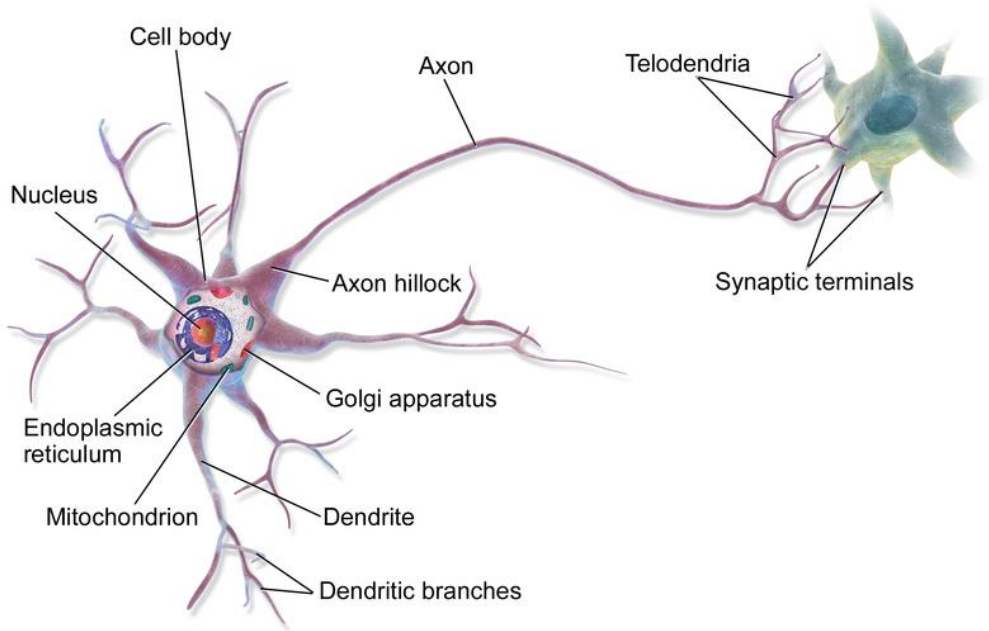
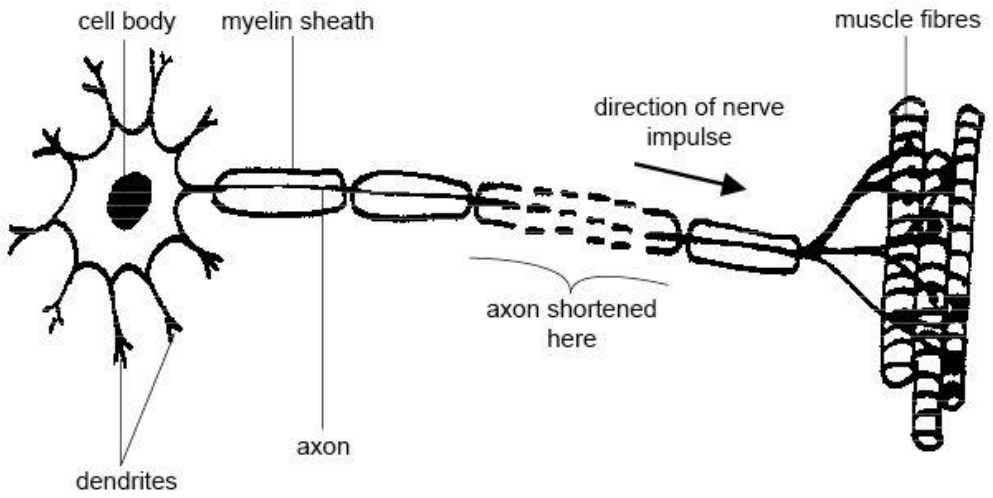
3. Transport proteins at work in the body

Transport Proteins in the Body

- Nerve impulse
- Muscle contraction





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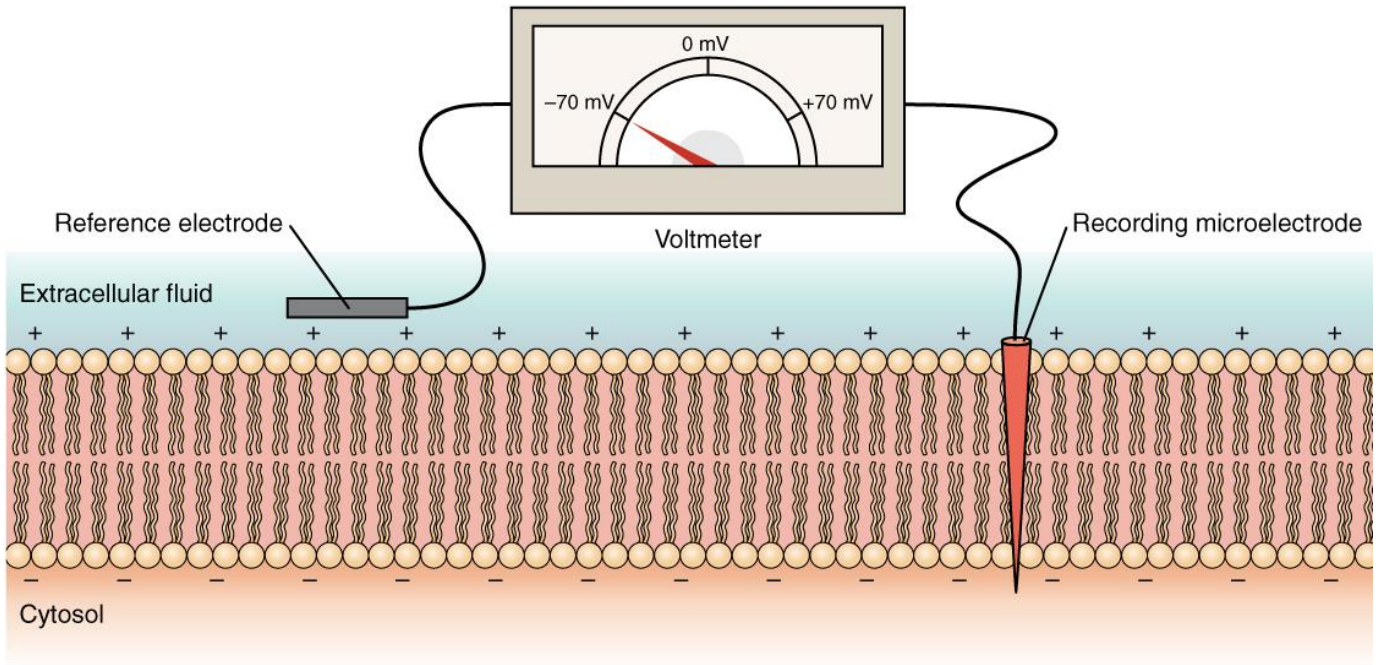
Nerve Impulses

- Key players: Na^+, K^+
- Resting membrane potential
  - -70mV



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Nerve Impulses

(1) Resting membrane potential (-70mV)

- Polarized

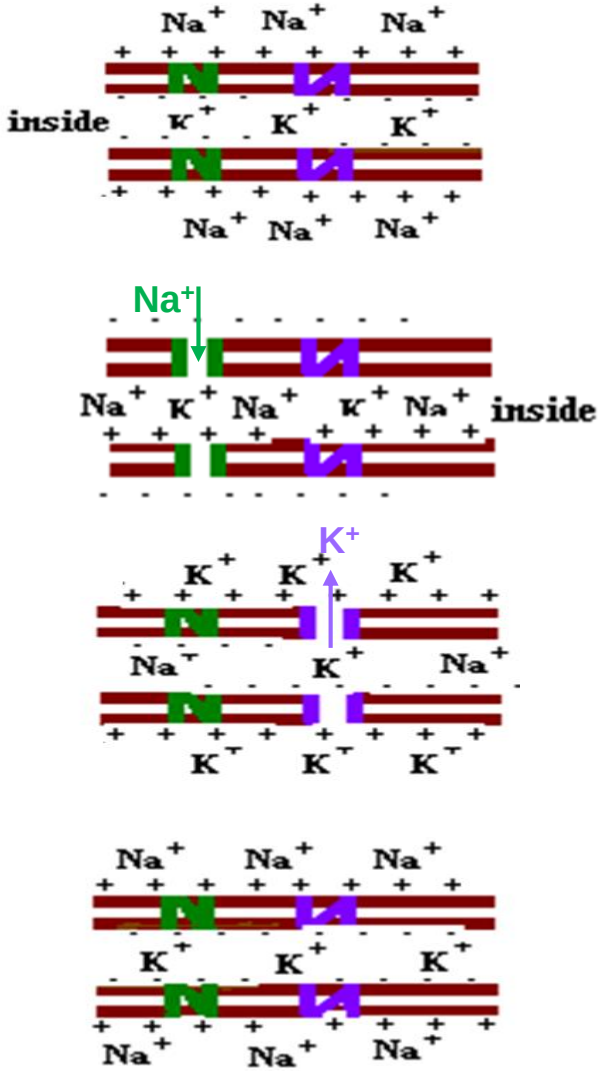
(2) Opening of Na^+ channel by stimulation

