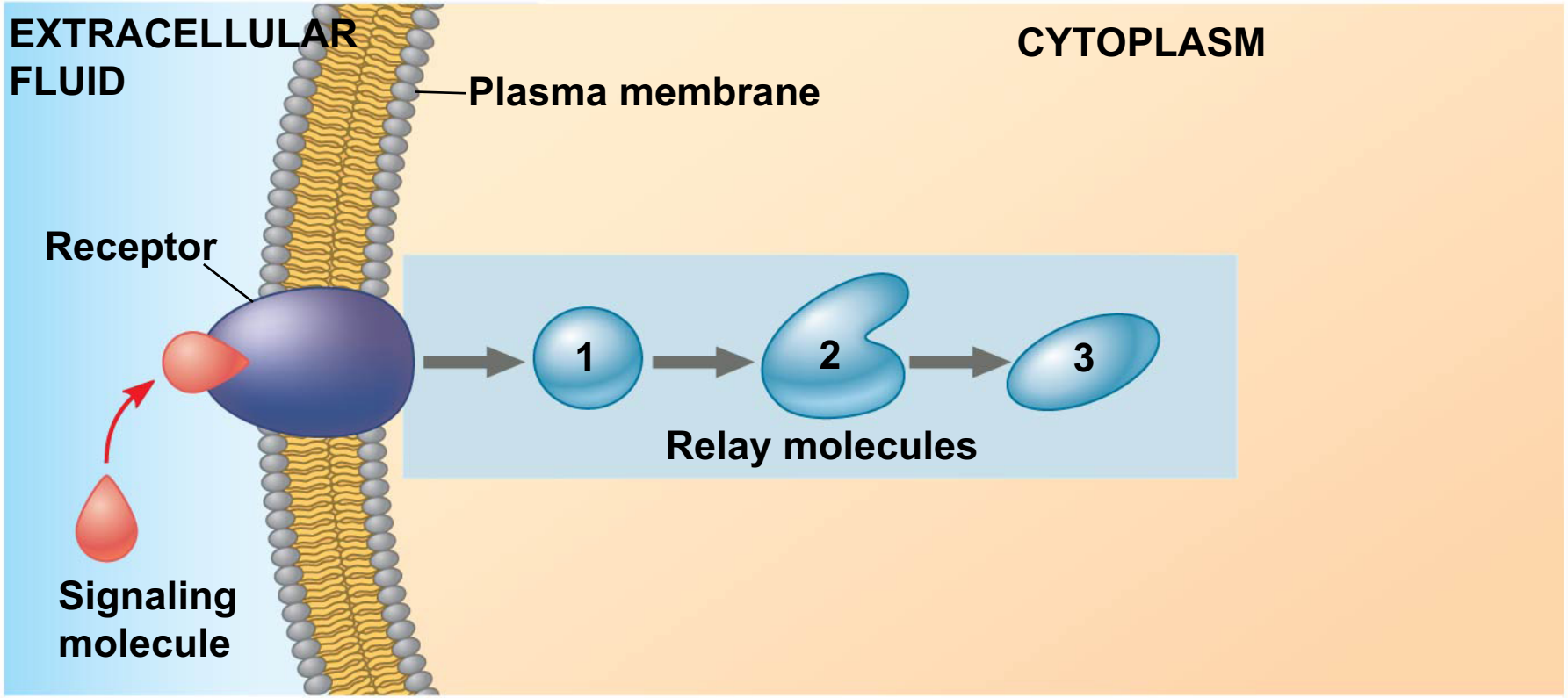
Signal transduction: 1. Reception



- A signaling molecule binds to a cell surface receptor
- Receptor is on the target cell

Figure 11.6 of Campbell Biology by Reece and others (10th edition)

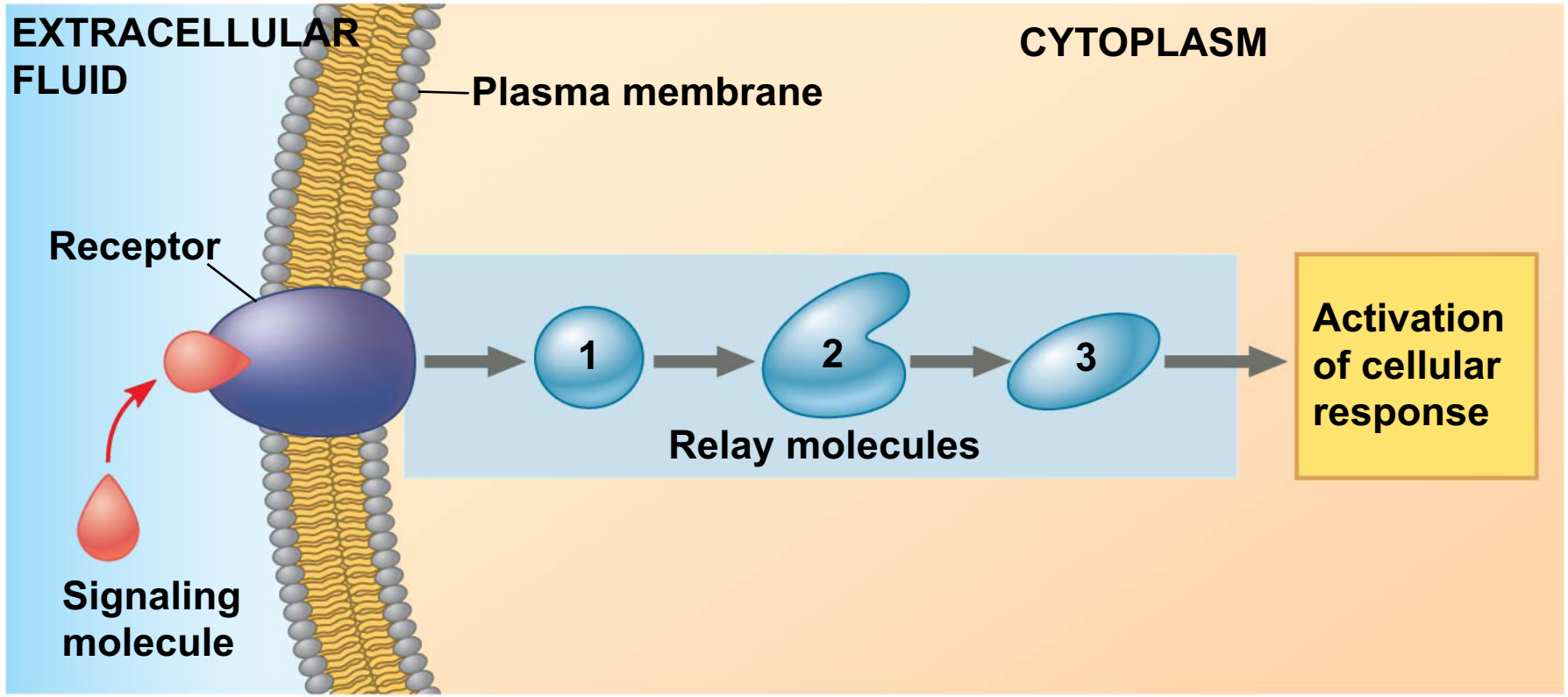
Signal transduction: 2. Transduction



- Binding leads to a change in the shape of the receptor
- Shape change leads to a cellular response
- Can be in one step; often, in multiple steps
  - involves relay molecules

Figure 11.6 of Campbell Biology by Reece and others (10th edition)

Signal transduction: 3. Response



- Response can be of different types:
  1. Catalysis of a reaction by an enzyme
  2. Activation of specific genes (gene expression)
  3. Rearrangement of the cytoskeleton

Figure 11.6 of Campbell Biology by Reece and others (10th edition)

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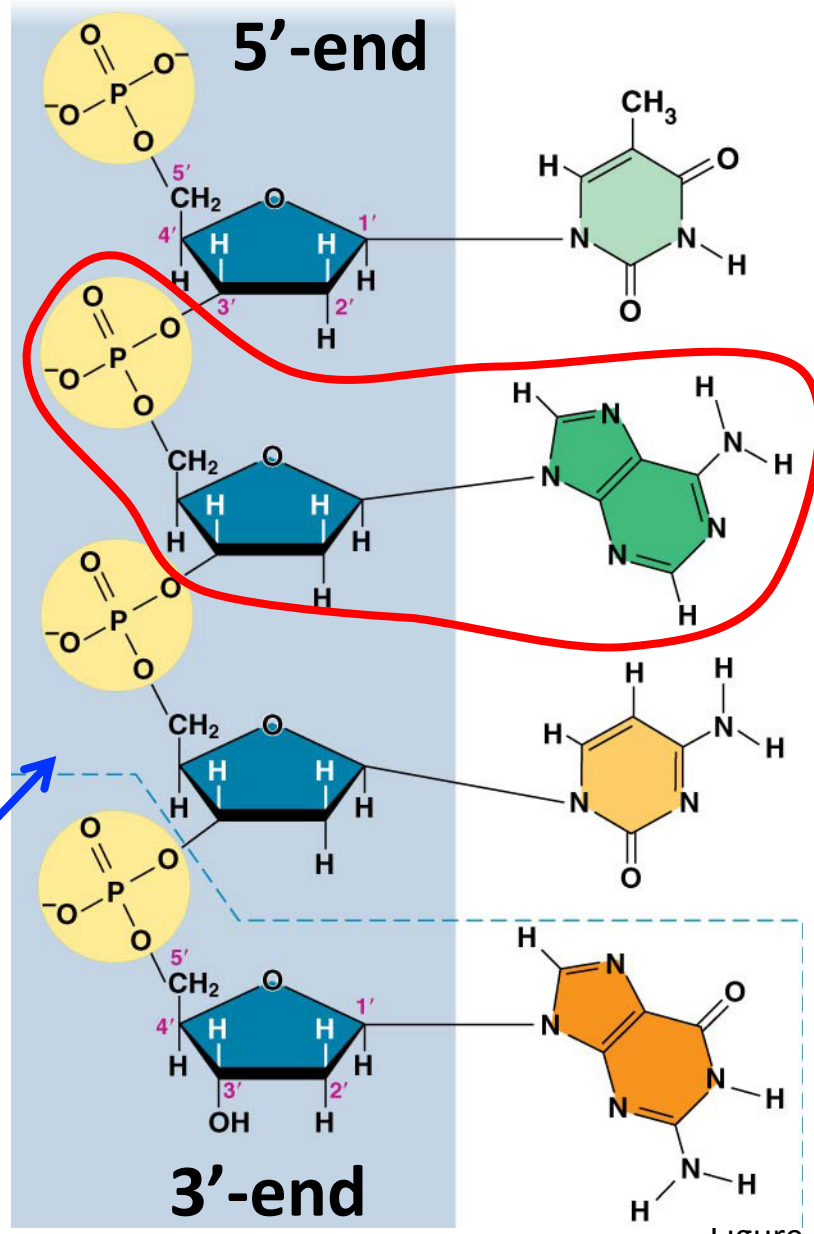
Nucleotides in DNA and RNA



Thymine (T)

Adenine (A)

Cytosine (C)

Guanine (G)

Nitrogenous bases

Sugar phosphate backbone

A nucleotide

Figure 16.5 of Campbell Biology by Reece and others (10th edition)

