

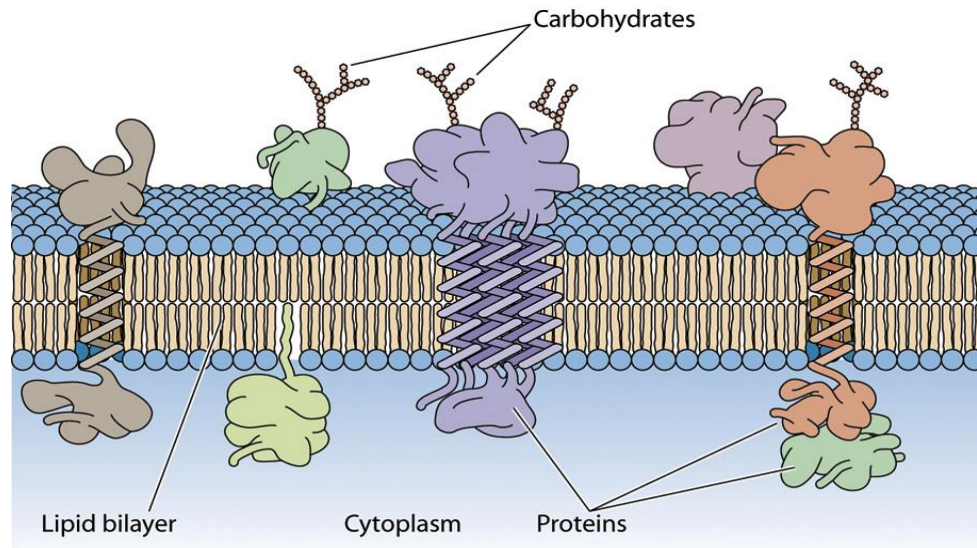
Chapter 7

Cells Maintain Their Internal Environments



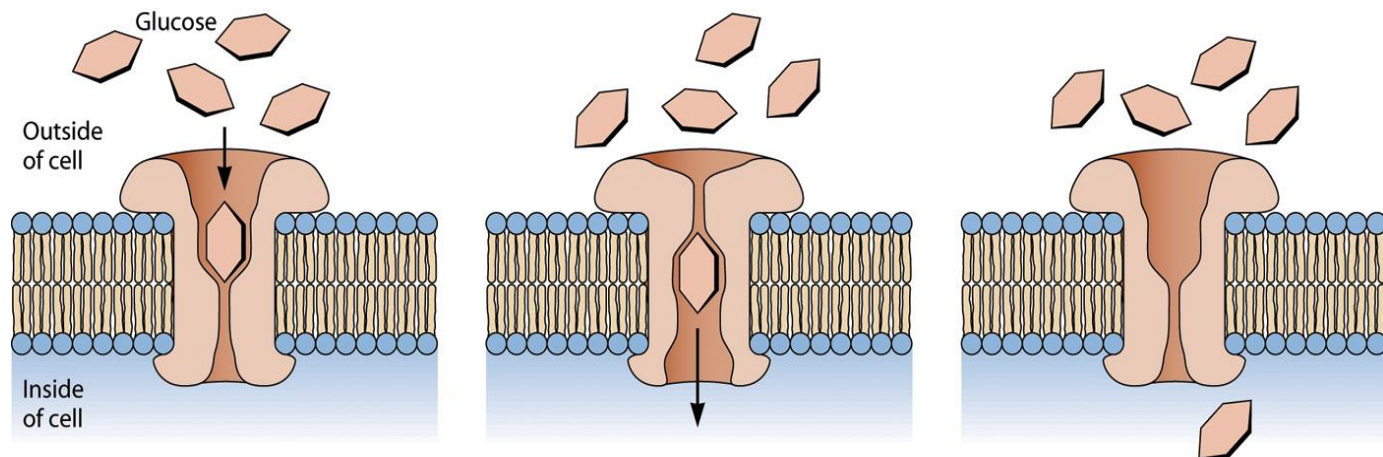
Cell Membrane

- Components of cell membrane
 - Lipid: phospholipids, sterols
 - Embedded proteins : receptor proteins, adhesion proteins, recognition proteins, transport proteins
 - Transmembrane proteins
 - Attachment to cytosolic or exterior face of membrane



Cell Membrane

- Membrane-spanning domains of membrane proteins
 - Hydrophobic surface and hydrophilic core
 - Transport of sugars, amino acids and ions (hydrophilic) through the hydrophilic core of transport proteins