- Depolarization

(3) Opening of voltage-gated K^+ channel

- Repolarization

(4) Back to resting state by Na^+/K^+ ATPase



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Nerve Impulses

(1) Resting membrane potential (-70mV)

- Polarized

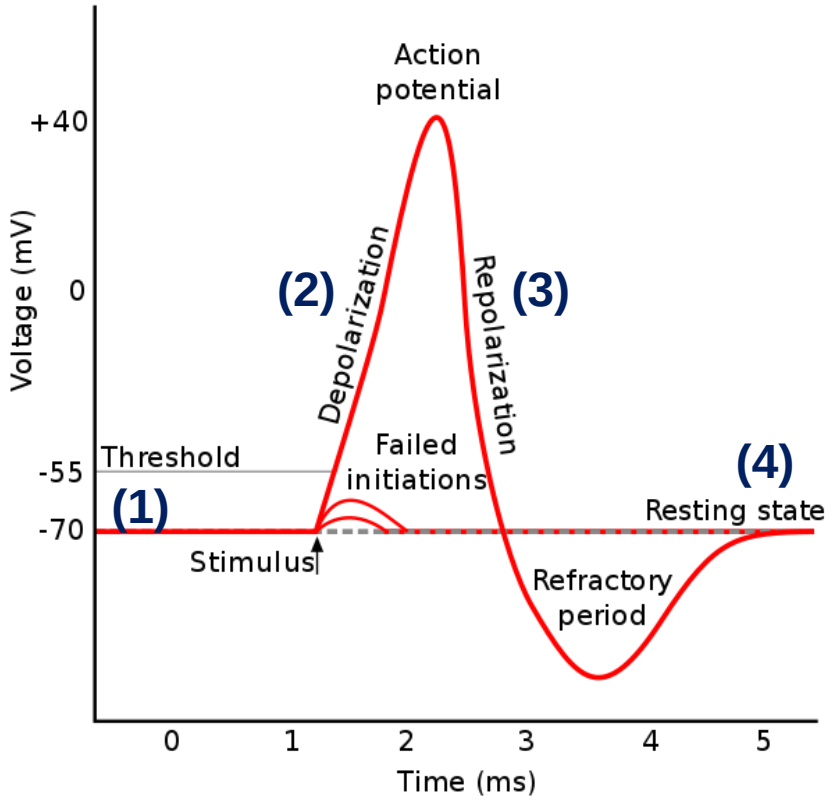
(2) Opening of Na^+ channel by stimulation

- Depolarization
- Rapid depolarization occurs when the threshold voltage (-55 mV) is reached.
- Generation of action potential

(3) Opening of voltage-gated K^+ channel

- Repolarization

(4) Back to resting state by Na^+/K^+ ATPase



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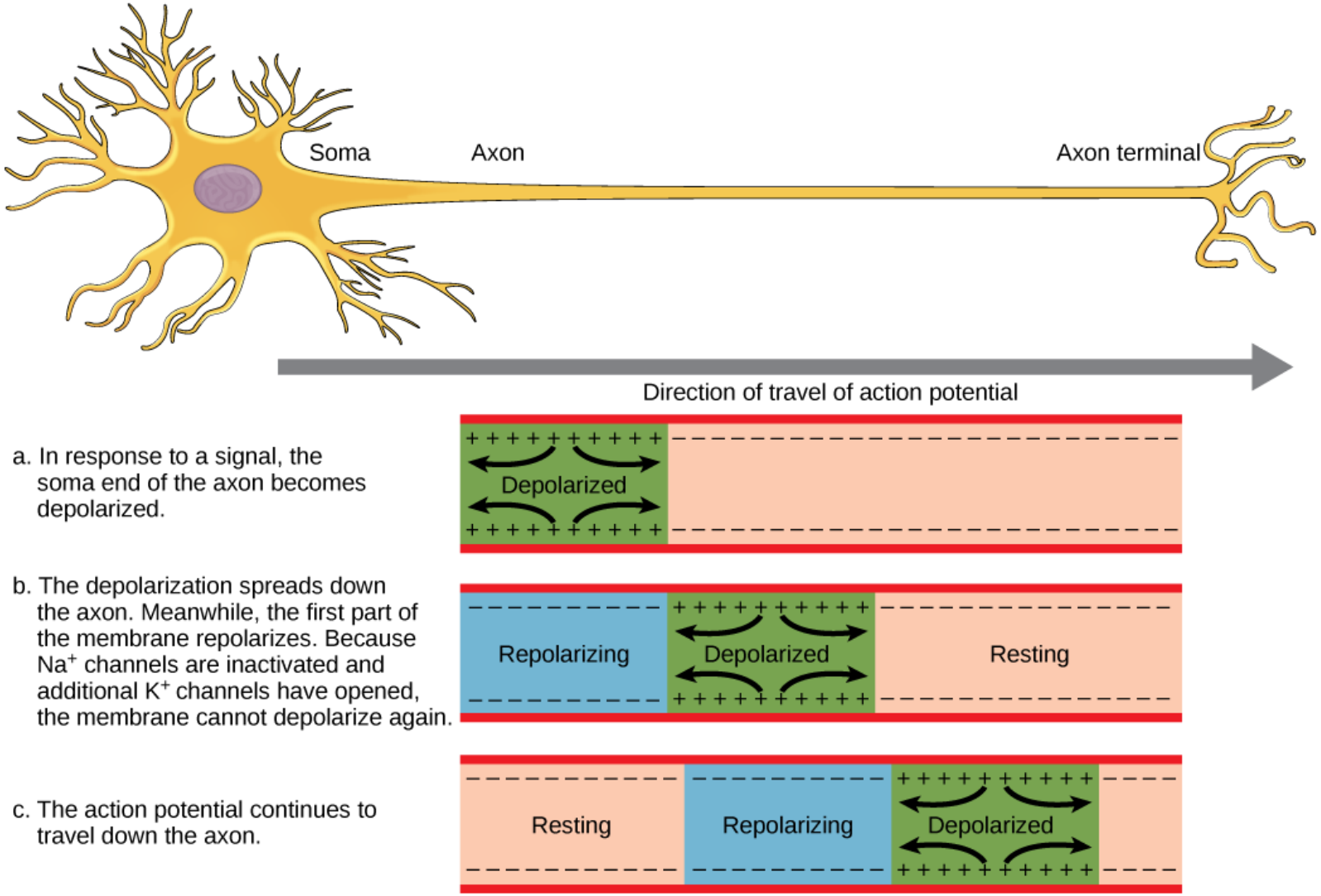
Nerve Impulses



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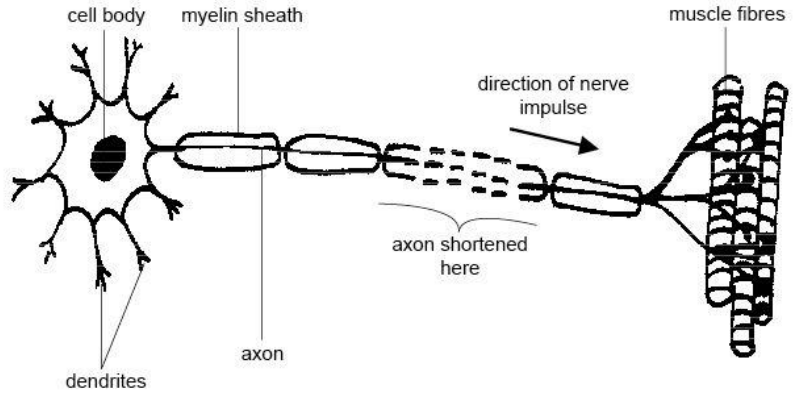
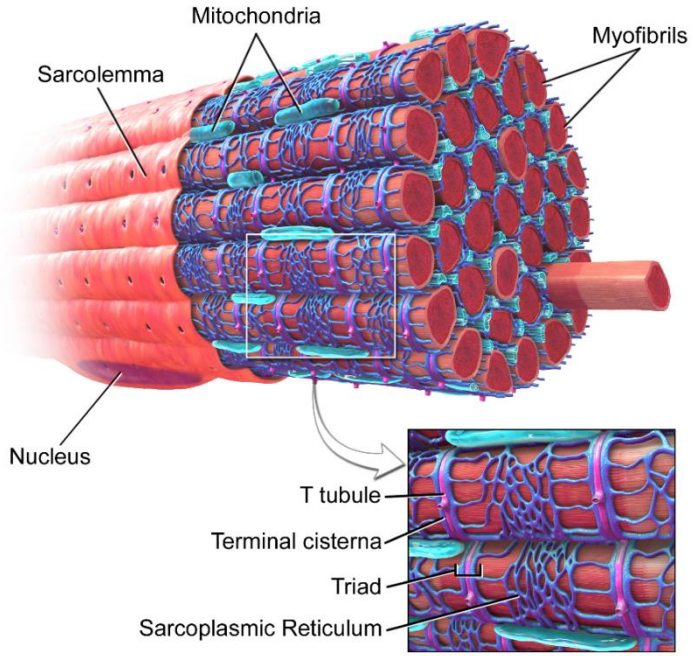
Muscle Contraction

- Key player: Ca^{2+}
- Inside muscle cells, Ca^{2+} are packed into a membrane-bound compartment called the sarcoplasmic reticulum (SR).
- When the nerve impulse (powered by Na^{+}/K^{+} gradients) reaches the muscle cells, it triggers Ca^{2+} channel in the SR to open.