Dual role of nucleotides

- ATP
  - Energy currency
- GTP
  - Signal transduction

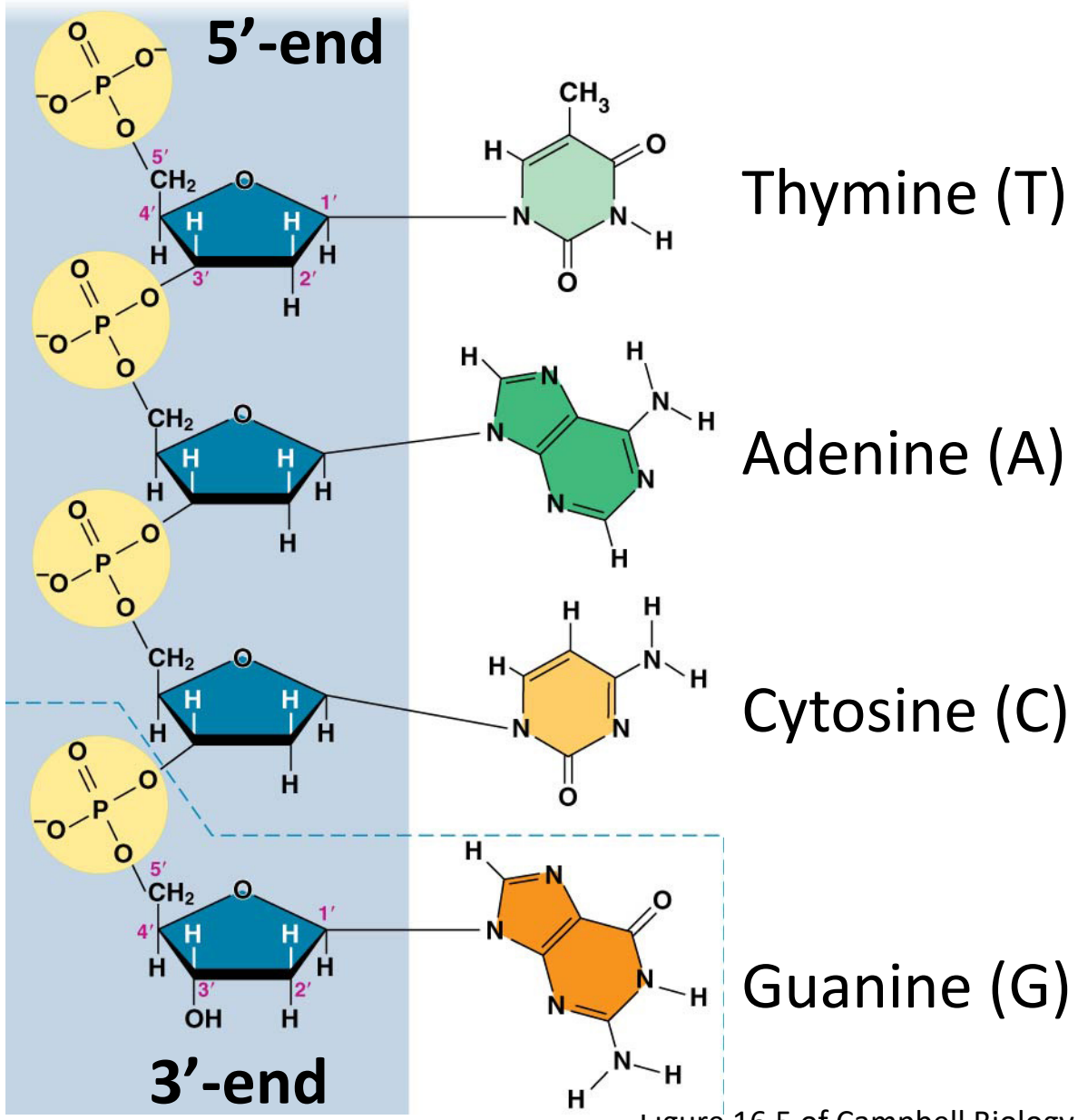


Figure 16.5 of Campbell Biology by Reece and others (10th edition)

https://www.nobelprize.org/prizes/uncategorized/the-nobel-prize-in-physiology-or-medicine-1994/ 90%

THE NOBEL PRIZE

Nobel Prizes & Laureates | Nomination | Alfred Nobel | News & insights | Events | Educational

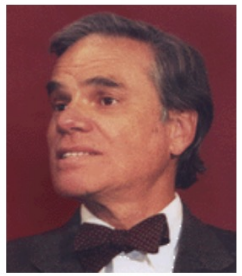
The Nobel Prize in Physiology or Medicine 1994

Discovery of G-proteins

BACK

The Nobel Assembly at the Karolinska Institute in Stockholm, Sweden, has awarded the Nobel Prize in Physiology or Medicine for 1994 jointly to **Alfred G. Gilman** and **Martin Rodbell** for their discovery of "G-proteins and the role of these proteins in signal transduction in cells".

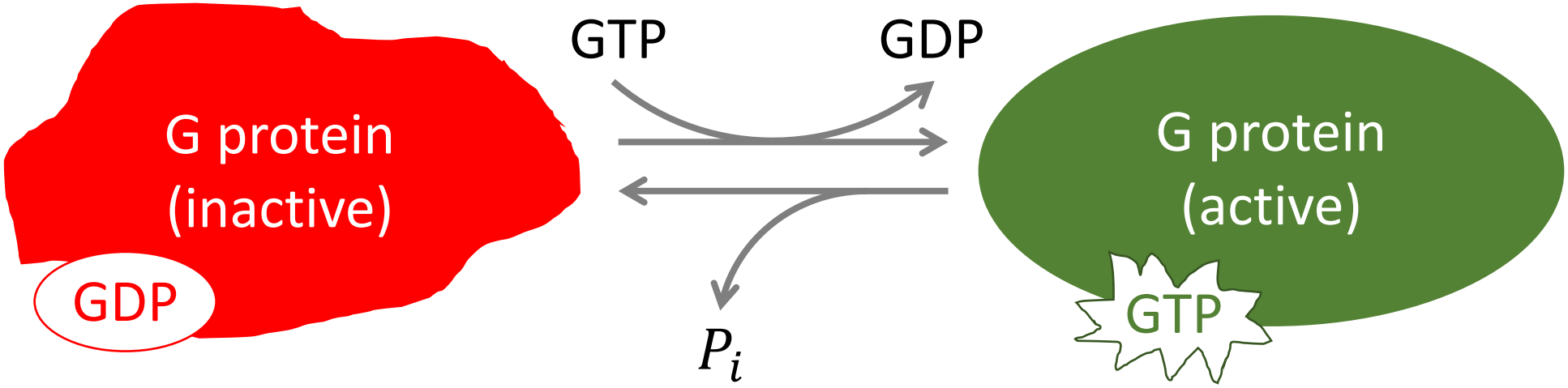
Alfred Gilman



Martin Rodbell

G-proteins (GTP/GDP binding proteins)

- G-proteins are a large family of proteins found ubiquitously
- They act as molecular switches
- Exchange GTP/GDP as part of signaling events



Energy is spent in conversion from active to inactive state

Change in shape or conformation

G-protein coupled receptors (GPCRs)

- Extremely widespread
- Involved in a variety of processes e.g., embryonic development, vision, taste, smell, …
- Involved in several human diseases e.g., cholera, pertussis, botulism
- ~60% of all medicines used today target GPCRs
- Share a common architecture of seven transmembrane domains

G-protein coupled receptors (GPCRs)

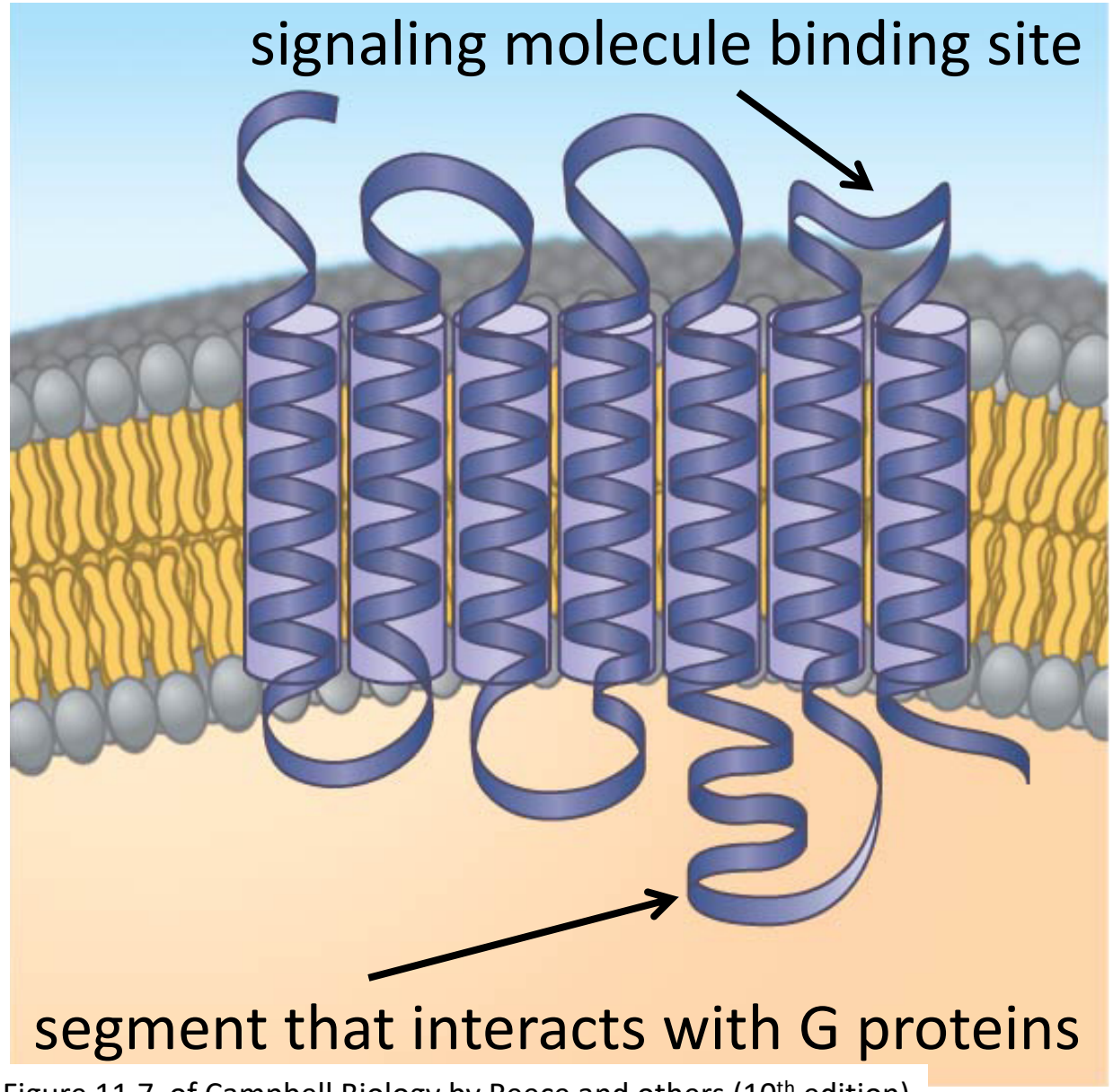
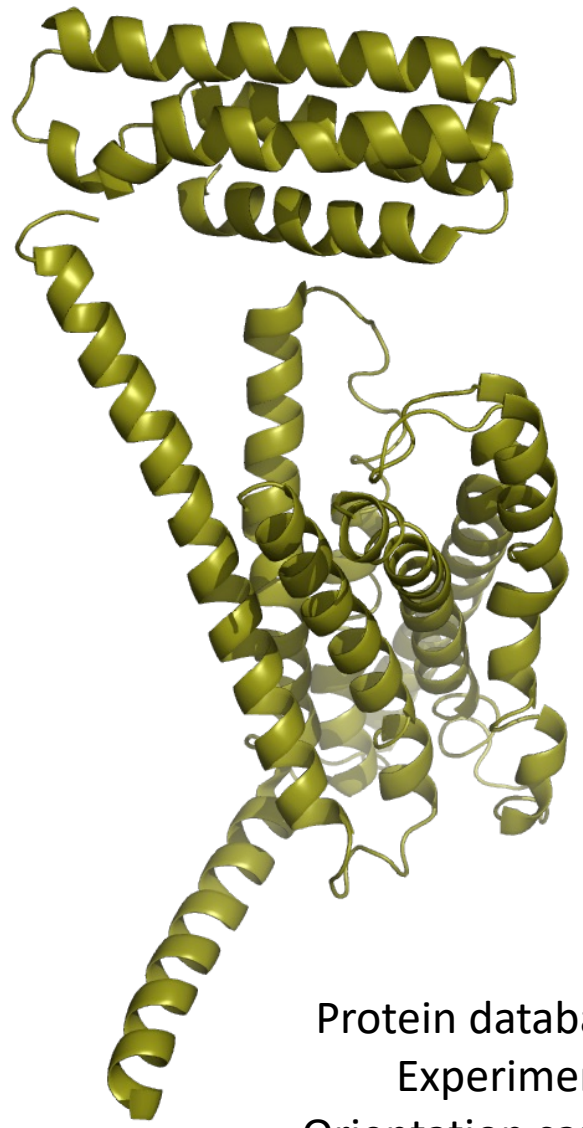