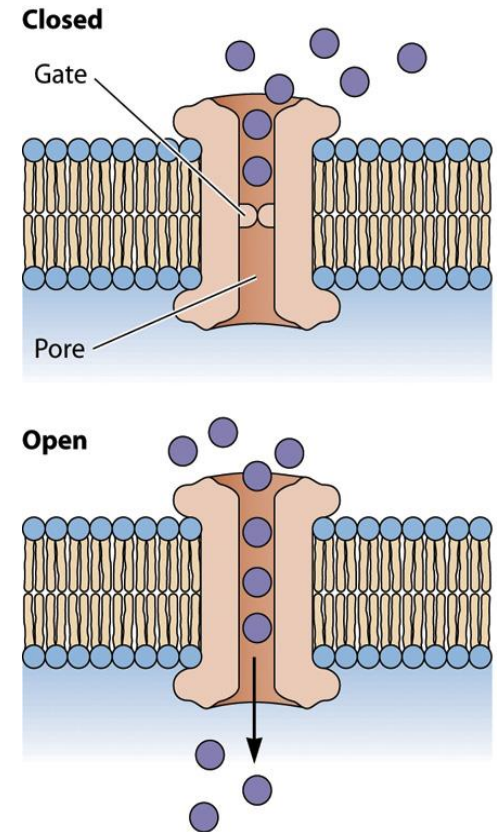


Transport Across Membrane

- Hydrophobic substances and very small molecules can cross the membrane unassisted.
- Diffusion
 - Free diffusion by concentration gradient
 - Hydrophobic substance, nonpolar molecules (O_2 , CO_2), small polar molecules (water, ethanol)

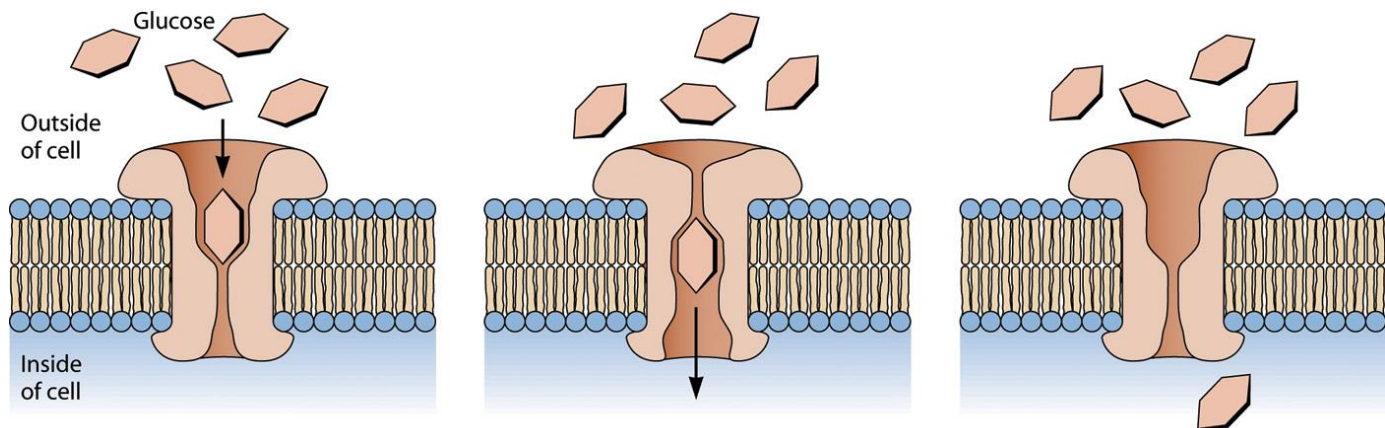
Transport Proteins

- Channel proteins
 - Transport of ions (Na^+ , K^+ , Ca^{2+} , Cl^-)
 - Along their concentration gradients
 - Aquaporin: channel for water (much faster than the diffusion across the membrane)
 - Gated channel



Transport Proteins

- Carrier proteins
 - Escort energy substrates and metabolic building blocks, such as glucose, amino acids, and nucleosides
 - Along the concentration gradient
 - Slower than simple diffusion



Active Transport

■ Pump

- One type of proteins that uses **energy** to move substances
- Transport against the concentration gradient
- Different concentrations between intracellular and extracellular fluids are maintained through pumps.