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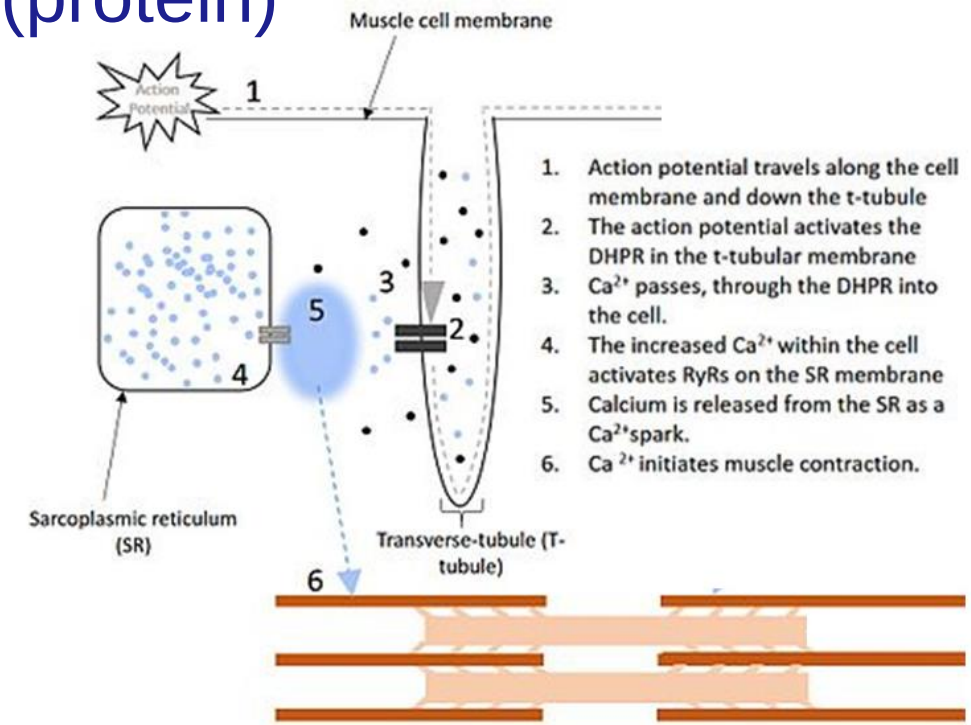
Muscle Contraction

- Opening of Ca^{2+} channel in SR
  → Release of Ca^{2+}
  → Released Ca^{2+} binding to troponin (protein)
  → Muscle contraction

- When the stimulus to contract your muscle ceases
  → Ca^{2+} is pumped back to the SR by ATP-using ion pump.
  → Your muscle relaxes.



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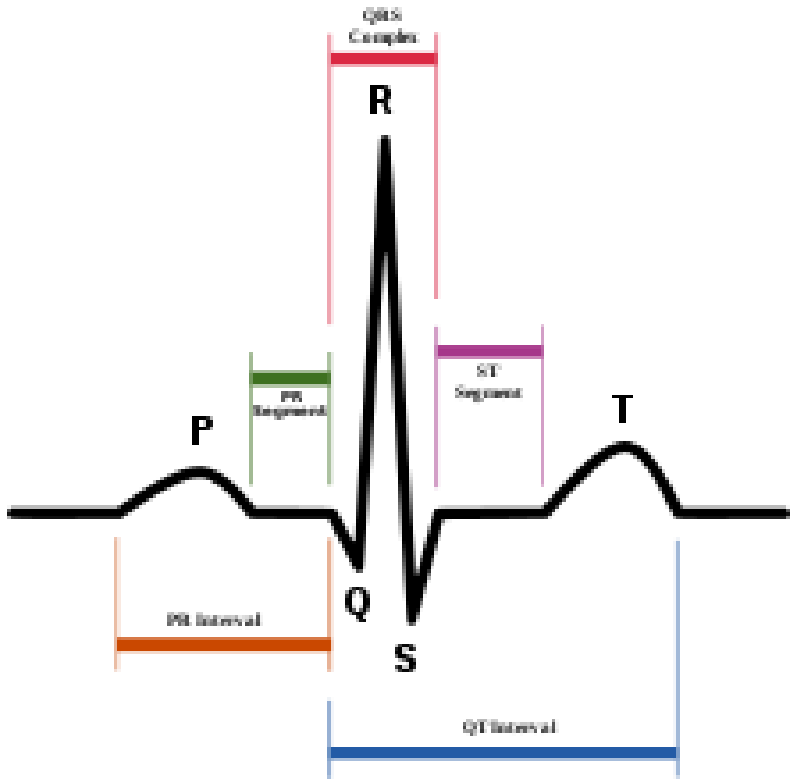
When Gradients Fail

- Long QT (LQT) syndrome
  - Long recovery periods before new heart contraction
  - Cell to cell variation of recovery periods
    - Can cause arrhythmia (lack of rhythm)
  - Defects in K^+ or Na^+ channels

Electrocardiogram (ECG)



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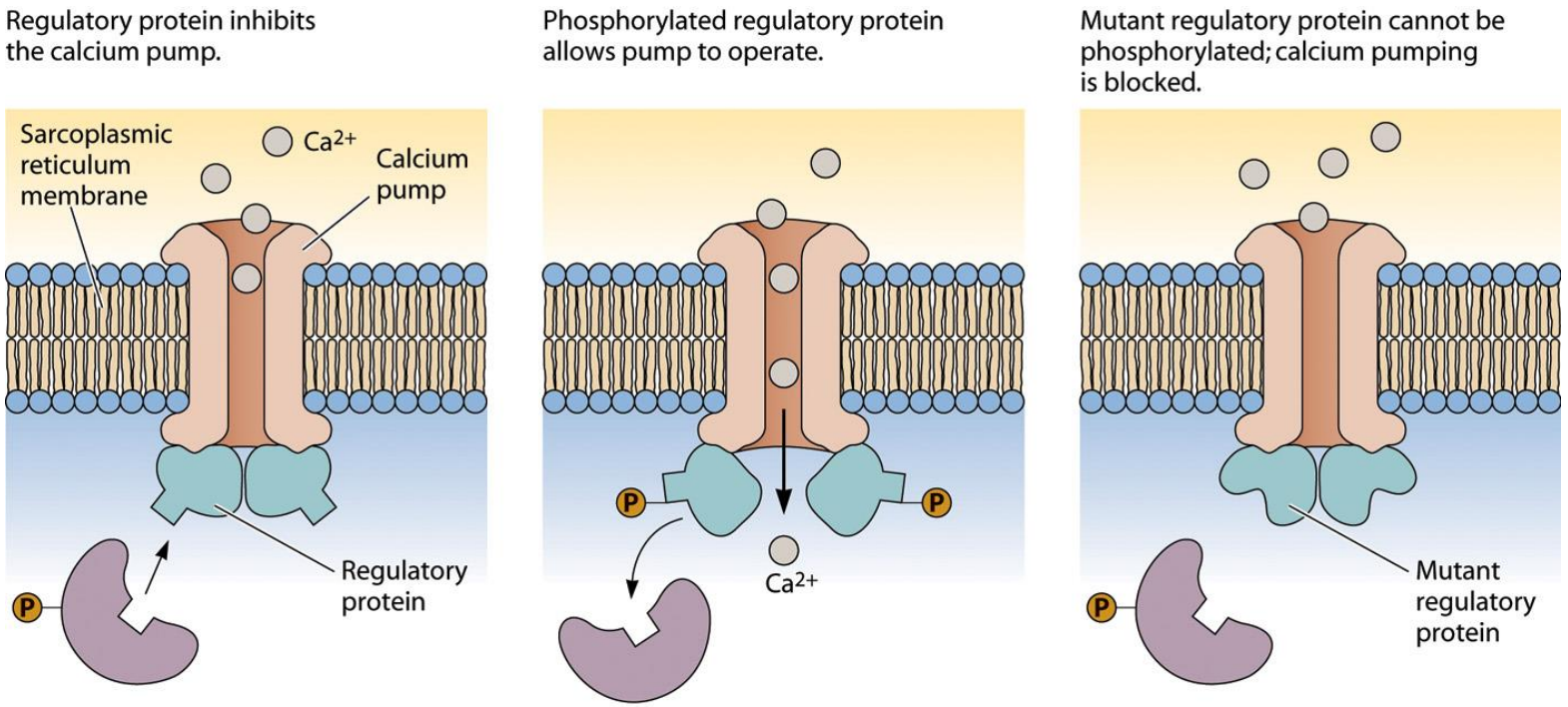
Inherited Heart Failure