Figure 11.7 of Campbell Biology by Reece and others (10th edition)



Nature (2013) 499:444
Protein databank accession no. 4L6R.pdb
Experimentally determined structure
Orientation same as that in the schematic
Surrounding lipid bilayer membrane is NOT shown

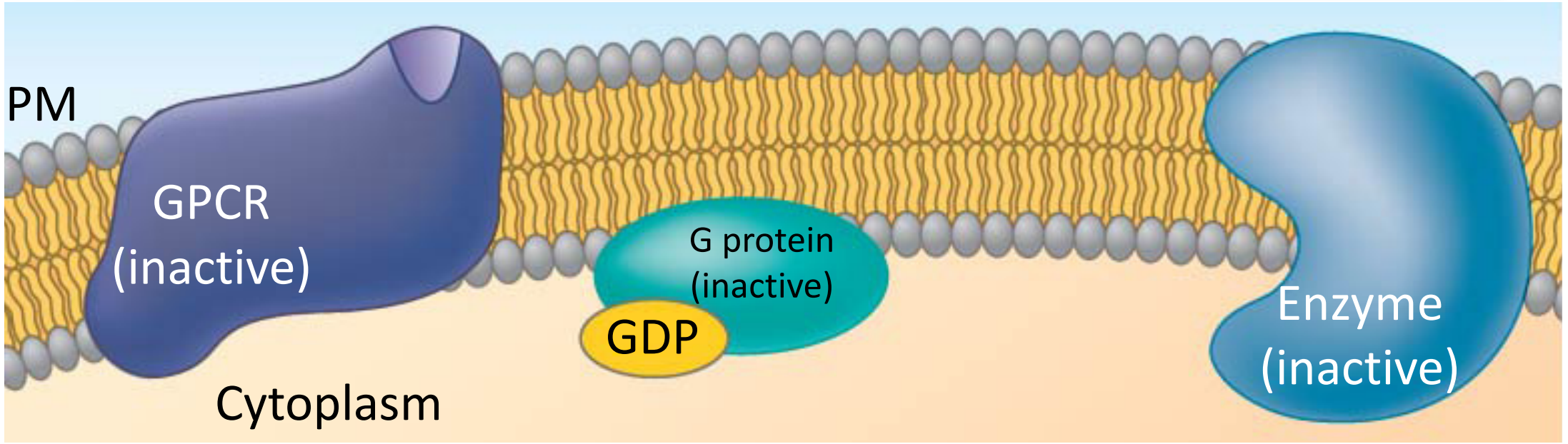
Drugs that target GPCRs

GPCR Class	Drug(s)	Indication
Adrenoreceptor		
Alpha-1	alfuzosin, terazosin	Benign prostate hyperplasia, high blood pressure
Alpha-2	clonidine, bisoprolol, betaxolol	High blood pressure
Beta-1	metoprolol, atenolol	High blood pressure
Beta-2	albuterol, nadolol, penbutolol	Asthma
Acetylcholine Receptor		
M1, M2, M3, M4 and M5	tolterodine	Overactive bladder
M1, M2, M3, M4 and M5	atropine	Poisoning
M1	scopolamine	Motion sickness; diarrhea
Calcitonin	calcimar	Osteoporosis
Dopamine		
D2	metoclopramide	Heartburn
D2	haloperidol, olanzapine	Schizophrenia
D2	ropinirole, pramipexole	Parkinson's disease; Restless legs syndrome

Histamine		
H1	loratadine, cetirizine	Allergies
H1	demenhydrinate	Motion sickness
H2	cimetidine, ranitidine	Ulcers/heartburn
5-HT (serotonin)		
5-HT1B	trazodone	Anxiety; depression
5-HT1D	sumatriptan	Migraine headaches
GLP-1	exenatide	Type-2 diabetes
Opioid		
Mu	fentanyl, codein, meperidine	Pain
Mu/kappa	oxycodone	Pain
CysLT1	montelukast	Asthma
Prosta-glandin E2 receptors	misoprostol	Gastric ulcers

https://www.drugdiscoverytrends.com/gpcrs-desirable-therapeutic-targets-in-oncology/

How do GPCRs receive and transduce signals?

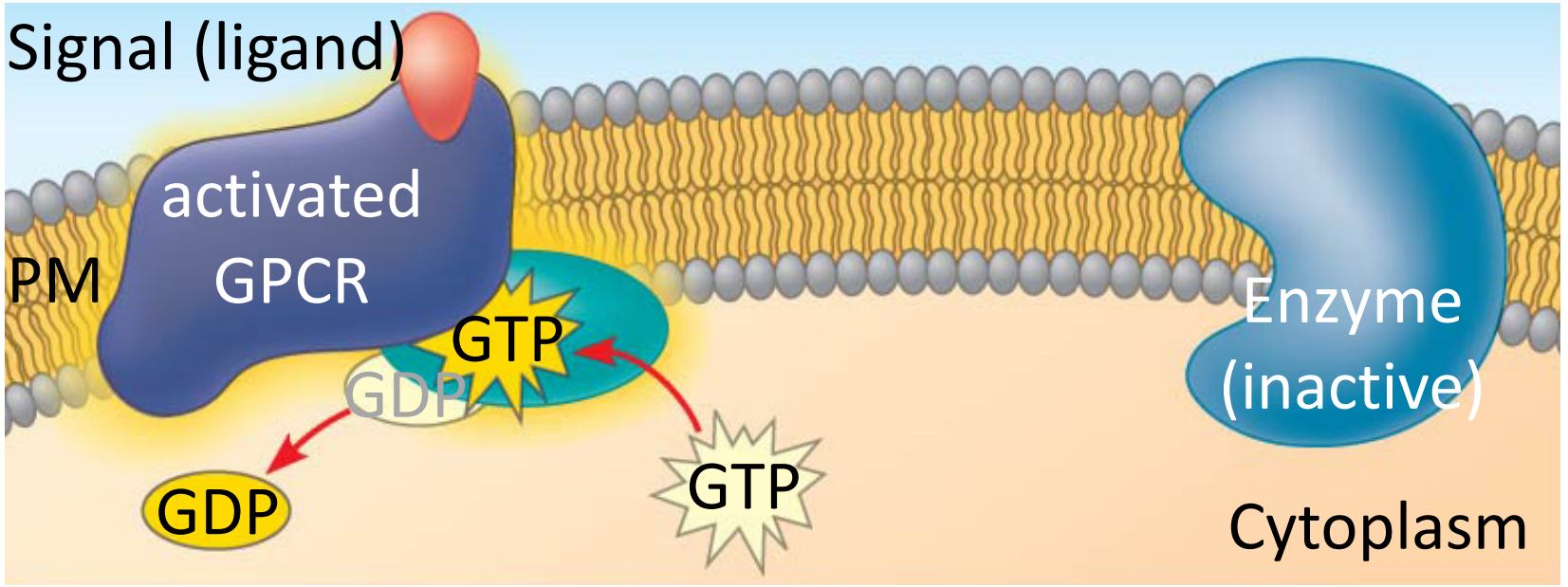


GPCR	Inactive	Ligand binding site is empty
G-protein	Inactive	It is bound to GDP, not GTP
Enzyme	Inactive	NOT bound by G-protein

PM: Plasma membrane

Figure 11.7 of Campbell Biology by Reece and others (10th edition)

How do GPCRs receive and transduce signals?

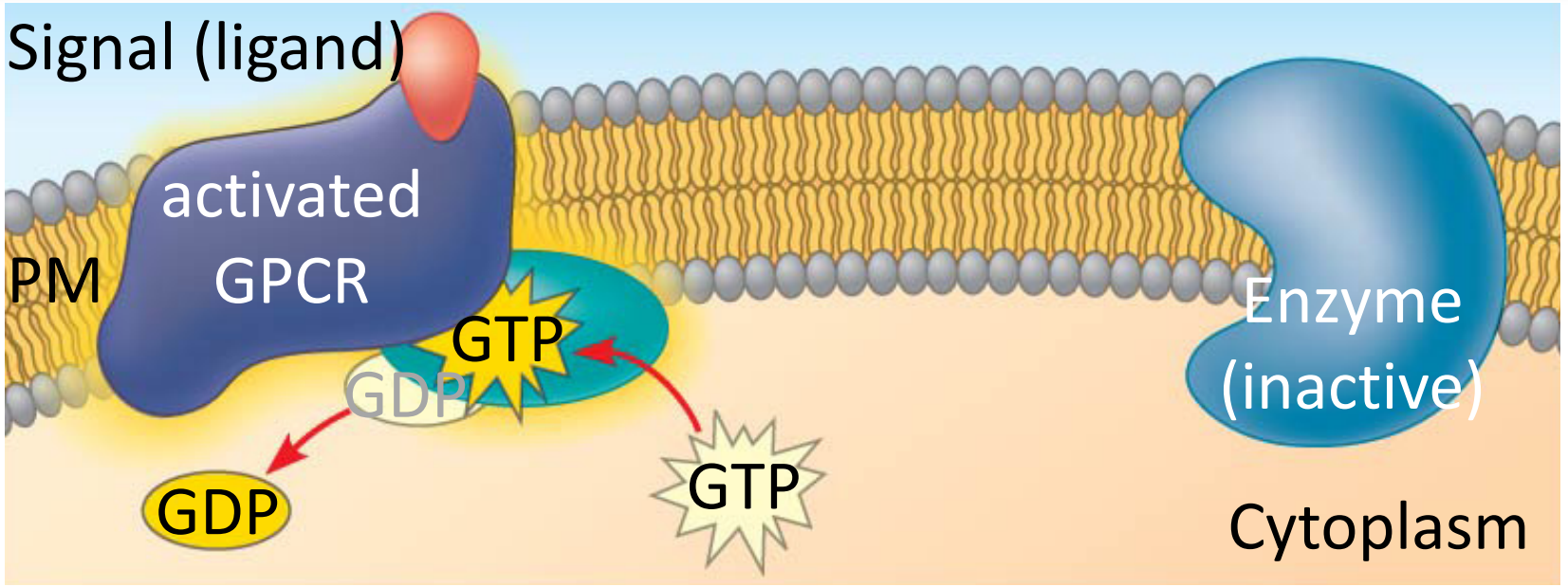


1. Signaling molecule (ligand) binds to GPCR on the outside
2. Binding induces shape change in GPCR (conformation)
3. Shape change leads to binding of G-protein on the inside

PM: Plasma membrane

Figure 11.7 of Campbell Biology by Reece and others (10th edition)

How do GPCRs receive and transduce signals?