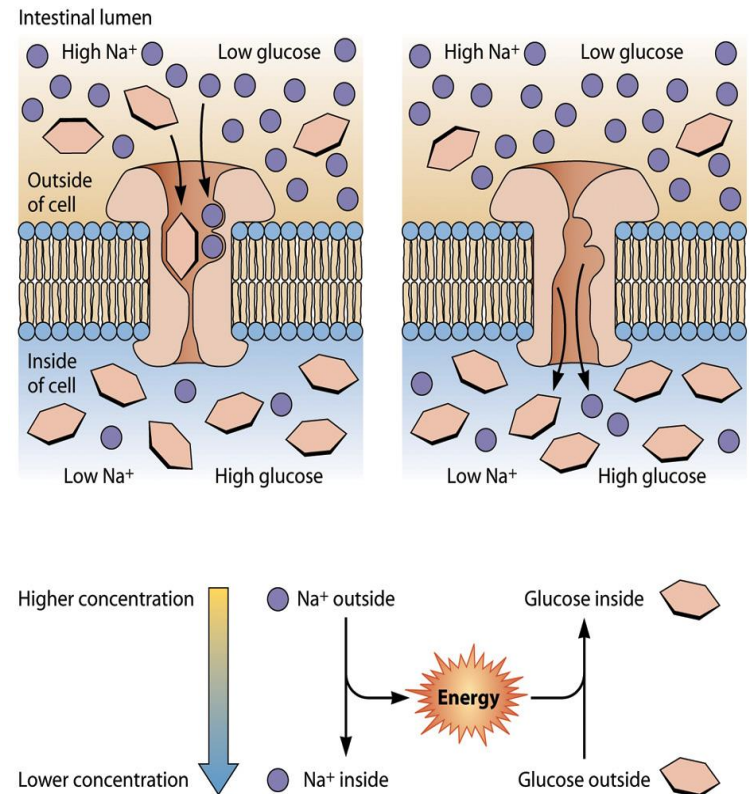
Table 7.1 Approximate concentrations of ions in intracellular and extracellular fluids

Ion ^a	Intracellular concn (mM)	Interstitial concn (mM)
Sodium (Na ⁺)	10	145
Potassium (K ⁺)	150	5
Calcium (Ca ²⁺)	0	3
Chloride (Cl ⁻)	5	110

^aThe most abundant ions in interstitial fluid are sodium and chloride ions, which are the components of table salt.

Pump

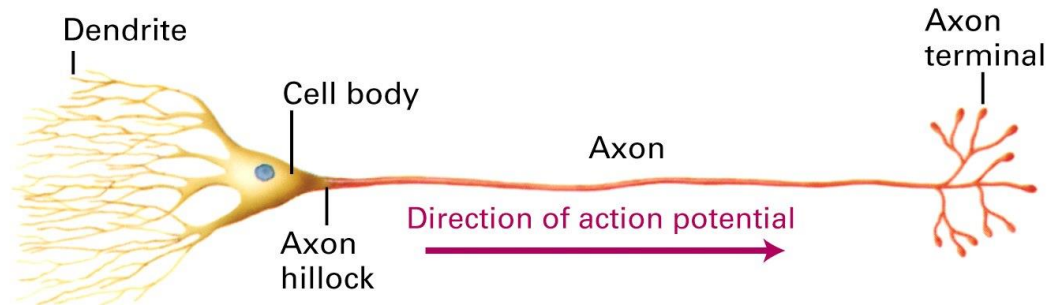
- Two different energy sources
 - ATP
 - e.g. Pumping Na^+ and K^+ against their gradients using ATP (Na^+/K^+ ATPase)
 - Energy inherent in gradient