- Mutation in the regulatory protein of Ca^{2+} channel in SR (The pump can not transport Ca^{2+} back into SR)



4. Nutrient distribution in the body

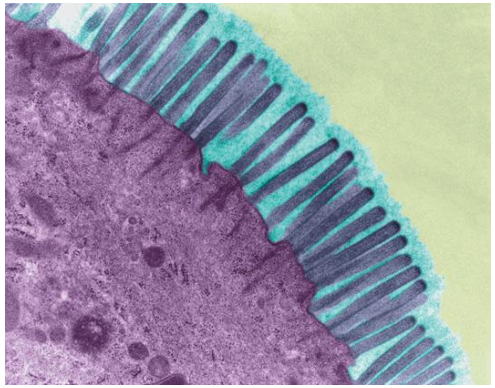
Pumps, Carriers, and Nutrient Distribution

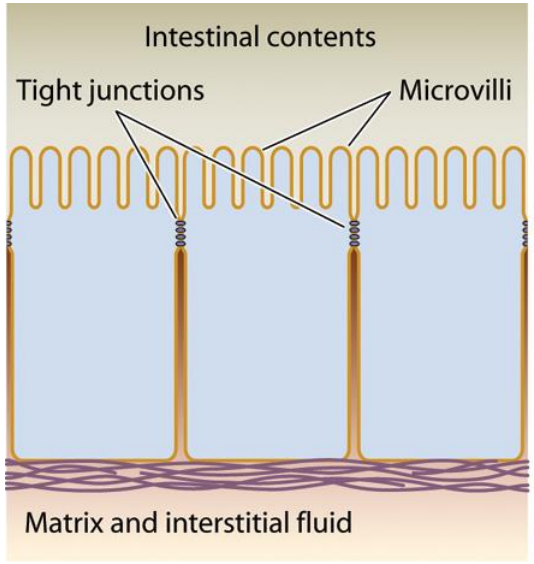
- Nutrient components must move from the intestine to the blood stream through intestinal epithelium.
- Epithelium
  - The body's version of a cell's membrane
  - Epithelial cells
    - Cells cover body surfaces and line internal organs
- Intestinal epithelium
  - Cells lining the digestive tract

Intestinal Epithelium

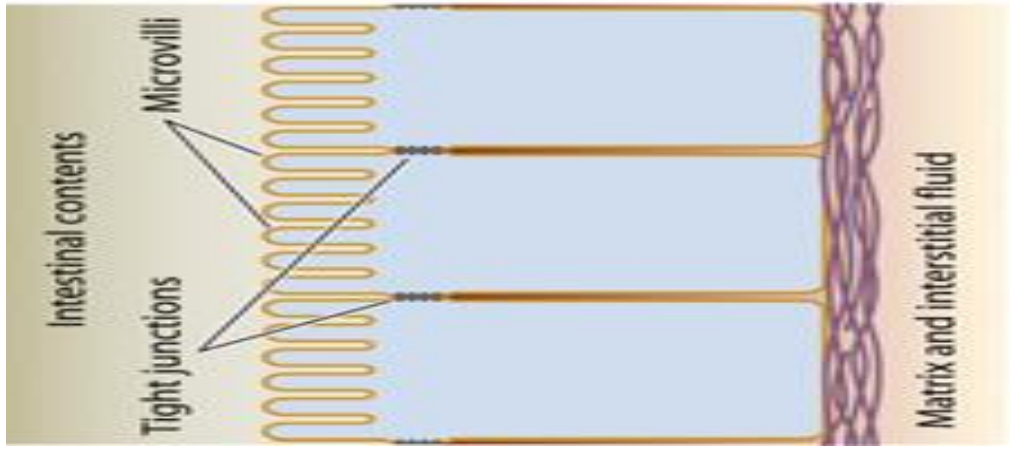
- Microvilli
  - Facing the intestinal track
  - Enzymes and transport proteins are located.
    - The enzymes break down complex sugars into simple sugars.

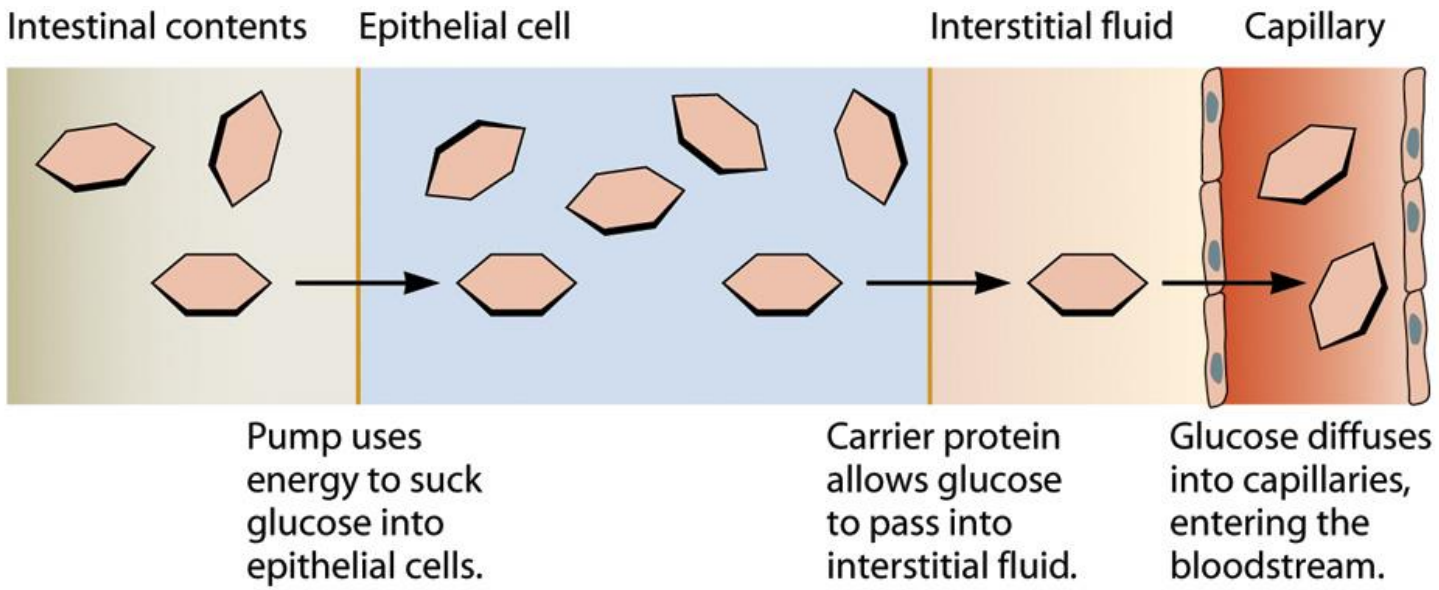
      lactose, sucrose → glucose
- Tight Junction between Cells
  - Preventing transport of large molecules
  - Barrier between the intestinal contents and the interstitial fluid
- Extracellular Matrix
  - Supporting epithelial cells
  - Tough network of extracellular proteins and carbohydrates





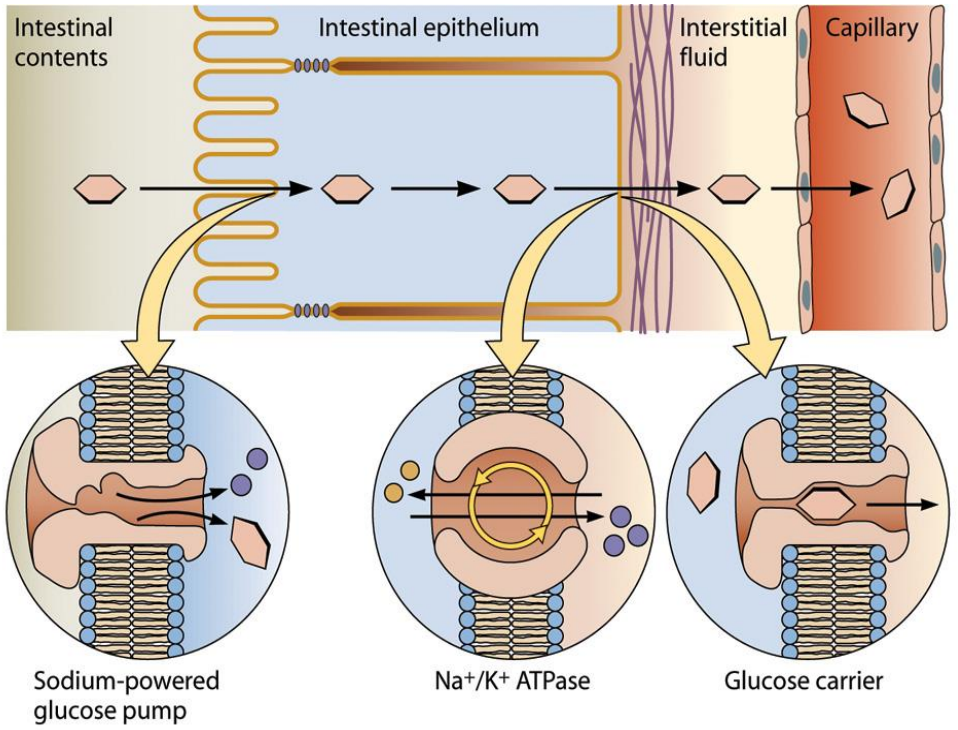
Transport of Nutrients across Epithelial Cells