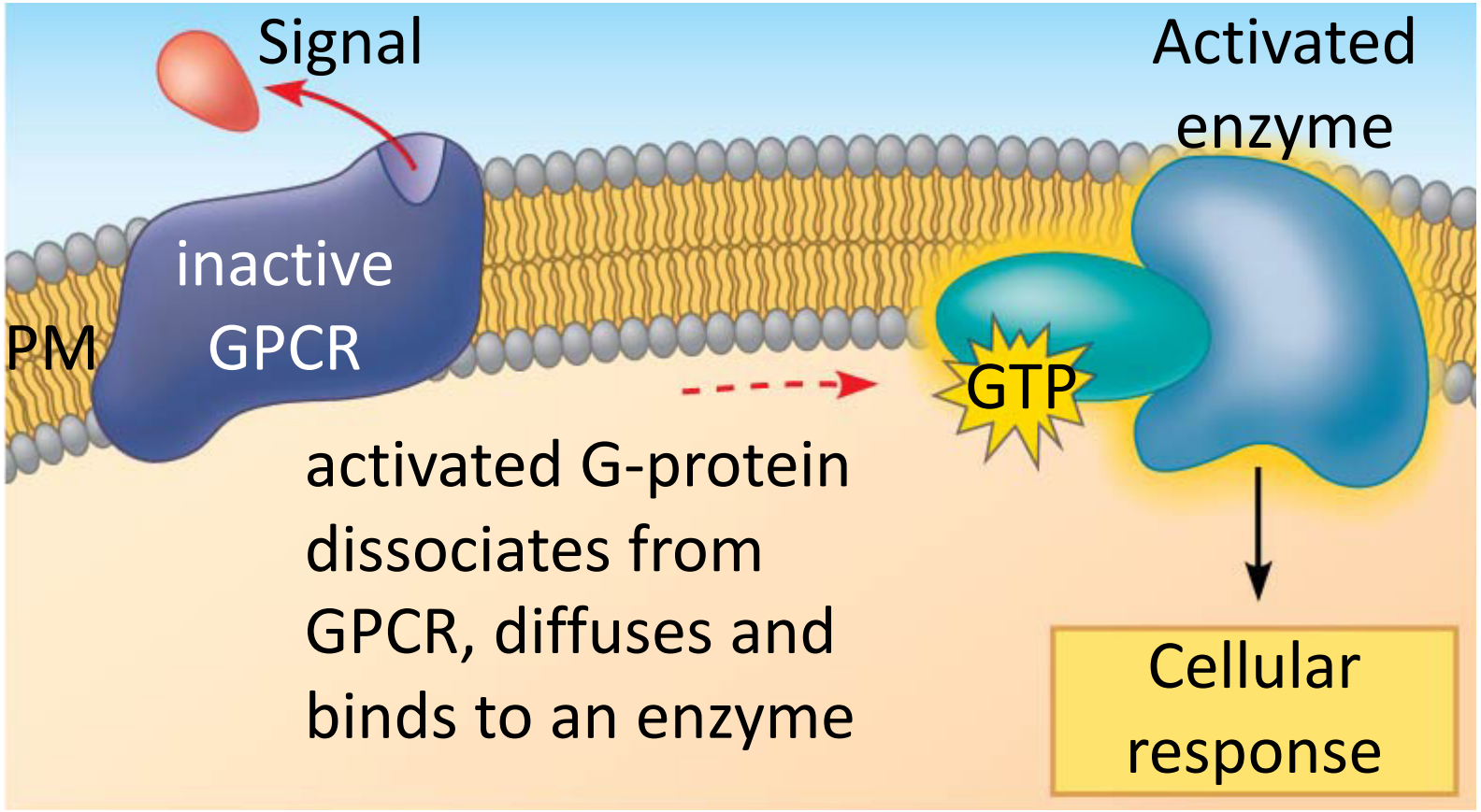
4. Upon binding to GPCR, G-protein exchanges GDP with GTP
5. GTP binding activates the G-protein
6. G-protein dissociates from GPCR (not shown above)

PM: Plasma membrane

Figure 11.7 of Campbell Biology by Reece and others (10th edition)

How do GPCRs receive and transduce signals?

Reversible binding of the signal (ligand)
$[ligand]$ determines $binding \rightleftarrows dissociation$

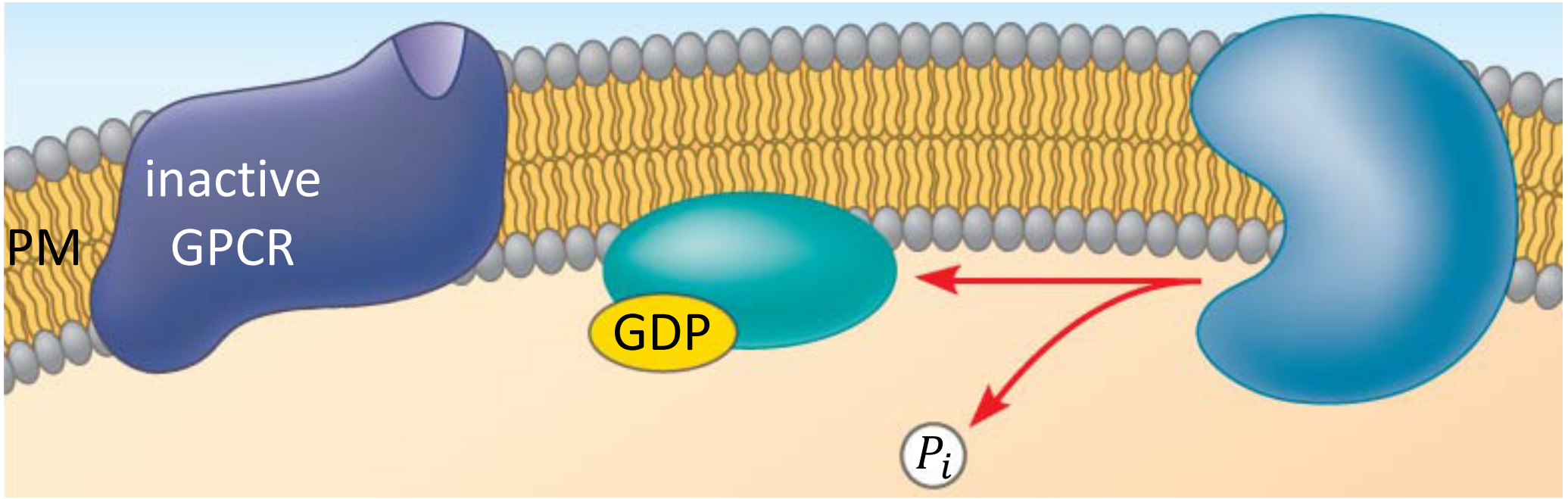


Activated enzyme triggers a cellular response

PM: Plasma membrane

Figure 11.7 of Campbell Biology by Reece and others (10th edition)

How do GPCRs receive and transduce signals?



- Changes in the enzyme and G-protein are transient
- G-protein has GTPase activity – hydrolyzes GTP to GDP and P_i
- G-protein is now GDP-bound – dissociates from the enzyme

This is a built-in controlling mechanism

PM: Plasma membrane

Figure 11.7 of Campbell Biology by Reece and others (10th edition)

cAMP and G-protein signaling pathways

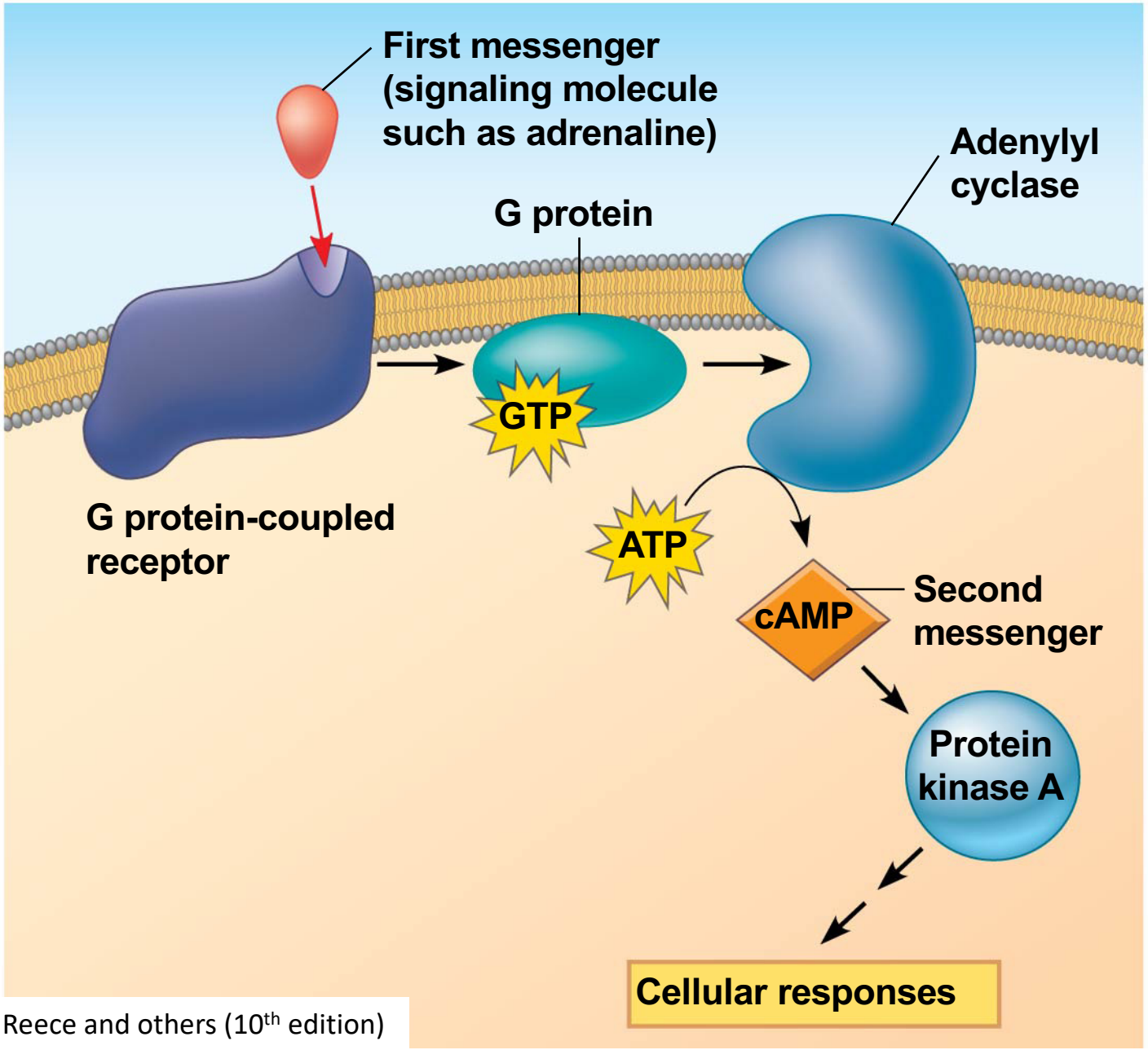


Figure 11.12 of Campbell Biology by Reece and others (10th edition)