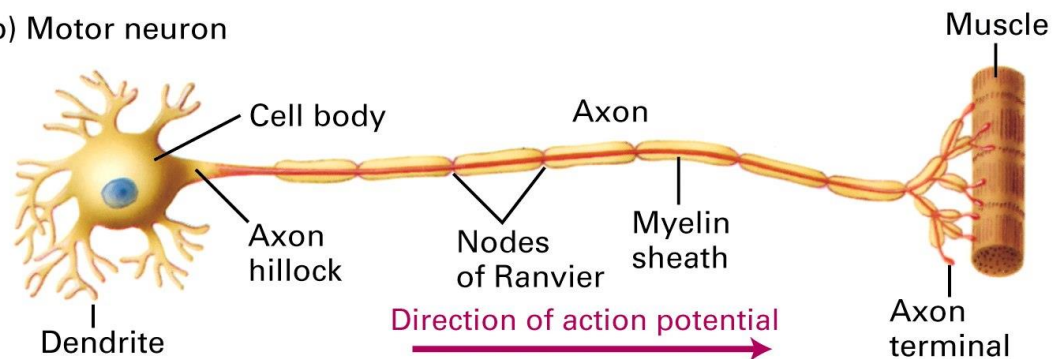
Transport Proteins in Animals

- Nerve Impulses

(a) Multipolar interneuron

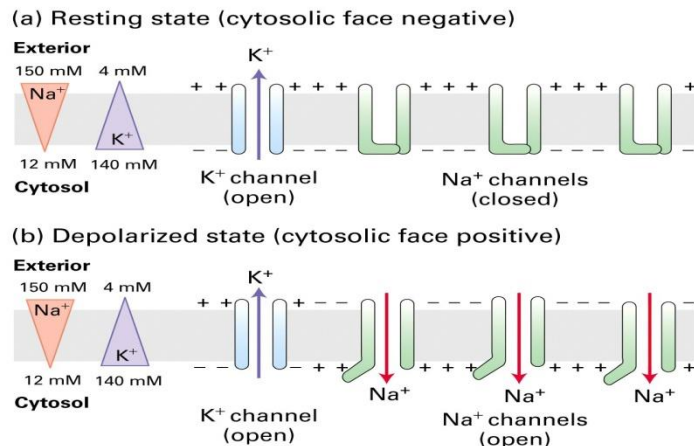


(b) Motor neuron



Nerve Impulses

- Key players: Na^+ , K^+
- Resting membrane potential of -70mV
 - (Some K^+ channels are open.)
- Opening of Na^+ channel by stimulation
 - Generation of action potential 50 mV



- Opening of voltage-gated K^+ channel
 - Repolarization of membrane potential
- Restoration of membrane potential by Na^+/K^+ ATPase

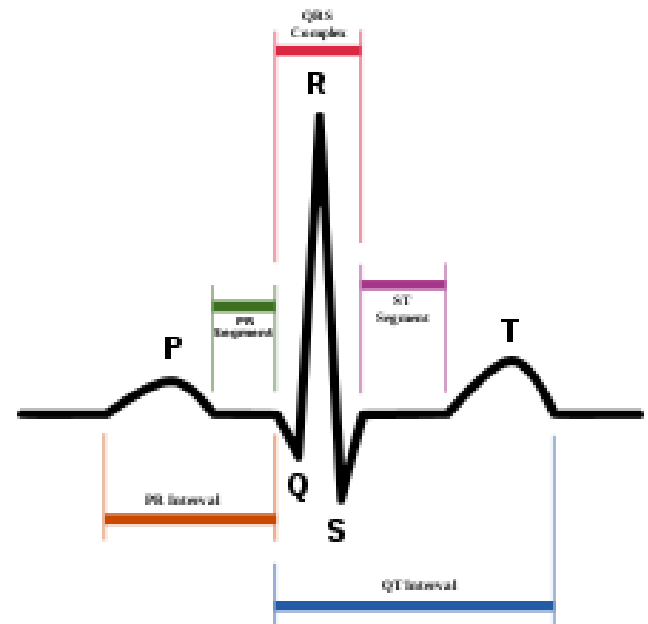
Muscle Contraction

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

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

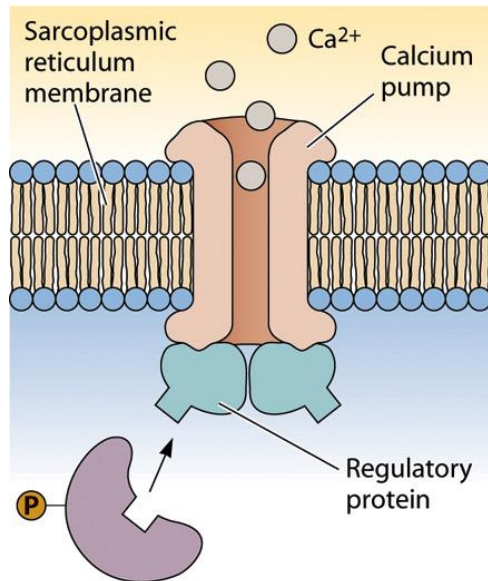
Electrocardiogram (ECG)