Transport of Nutrients across Epithelial Cells

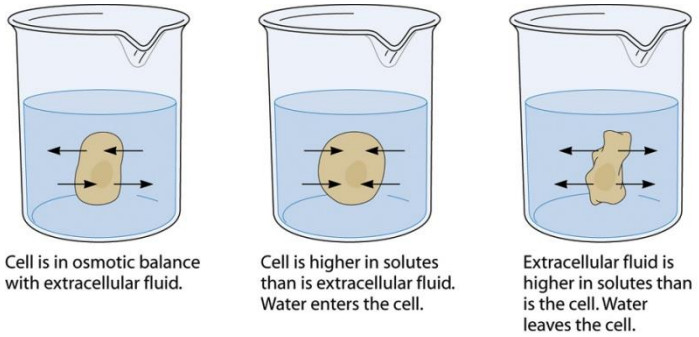
- Intestinal side
  - active transport of glucose powered by Na^+ gradient
  - co-transport of two Na^+ and one glucose molecule
- Interstitial fluid side
  - glucose
    -- by carrier proteins
  - Na^+
    -- by Na^+/K^+ ATPase
- Capillary wall
  - Glucose diffusion
  - Designed to let all but the large molecules (e.g. blood proteins) cross over

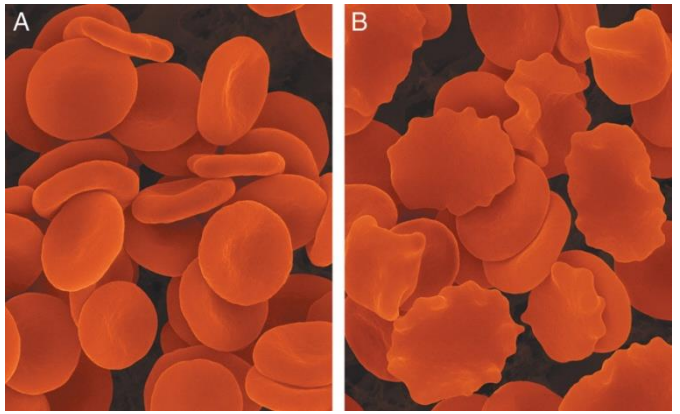


5. Water balance

Cells, Salts, and Water Balance

- Movement of water across the cell
  - Water movement to equalize the total concentration of solutes
  - Osmosis: movement of water across membranes
  - Osmotic balance: no net water movement





Cells, Salts, and Water Balance

- Cells in osmotic balance
  - Cells contain many proteins, amino acids, and other small molecules.
  - Concentration of total ions is higher outside than inside cells to keep the osmotic balance.

Table 7.1 Approximate concentrations of ions in intracellular and extracellular fluids

Ion[a]	Intracellular concn (mM)	Interstitial concn (mM)
Sodium (Na^+)	10	145
Potassium (K^+)	150	5
Calcium (Ca^{2+})	0	3
Chloride ($C1^-$)	5	110

[a]The most abundant ions in interstitial fluid are sodium and chloride ions, which are the components of table salt.

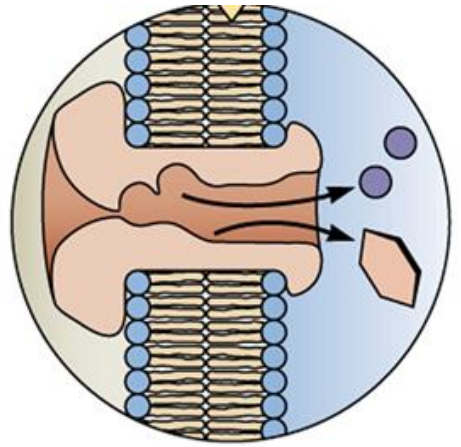
Water follows salt

- Water in human body (75 kg man)
  - 45 L of water
    - 30 L: intracellular
    - 3.75 L: blood plasma
    - 11.25 L: extracellular fluid

  Almost same solute (salt), since blood capillaries are permeable to small molecules
- Water balance
  - Lactose intolerance
    - Lack of lactase breaking lactose into glucose and galactose
    - No digestion of lactose → movement of water into the intestine
    - Metabolize of lactose by intestinal bacteria → gas production
  - High-magnesium laxative : relieving constipation
  - Cystic fibrosis (by impaired salt transport)
    - Mutation in Cl^- channel : reduced water secretion → thick mucus in epithelia of respiratory and gastrointestinal tracts

Biotechnology

- Rehydration therapy
  - Diarrhea: kill 2 million children/year by dehydration
  - Solution of sugar and salt is effective to treat dehydration: e.g. sports drinks
- Enzyme treatments
  - Lactose intolerance
    - Add lactase (β-galactosidase) in milk or dairy products
  - When you eat a bean-rich meal in a Mexican restaurant
    - Beans contain galactose-containing sugars (galactosides)
    - Humans lack enzymes for breaking down galactosides.
    - Microbial munching on galactosides → gas production
    - Buy α-galactosidase (Beano) in a drugstore



Chapter 8

Cells Respond to Their External Environments

목 차

1 신호와 수용체

2 오페론 (Operon)

3 호르몬

4 혈당 조절

1. 신호와 수용체(Signals and Receptors)

Response to External Environments

- Single-celled organism
  - Respond to environmental changes
  - Temperature, salinity, pH, toxins, mating factors
- Multicellular organism
  - Environment is the inside of the organism
  - Respond to external conditions and maintain cellular homeostasis

Signals and Receptors

- Response to signal
  - Signal
    - Chemicals, light, sound, electrical impulses, solutes concentration, pressure
  - Detection of signal
    - Receptors
  - Induction of cellular response
    - Cellular changes
    - Cellular responses

Response to Signal

- Cellular changes
  - Activation or suppression of enzyme activity
  - Activation or suppression of transcription or translation
  - Changes in the permeability of the cell
  - Release of stored proteins
- Cellular responses
  - Generation of nerve impulse
  - Metabolizing nutrient
  - Migration
  - Growing and dividing
  - Differentiation
  - Dying