Cyclic AMP: second messenger

AMP: adenosine monophosphate

cyclic AMP: cAMP

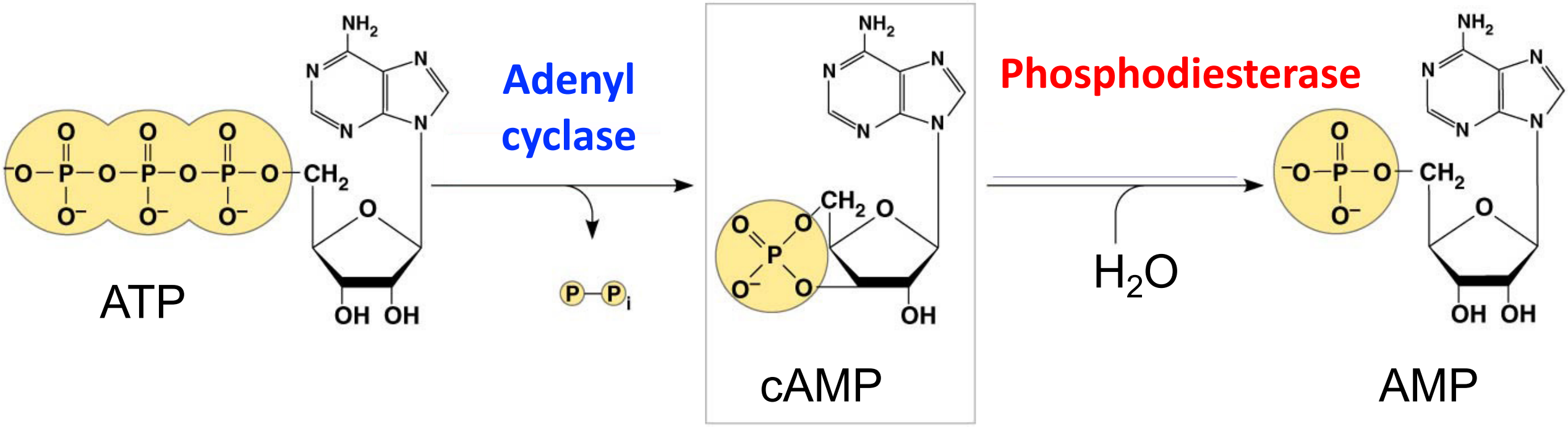


Figure 11.11 of Campbell Biology by Reece and others (10th edition)

Today's topics

- Example of cell communication: quorum sensing
- Signal transduction in eukaryotes – an overview
- G-proteins
- Signal amplification
- Signaling mechanisms in living systems

Cascade

- Cascade means

  a large number of “actions” or “events”

  that happen one after the other and

  in quick succession

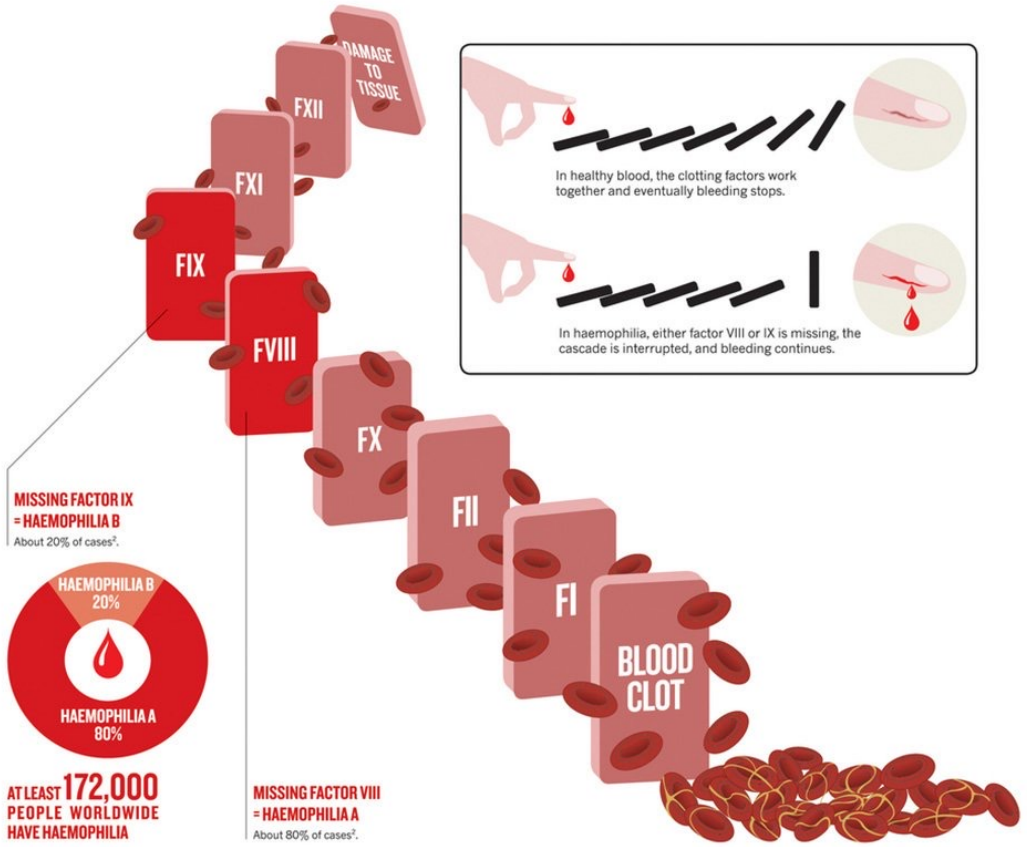
- First event triggers the second,

  second event triggers the third,

  and so on...

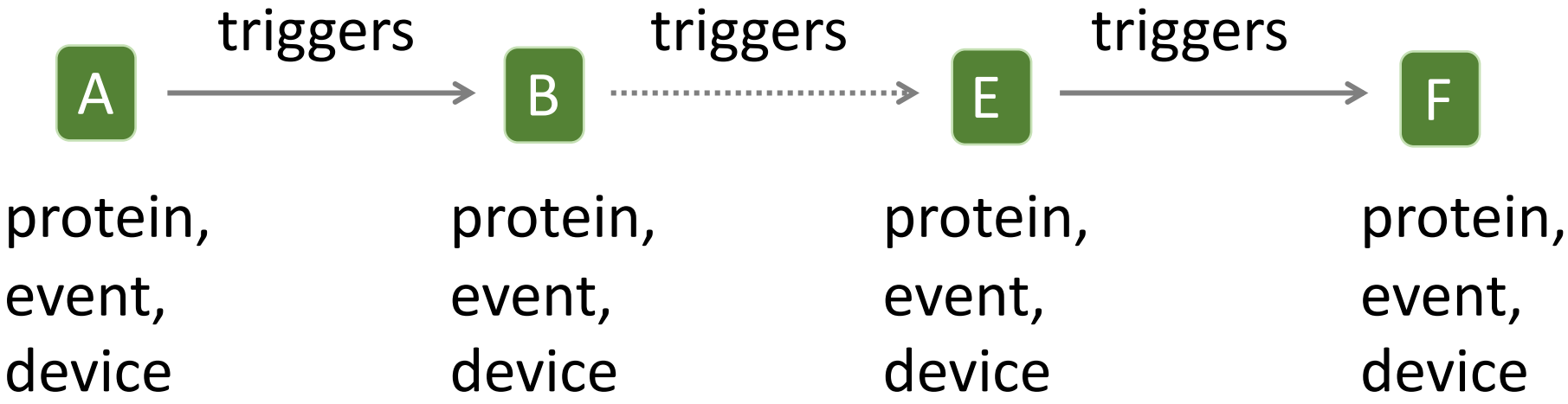
https://upload.wikimedia.org/wikipedia/en/5/55/Silver_Cascade_3-4.JPG

Blood clotting



- Blood clotting is a cascading event
- Several proteins, called as “factors”, are involved
- An individual who inherits defective Factor IX suffers from the disease hemophilia
  - Factors are NOT numbered in the sequence in which they act

Cascade



What is the advantage?

Phosphorylation cascade

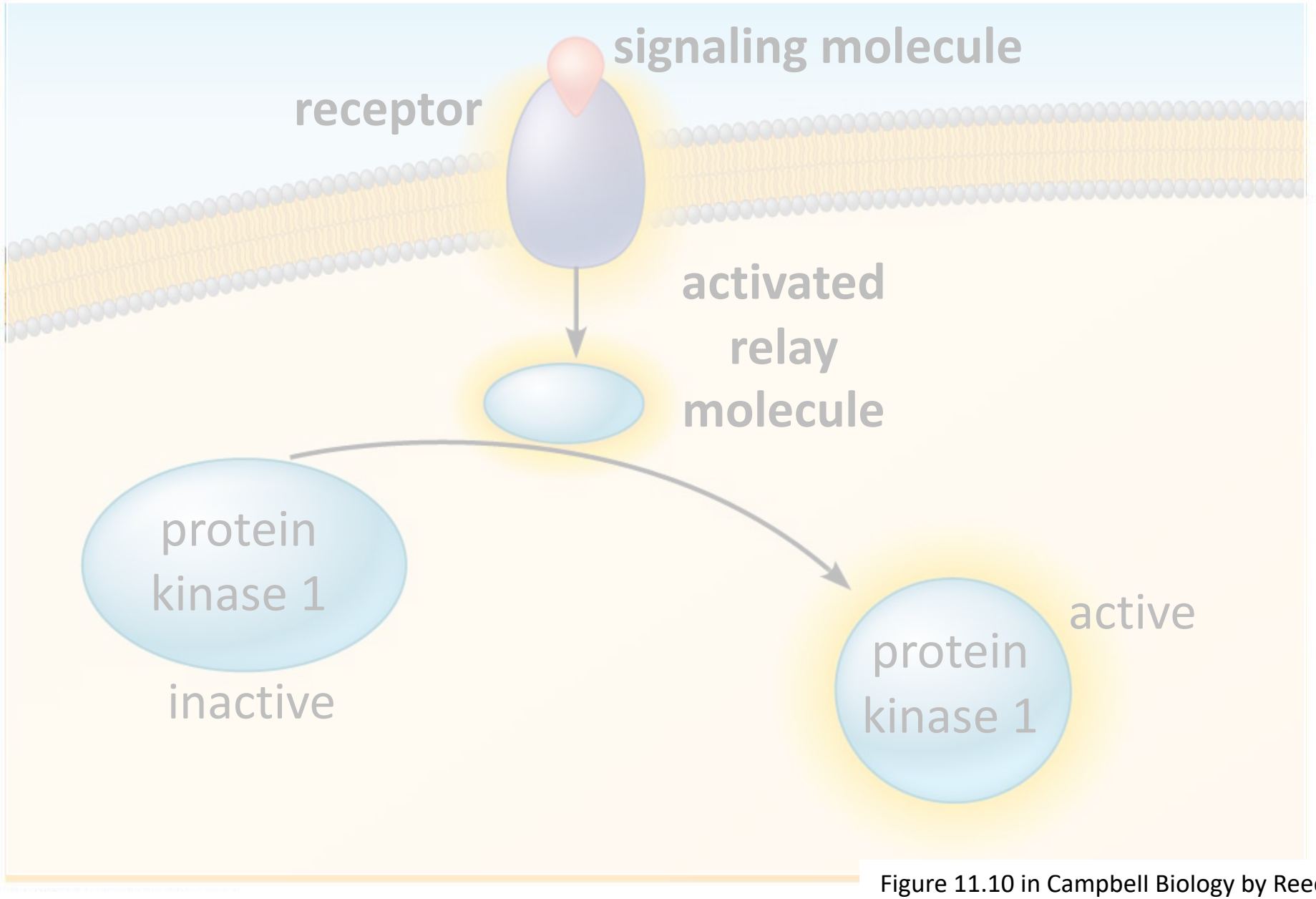


Figure 11.10 in Campbell Biology by Reece et al., (10th edition)