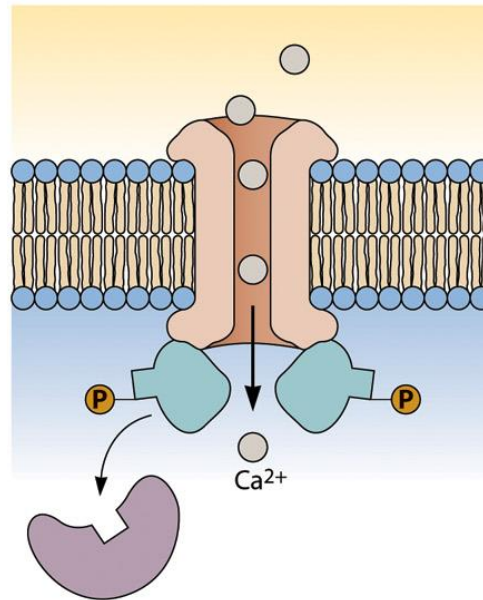
When Gradients Fail

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

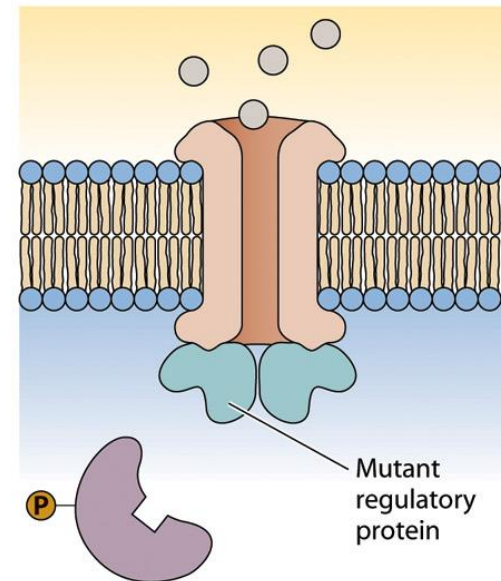
Regulatory protein inhibits the calcium pump.



Phosphorylated regulatory protein allows pump to operate.



Mutant regulatory protein cannot be phosphorylated; calcium pumping is blocked.



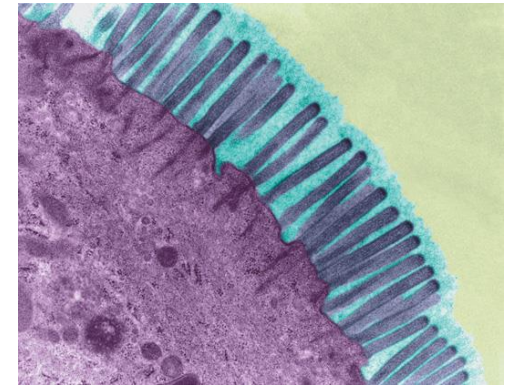
Pumps, Carriers, and Nutrient Distribution