Types of Receptors

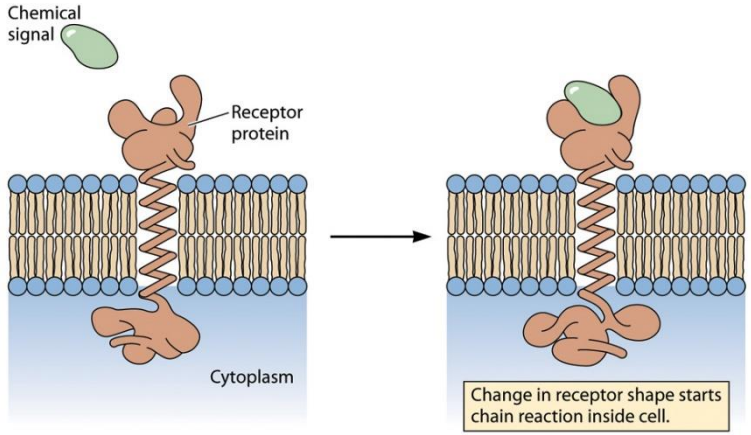
- Receptors of the five senses

Table 8.1 Receptors and the five senses

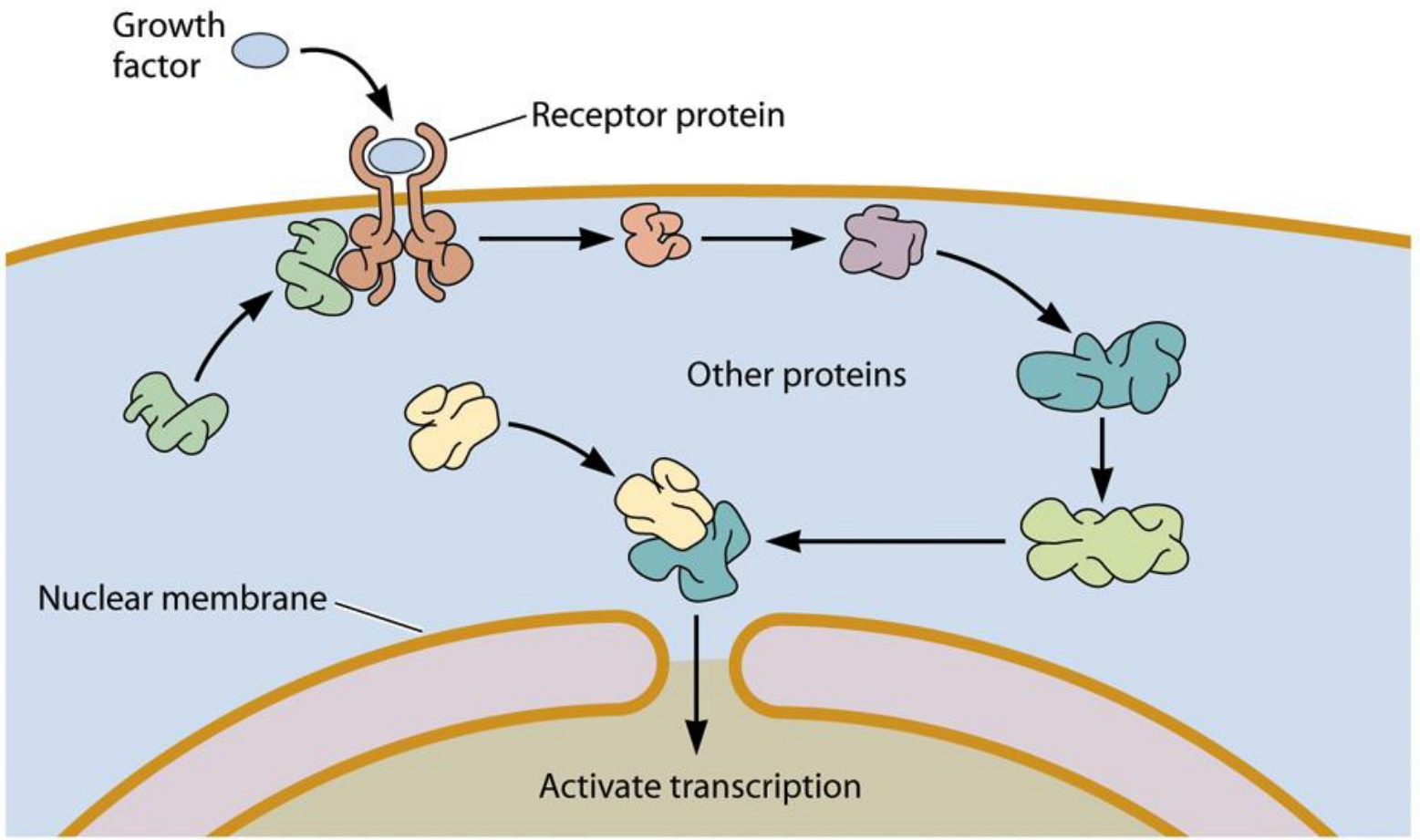
Type of receptor	Activating stimulus	Cellular response	Brain's interpretation of nerve impulse
Photoreceptor	Light	Change in membrane channels	Vision
Auditory receptors	Vibration	Release of stored neurotransmitters	Sound
Olfactory receptors	Various molecules in the air	Change in membrane channels	Smell
Taste receptors for sweet and bitter	Various dissolved molecules	Change in membrane channels	Sweet or bitter taste
Taste receptors	Na^+, $C1^-$, K^+ (salty) H^+ (sour)	Release of stored neurotransmitters	Salty or sour taste
Baroreceptor	Deformation of cell	Change in membrane channels	Touch, pressure

Signal Transduction

- Receptors
  - Membrane receptor: Binding of signal molecules which cannot cross the membrane
  - Intracellular receptors: Binding of signal molecule which can cross the membrane
- Signal transduction
  - Conformational change of receptor upon binding to the signal
  - Triggering cascade of reactions



Signal Transduction



2. 오페론 (Operon)

Responses of Single-Celled Organisms

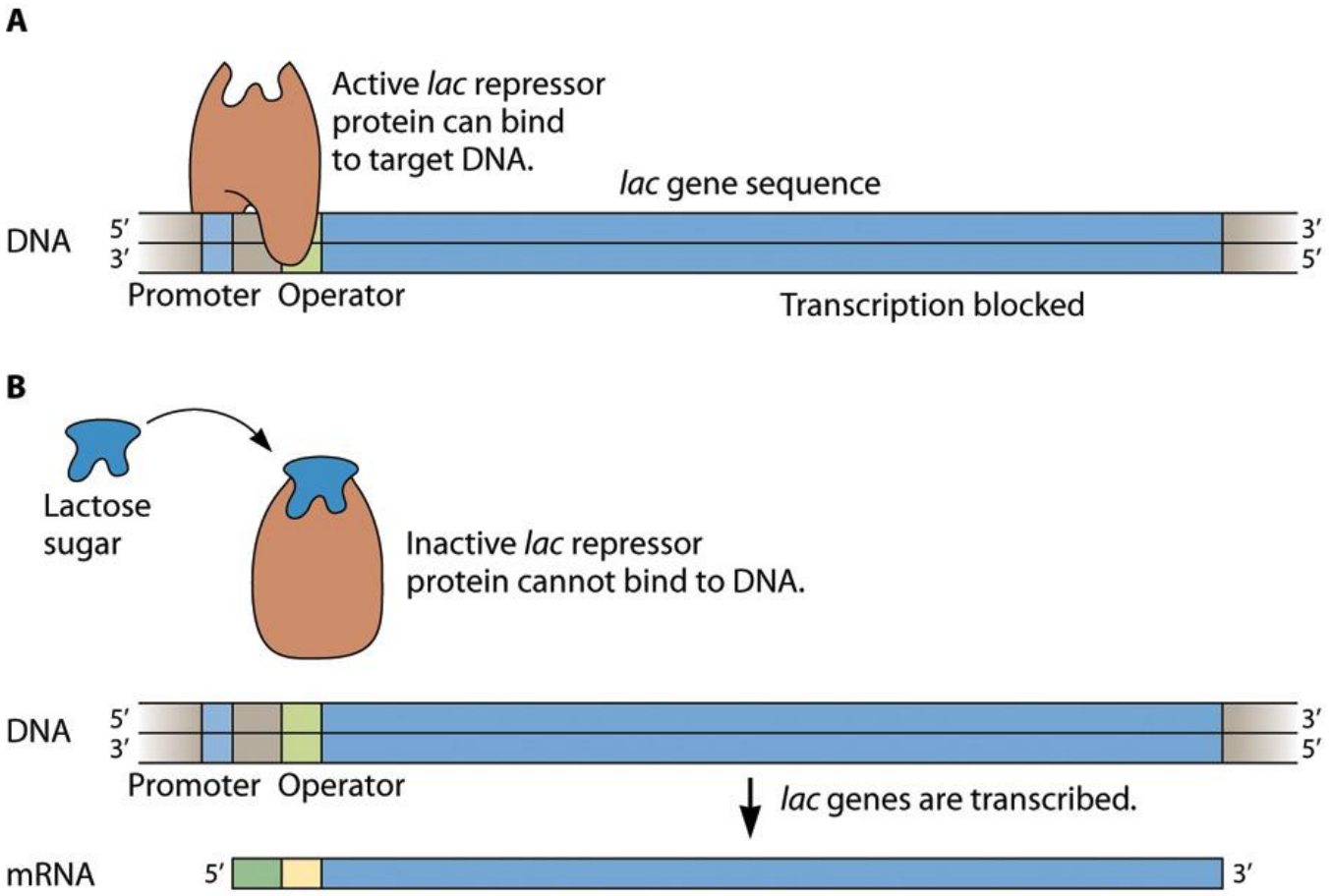
- Lactose breakdown in *E. coli*
  - Turning on lactose utilizing genes (*lac* genes) only in the presence of lactose
  - In the absence of lactose

    --- The *lac* repressor represses *lac* genes by binding to operator of *lac* operon.
  - In the presence of lactose