Phosphorylation cascade

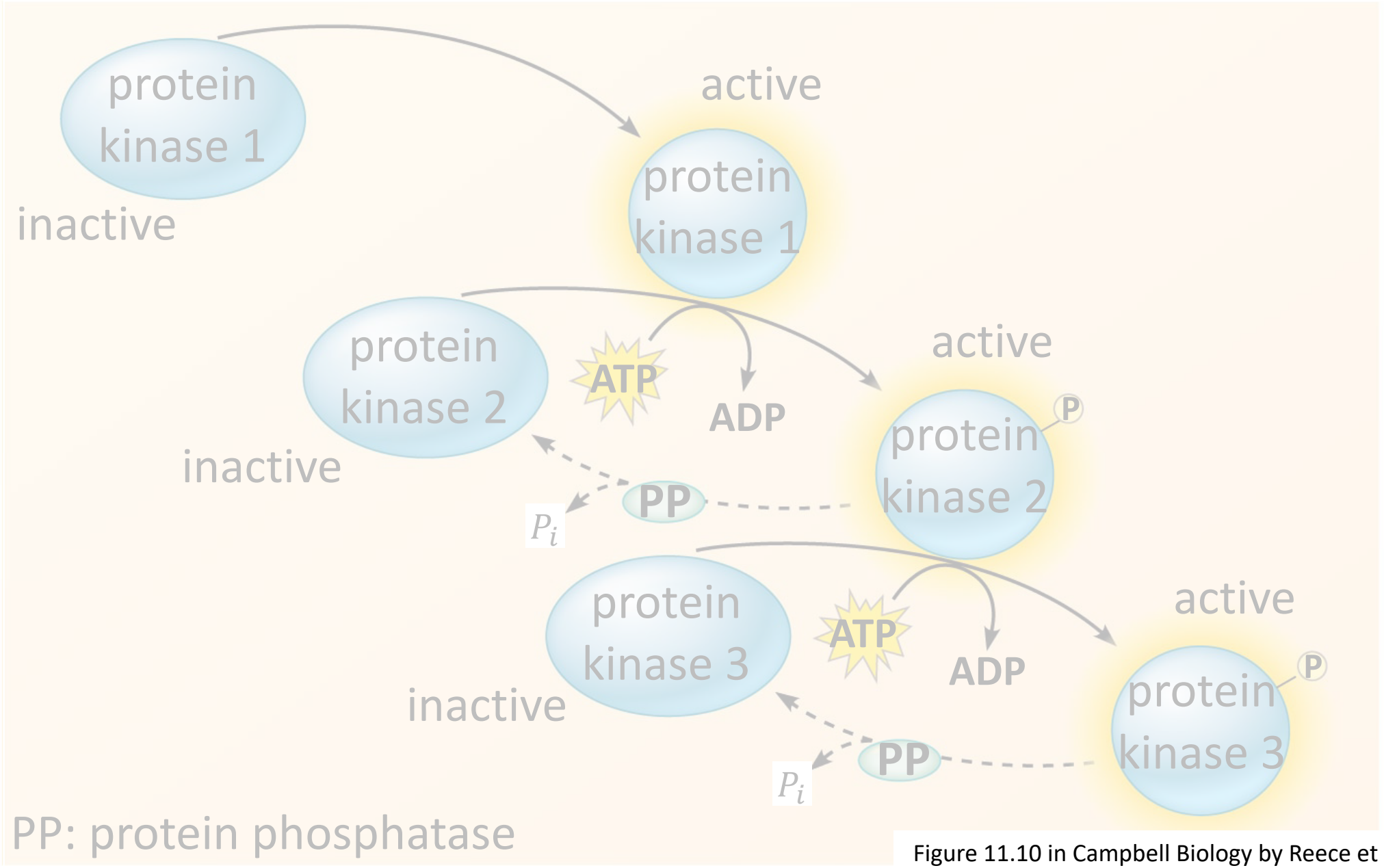


Figure 11.10 in Campbell Biology by Reece et al., (10th edition)

Phosphorylation cascade

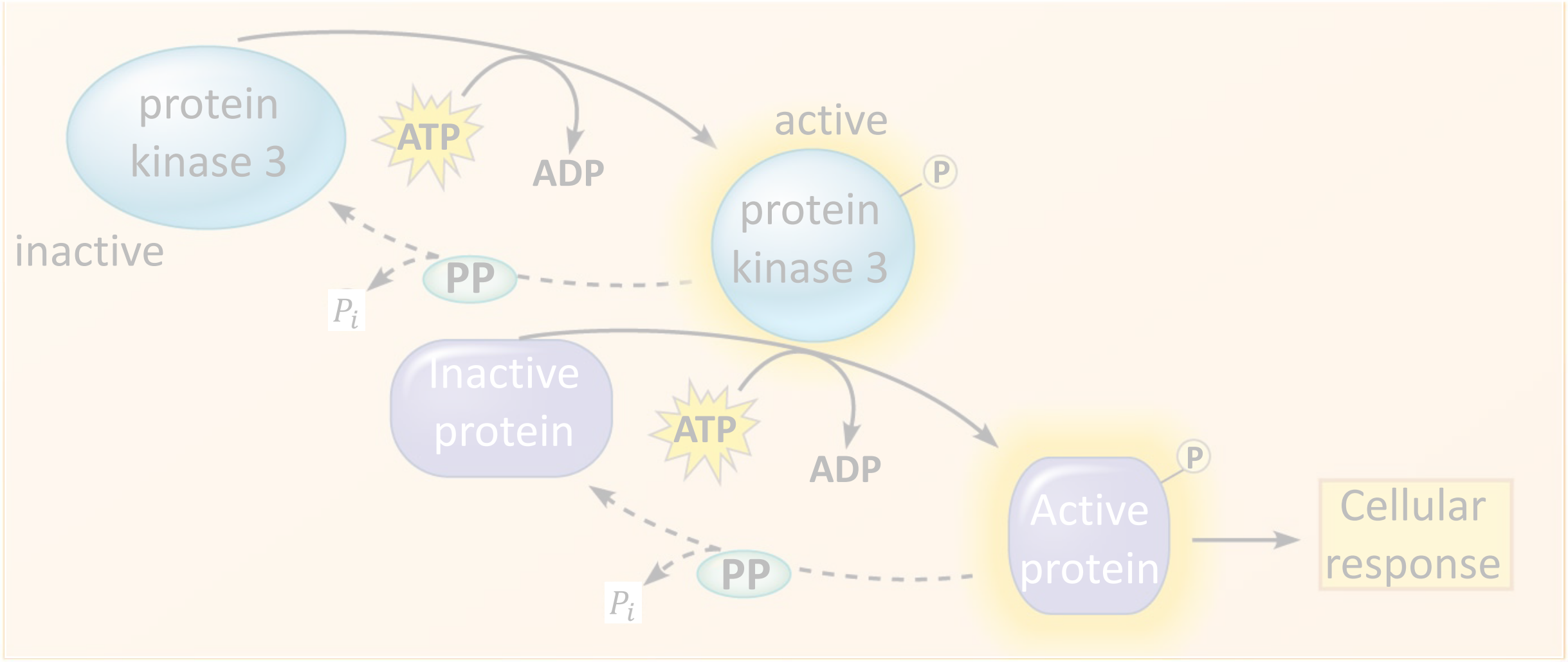
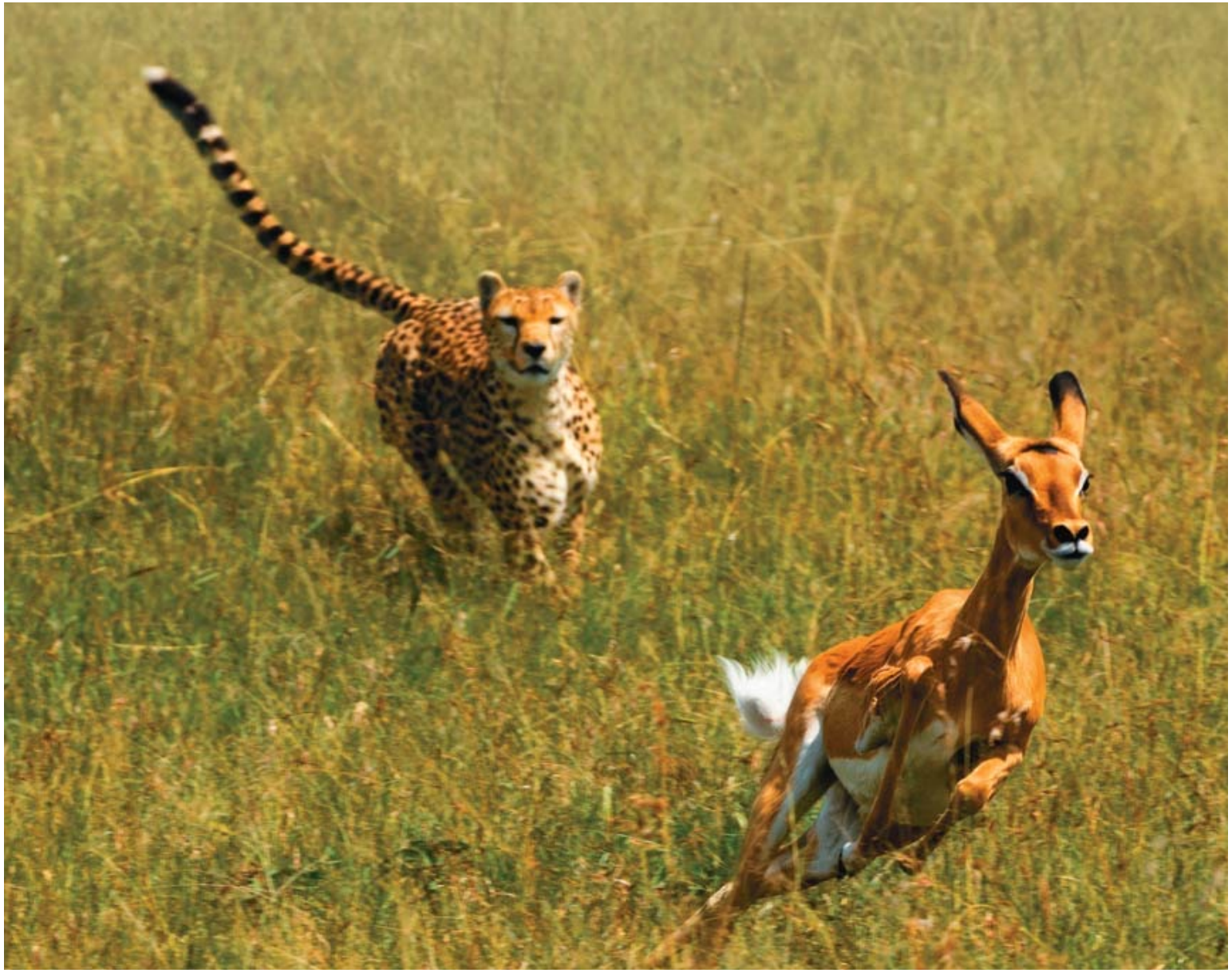
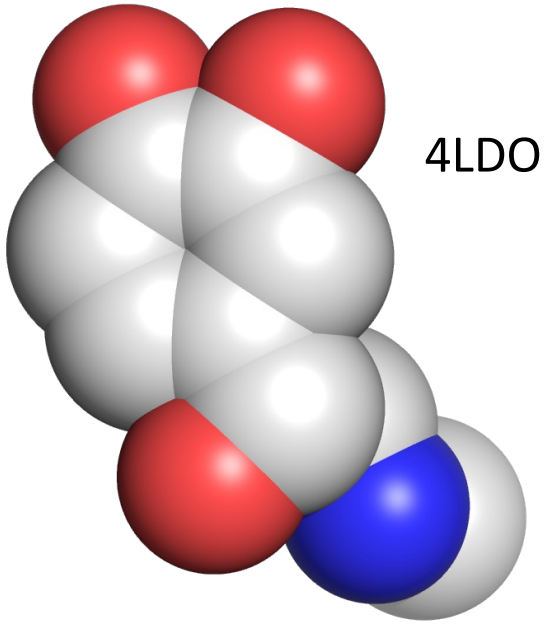


Figure 11.10 in Campbell Biology by Reece et al., (10th edition)

How does adrenaline mobilize energy quickly?