- 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

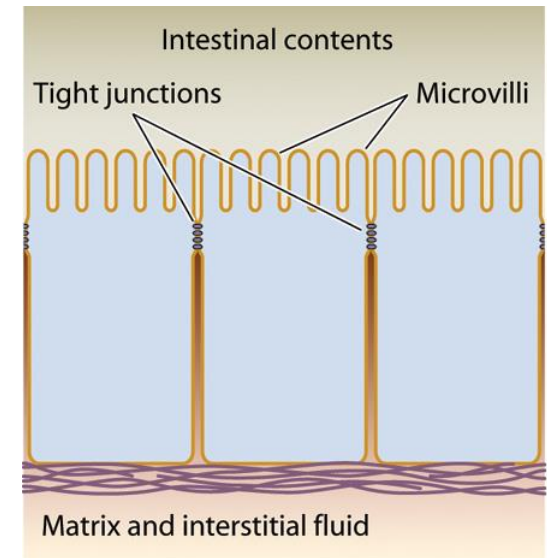


■ Tight Junction between Cells

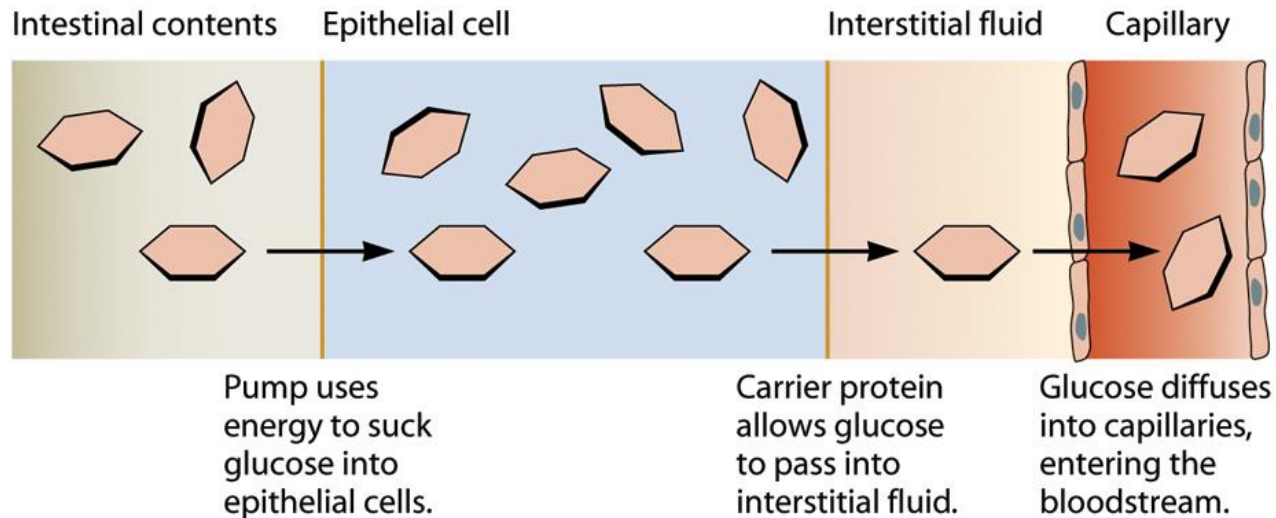
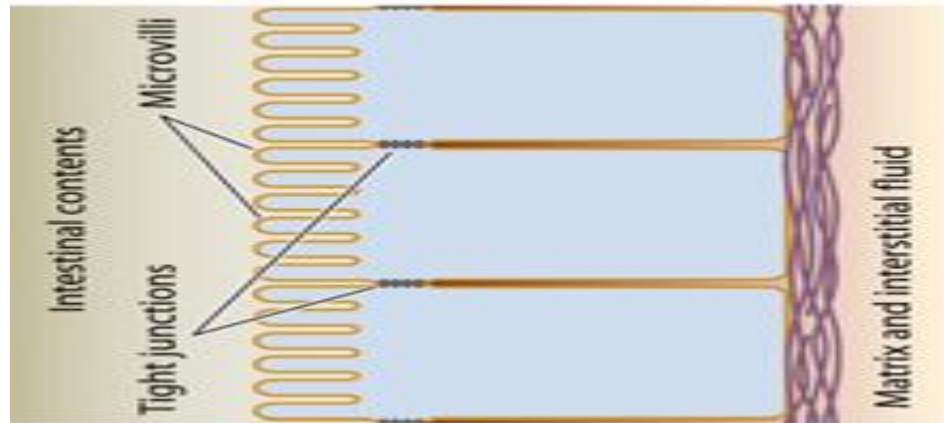
- Preventing transport of large molecules
- Barrier between the intestinal contents and the interstitial fluid

■ Extracellular Matrix

- Supporting epithelial cells
- Tough network of extracellular proteins and carbohydrates