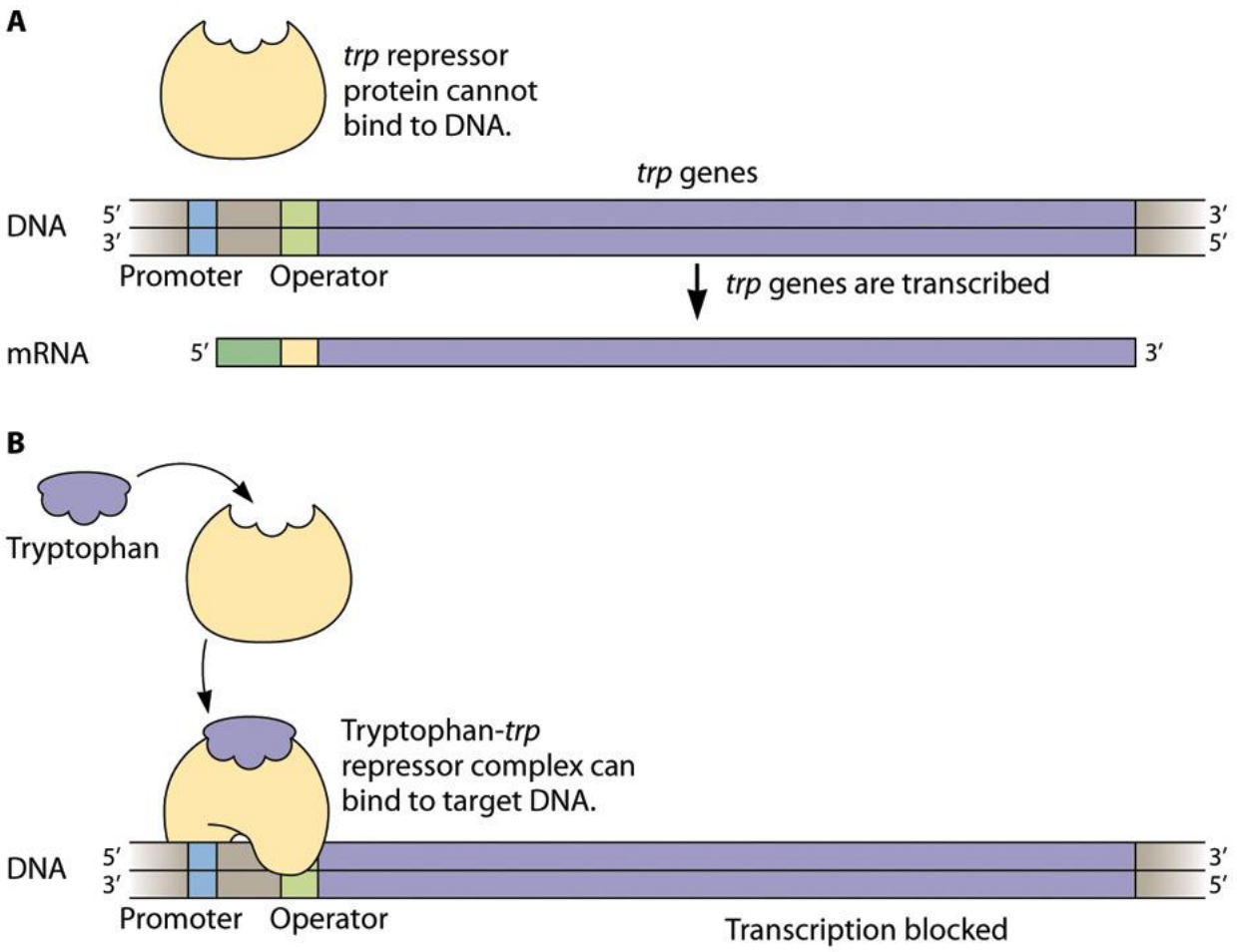
    --- Lactose binding to *lac* repressor leads to release from the *lac* operator

    → Transcription on

lac Operon


A
Active lac repressor protein can bind to target DNA.
lac gene sequence
DNA
5′
3′
3′
5′
Promoter
Operator
Transcription blocked
B
Lactose sugar
Inactive lac repressor protein cannot bind to DNA.
DNA
5′
3′
3′
5′
Promoter
Operator
lac genes are transcribed.
mRNA
5′
3′

trp Operon


A
trp repressor protein cannot bind to DNA.
trp genes
DNA
5′
3′
3′
5′
Promoter
Operator
trp genes are transcribed
mRNA
5′
3′
B
Tryptophan
Tryptophan-trp repressor complex can bind to target DNA.
DNA
5′
3′
3′
5′
Promoter
Operator
Transcription blocked

3. 호르몬 (Hormone)

Coordination of Cellular Responses in Multicellular Organisms

Coordination of Cellular Responses in Multicellular Organisms

- Hormones
  - Produced in various glands and secreted into blood stream

Table 8.2 Examples of human hormones

Hormone	Where secreted	Target(s)	Primary effect(s)
Thyroxine	Thyroid	Many tissues	Stimulates and maintains metabolism; necessary for normal growth and development
Growth hormone	Anterior pituitary	Bones, liver, muscle	Stimulates protein synthesis and growth
Follicle-stimulating hormone	Anterior pituitary	Gonads	Stimulates growth and maturation of eggs in females; stimulates sperm production in males
Melanocyte-stimulating hormone	Anterior pituitary	Melanocytes	Controls pigmentation
Insulin	Pancreas	Muscles, liver, fat	Stimulates uptake and metabolism of glucose; increases glycogen and fat synthesis; reduces blood sugar
Glucagon	Pancreas	Liver	Stimulates breakdown of glycogen; raises blood sugar
Somatostatin	Pancreas	Digestive tract, pancreas	Inhibits release of insulin and glucagon; decreases activity in the digestive tract
ADH	Posterior pituitary	Kidneys	Stimulates water resorption and raises blood pressure
ANH	Heart	Kidneys	Increases sodium ion excretion; lowers blood pressure
Aldosterone	Adrenal cortex	Kidneys	Stimulates excretion of potassium and resorption of sodium ions
Estrogens	Ovaries	Breast, uterus, and other tissues	Stimulate development and maintenance of female sexual characteristics; necessary for proper bone development in males and females; proper seminal fluid formation in males
Androgens	Testes	Various tissues	Stimulate development and maintenance of male sexual characteristics

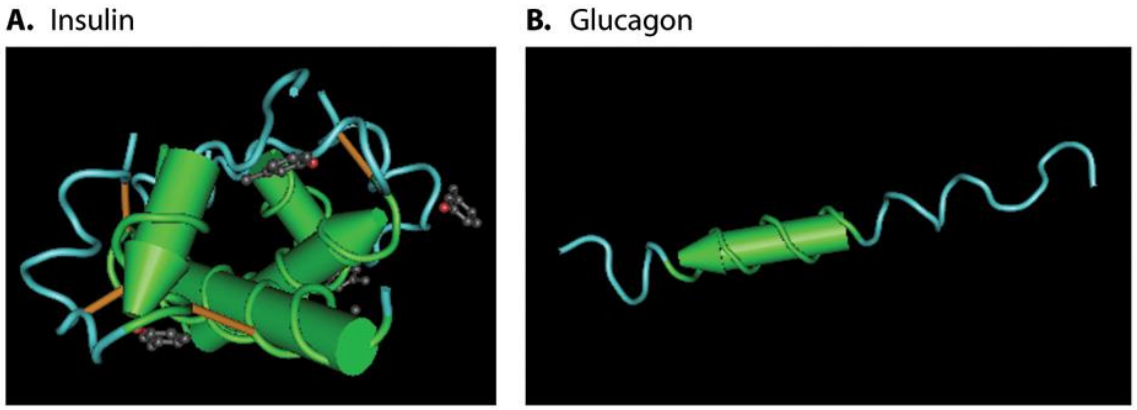
Hormones

- Hormone receptors
  - Membrane receptors (Many hormones are proteins.)
    → signal transduction
  - Intracellular receptors for steroid hormones
    The receptor-hormone complex binds to target DNA.
    → repression or activation of transcription
- Estrogen
  - Female hormone (steroid hormone)
    - The receptor-hormone complex activates the transcription.
      → Generation of new blood vessels in the uterus,
      Increase in lactoferrin (protein in breast milk)
  - Proper production of seminal fluid and development of skeletons in male

4. 혈당 조절(Regulation of Blood Glucose Concentration)

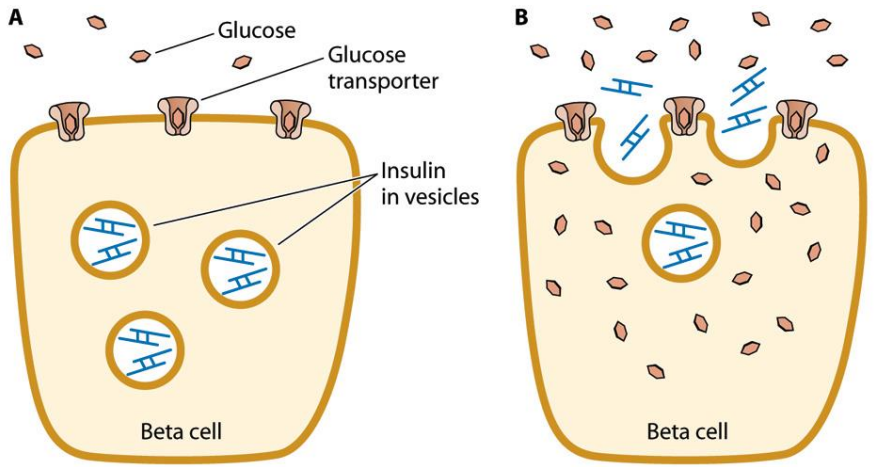
Regulation of Blood Glucose Concentration

- Importance of regulating glucose levels in blood stream
  - Low glucose: no energy source in the brain
    → unconsciousness, comma, and death
  - High glucose: mental confusion, dehydration etc.
- Hormones regulating blood glucose levels
  - Generated from pancreas
    - Insulin decreases glucose levels
    - Glucagon increases glucose levels