4LDO.pdb

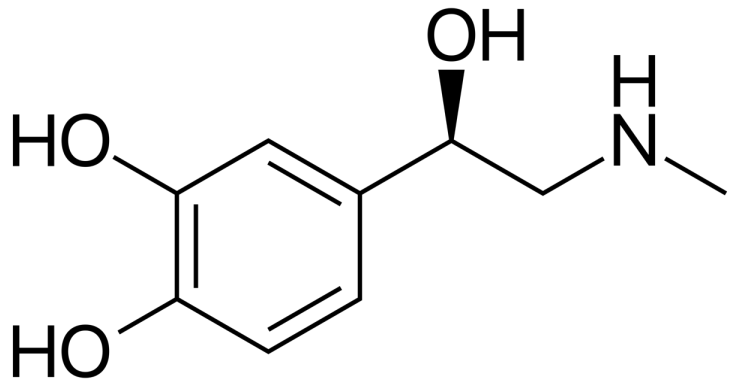
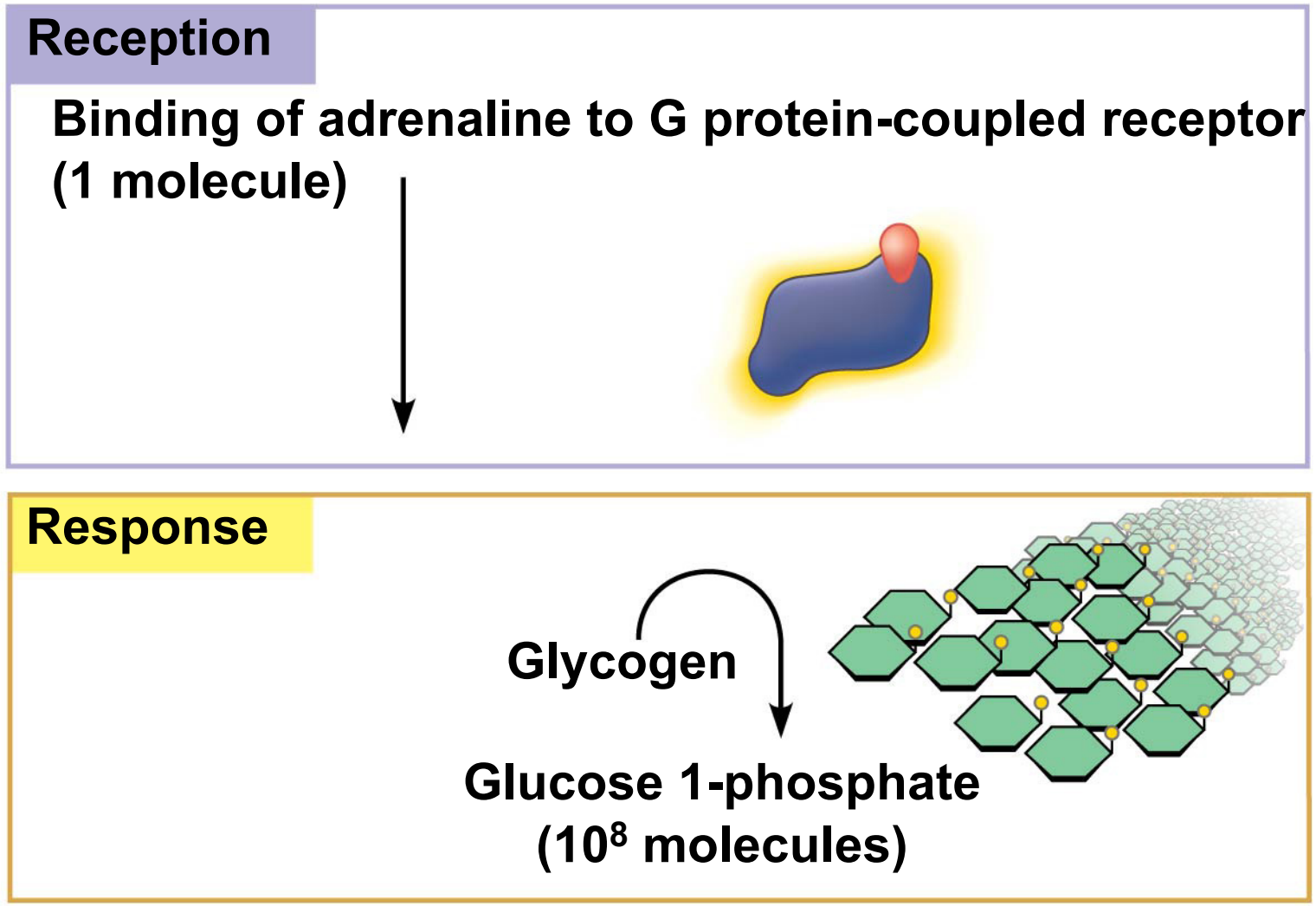


Figure 9.1 of Biology. A global approach

Signal amplification by cascades



Glucose is stored as glycogen

Adrenaline is produced

Signal transduction cascades will activate the enzyme to break down glycogen

Fight or flight response

Figure 9.16 of Biology. A global approach

Signal amplification by cascades

Step	Event	Number of molecules
1	Binding of adrenaline to G-protein coupled receptor	1
2	Activation of G-proteins	10^2
3	Activation of adenylyl cyclase (synthesis of cAMP)	10^2
4	Activation of protein kinase A	10^4
5	Activation of phosphorylase kinase	10^5
6	Activation of glycogen phosphorylase	10^6
7	Release of glucose phosphate	10^8

Figure 9.16 of Biology. A global approach

Amplification by phosphorylation cascades

Dominoes

- Signal transduction usually involves multiple steps
- Multiple steps greatly amplify a signal
- Binding of ligand to a receptor triggers the first step
- Domino effect: sequential activation of proteins
- Each step involves signal transduction e.g., change of shape of a protein

http://dataquarks.com/am-i-alright-jack-the-domino-effect-of-brexit

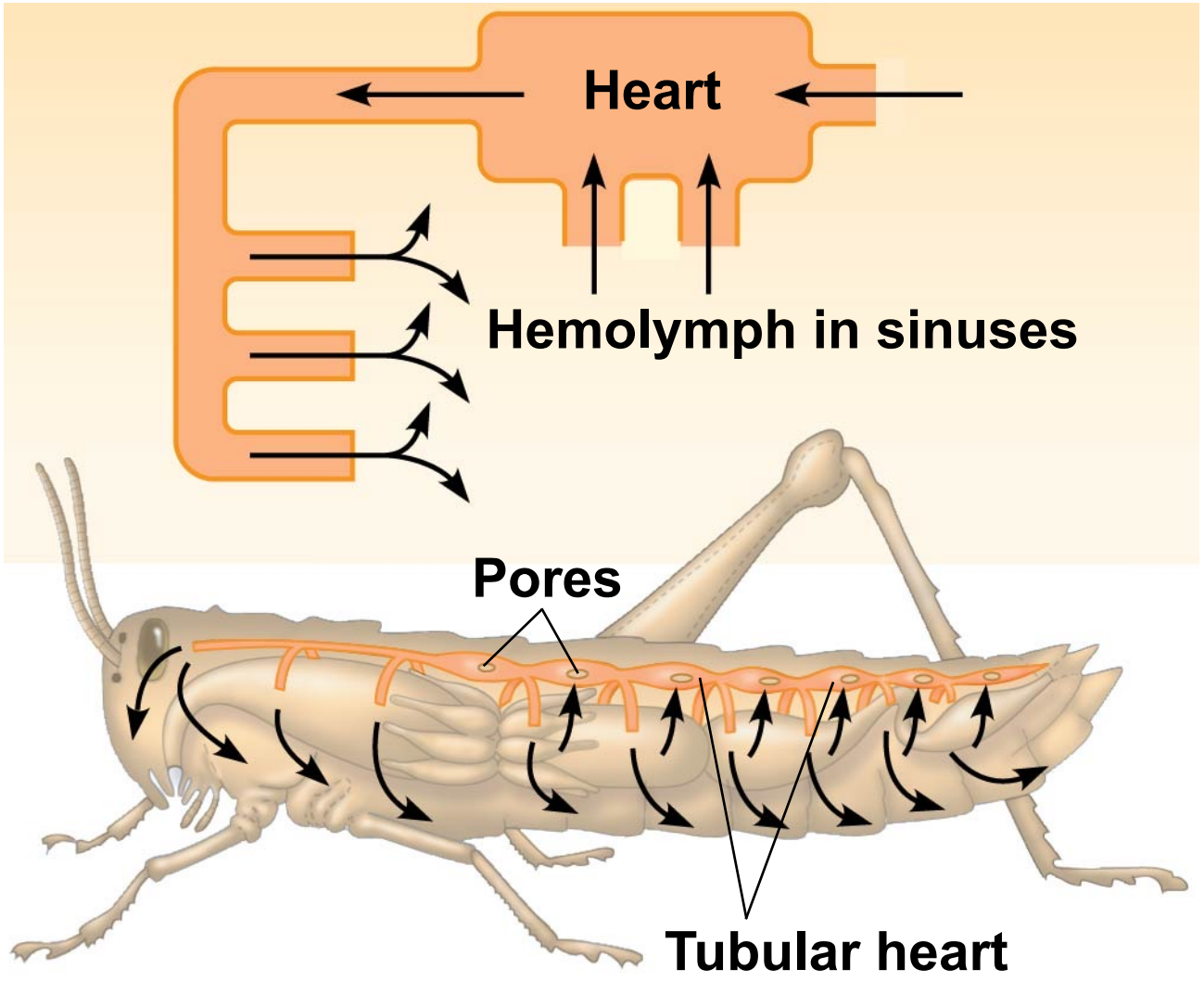
Today's topics

- Example of cell communication: quorum sensing
- Signal transduction in eukaryotes – an overview
- G-proteins
- Signal amplification
- Signaling mechanisms in living systems

Signaling mechanisms are conserved

- Even unicellular organisms talk to each other
- Mechanisms by which cells
  - send/receive signals,
  - process the signal, and
  - let other cells know about the signal…
  - are evolutionarily conserved...
- Same mechanisms are encountered again and again
  - Mechanisms are universal

Specificity of cell signaling



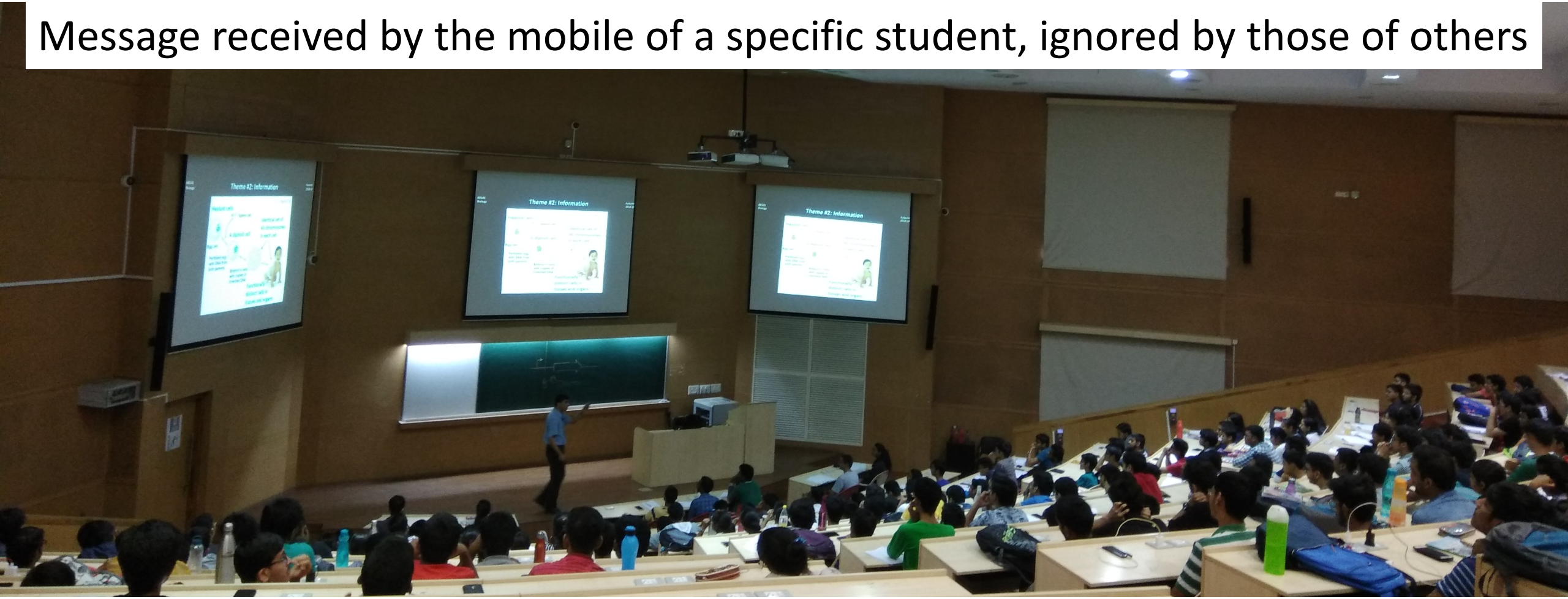
Grasshopper: open circulatory system

- Different organs (cell types) are in contact with the bloodstream
- Bloodstream contains a number of signaling molecules
- Response is elicited in only some cell types?
- How does such specificity arise?