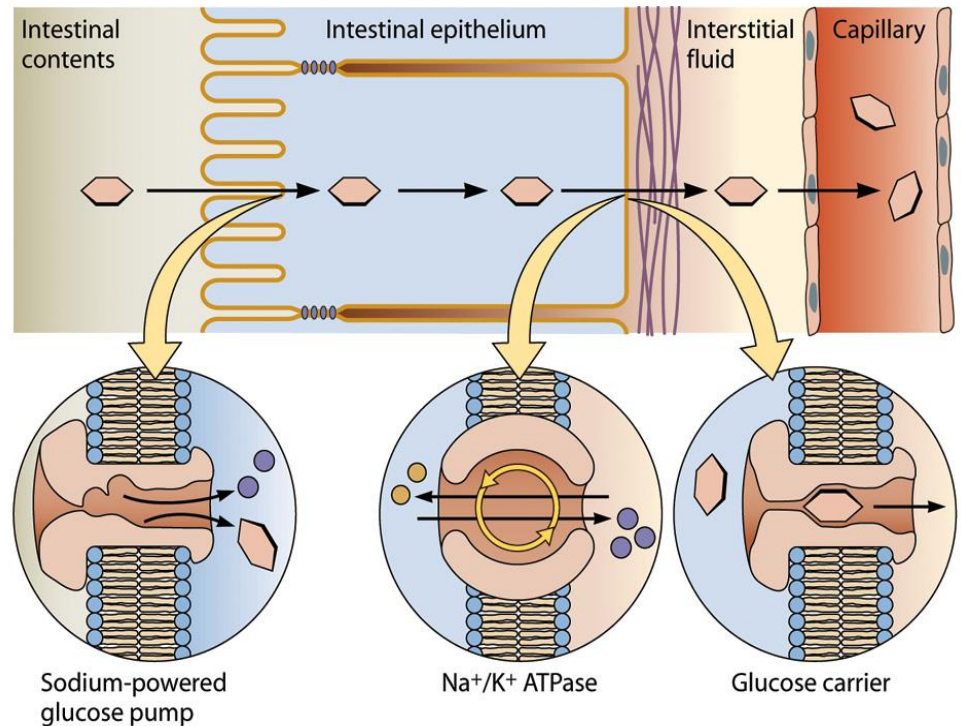


Transport of Nutrients across Epithelial Cells



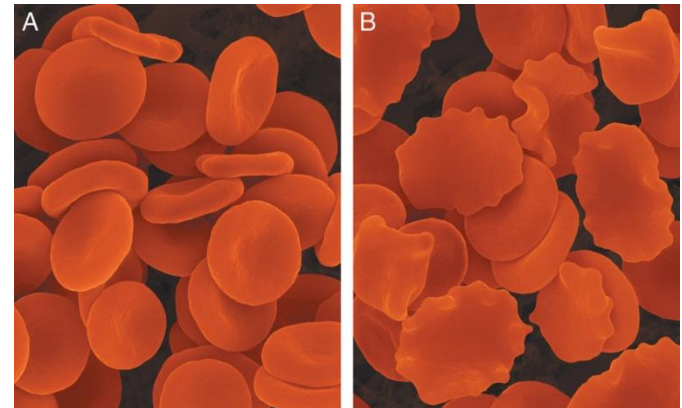
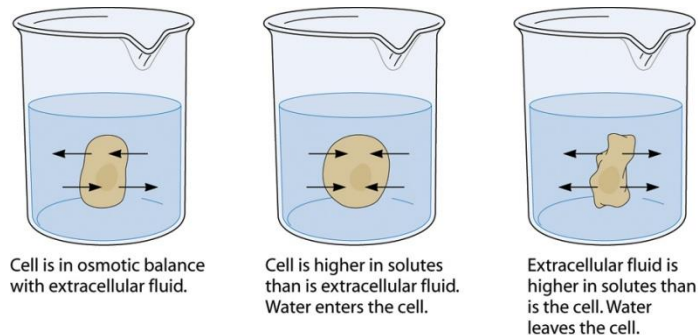
Transport of Nutrients across Epithelial Cells

- 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



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 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.

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 \rightarrow gas production
 - Buy α -galactosidase (Beano) in a drugstore

Chapter 8

Cells Respond to Their External Environments



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
 - 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