Insulin

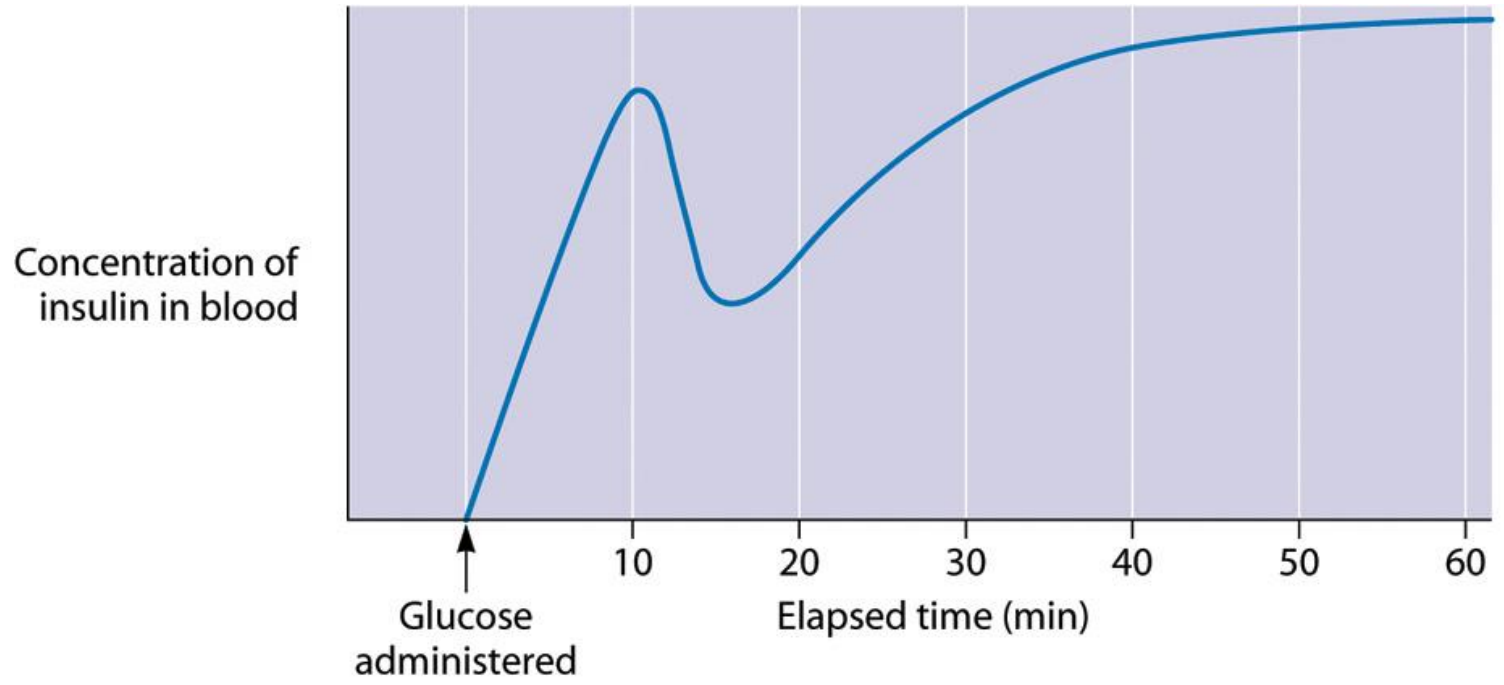
- Synthesized in the pancreatic β cells and packed into vesicles
- If glucose is high,
  - → the glucose enters the β cells via transport proteins
  - → Insulin vesicles fuses with cell membrane
  - → Insulin is released to the blood stream



Insulin

(1) Insulin packed in vesicles can be utilized immediately.

(2) Glucose stimulates the transcription of insulin gene.



Roles of Insulin

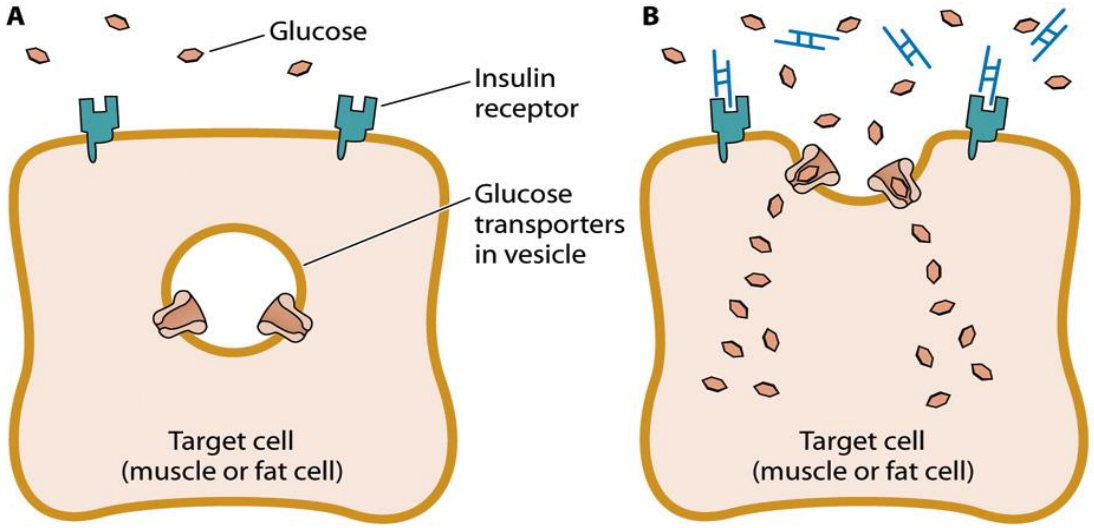
- Binding to cell type-specific insulin receptors
  - e.g. Muscle and fat cells

    Binding of insulin to insulin receptors

    → Increase in fusion of vesicles containing glucose transporters (GLUT4)

    → Stimulation of uptake of glucose from the blood

    cf. liver and brain: insulin-independent glucose transporter (GLUT1)

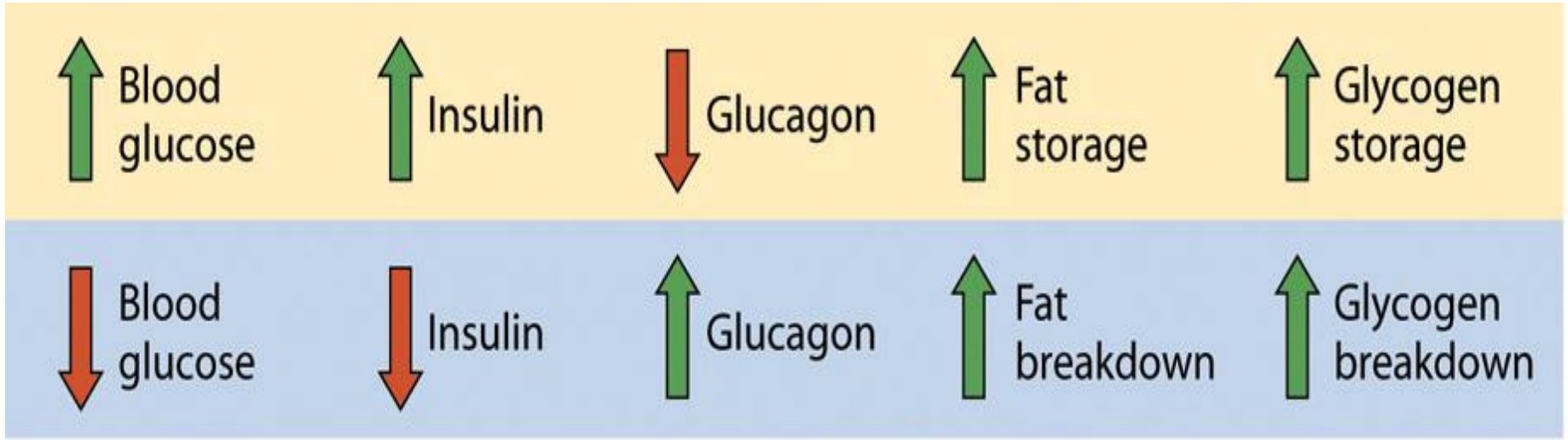


Glucagon

- Release of glucagon upon low glucose levels
- Binding to cell type-specific glucagon receptors
  - Liver
    - Inhibition of glycogen synthesis
    - Stimulation of breakdown of glycogen
      → Release of glucose
  - Fat cells
    - Activation of breakdown of fats
    - Fatty acids are used as E source, sparing glucose for brain cells

Insulin and Glucagon

- Insulin and glucagon cooperatively maintain 80-100 mg glucose / 100 ml of plasma.



Diabetes

- Diabetes mellitus
  - Diabetes: excessive urination in Greek
  - Mellitus: honey in Latin
- Problem in controlling blood glucose
  - Insufficient glucose absorption in the presence of high blood glucose
    → high concentration of glucose in the urine
- Types of diabetes
  - Type I, Juvenile, insulin-dependent diabetes
    - No insulin production
    - Autoimmune response --- destroying pancreatic β cells
  - Type II, insulin-resistant, non-insulin-dependent diabetes
    - No response to insulin (unknown cause, associated with obesity)
    - 90~95% of diabetes

Biotechnology Application

- Insulin production to treat diabetes
  - 1920's
    - isolation of insulin from pig and cow pancreases
  - 1980's
    - Recombinant human insulin expressed in *E. coli*