Figure 42.3 in Campbell Biology by Reece et al., (10th edition)

Signal reception by mobile phones

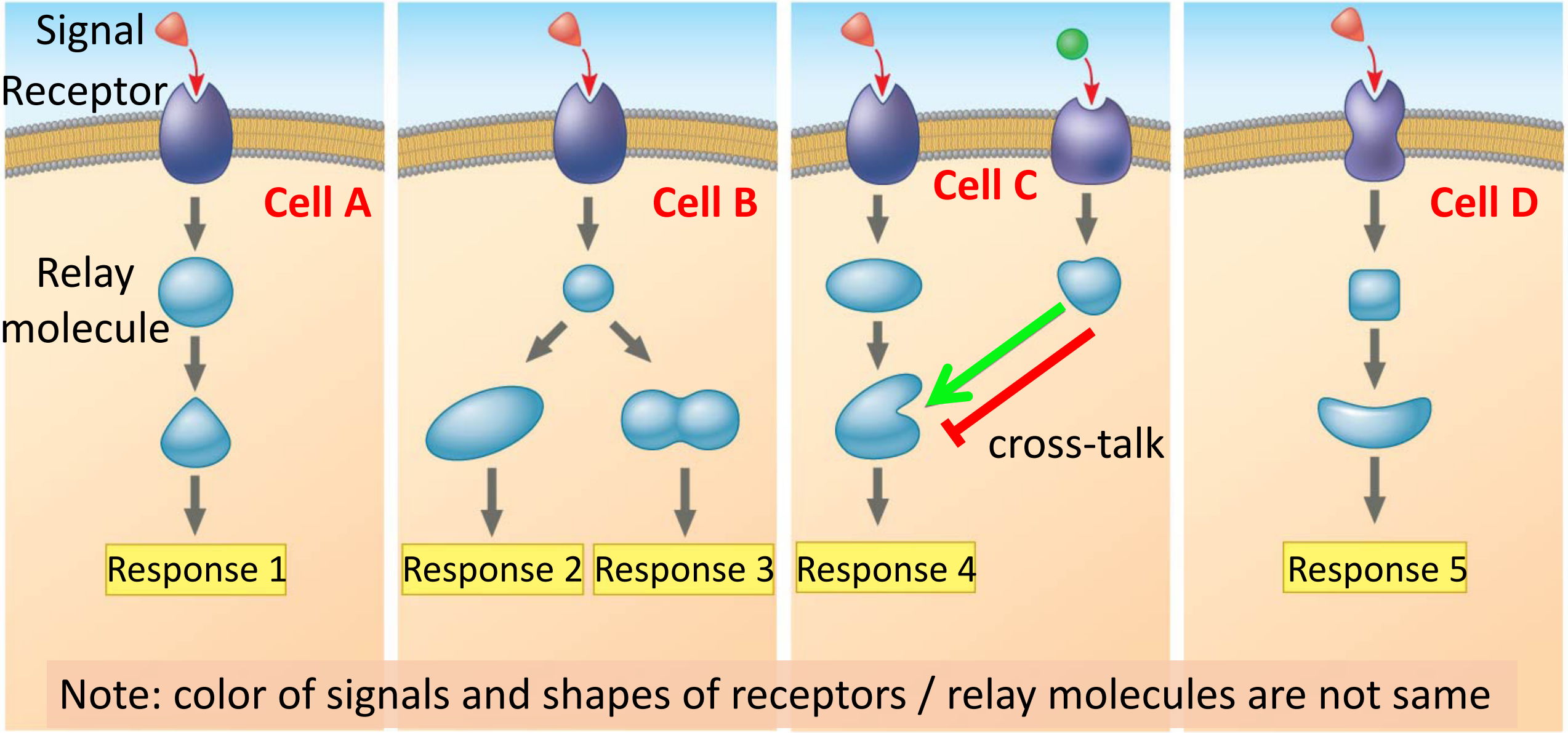
Message received by the mobile of a specific student, ignored by those of others



Cells have a variety of receptors; signaling molecules are also varied

Signaling molecules and receptors bind only their respective partners

Specificity achieved by different receptors



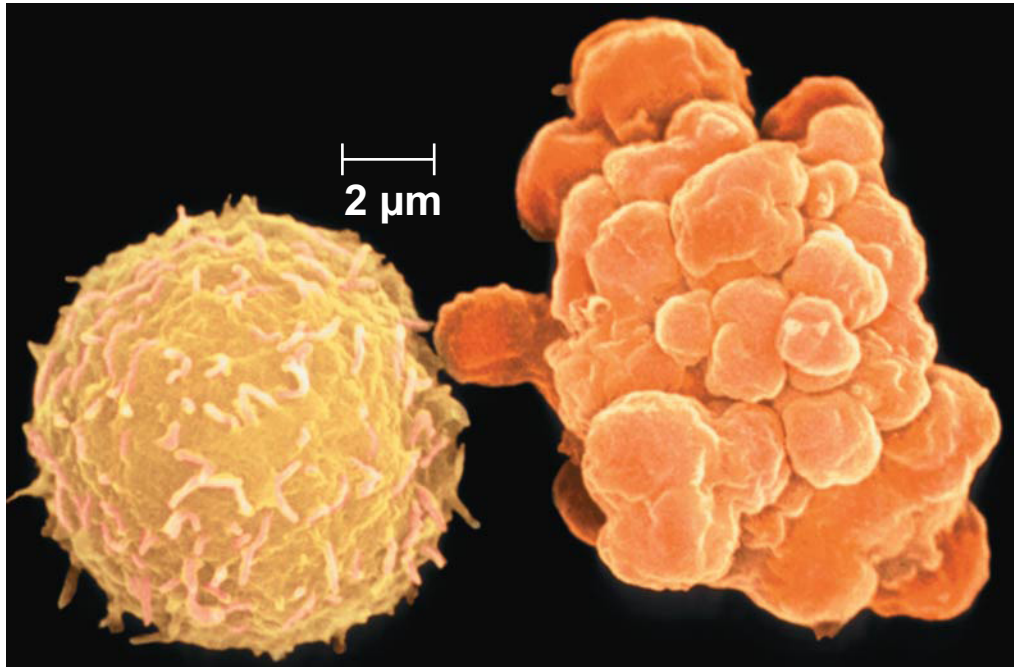
Note: color of signals and shapes of receptors / relay molecules are not same

Figure 11.18 in Campbell Biology by Reece et al., (10th edition)

Apoptosis: integration of several signaling pathways

Human white blood cell

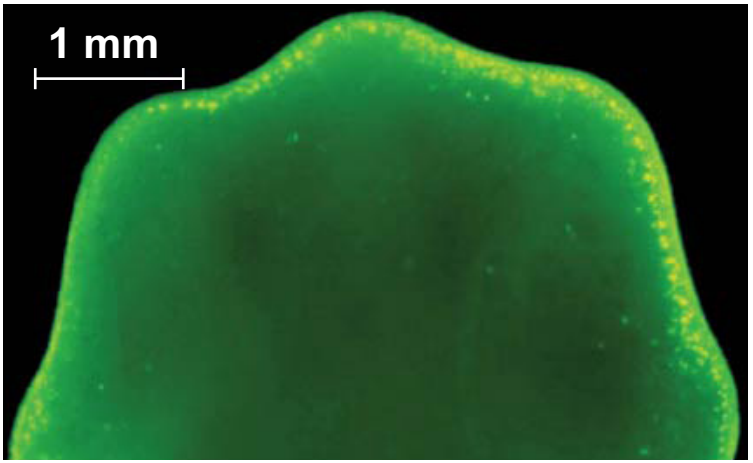
Normal



Undergoing apoptosis
(apoptosis=programmed cell death)

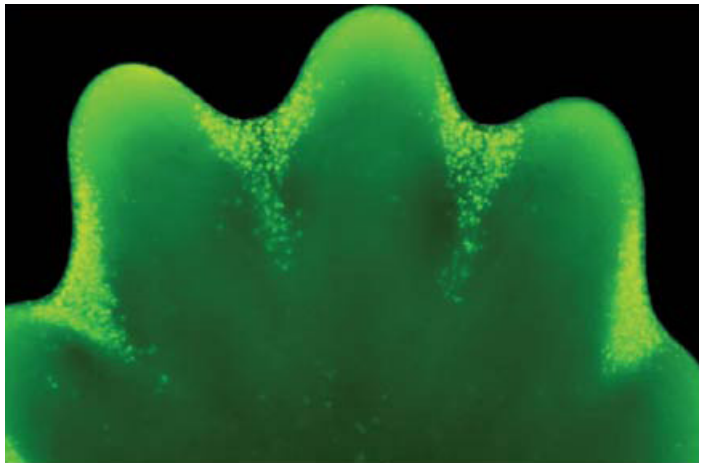
Figure 11.20 in Campbell Biology by Reece et al., (10th edition)

Apoptosis: development of paws in mouse



inter-digital tissue

cells undergoing apoptosis



space between digits

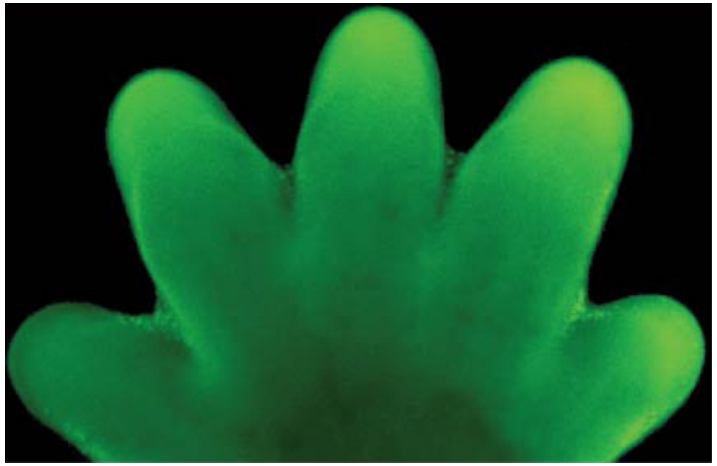


Figure 11.22 in Campbell Biology by Reece et al., (10th edition)