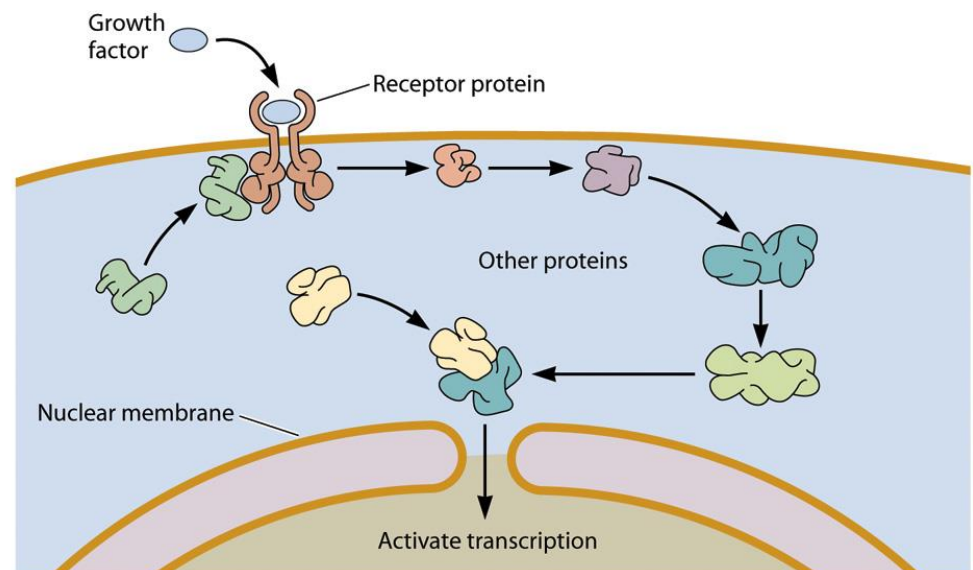
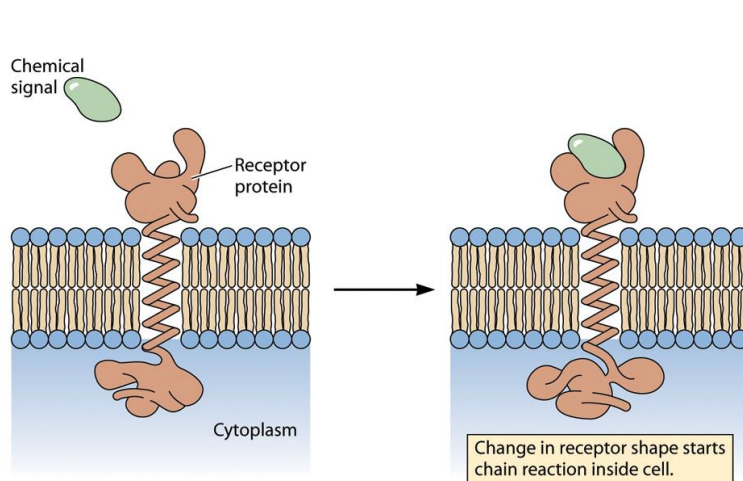
Type of receptor	Activating stimulus	Cellular response	Brain's interpretation of nerve impulse
Photoreceptor	Light	Change in membrane channels	Vision
Auditory receptors	Vibration	Release of stored neurotransmitters	Sound
Olfactory receptors	Various molecules in the air	Change in membrane channels	Smell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

- Osmoreceptors

- High salt → Cell shrinkage → Geometry change → Opening of ion channels → Generation of a nerve impulse

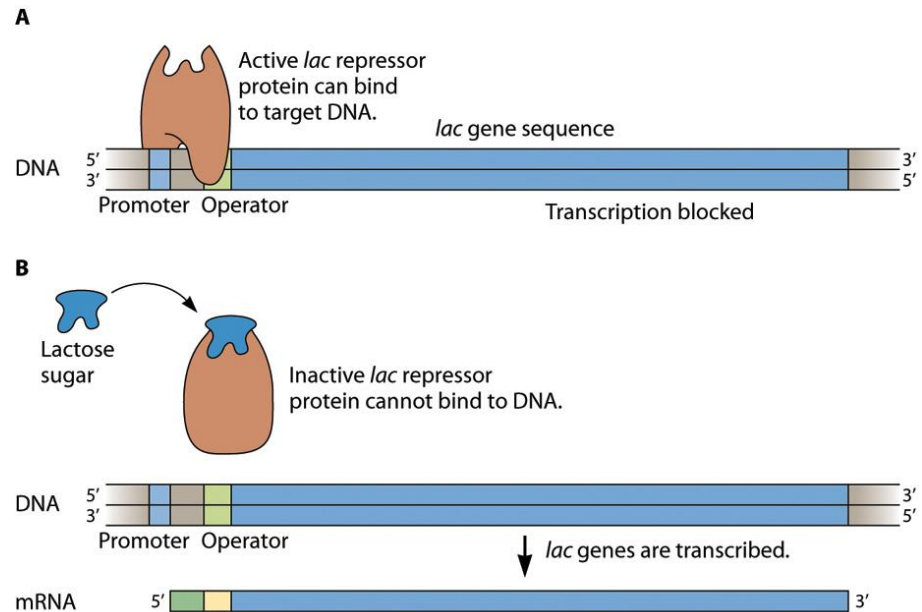
Signal Transduction

- **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



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



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

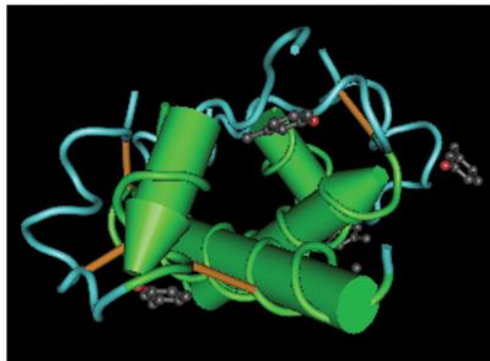
■ Estrogen

- 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

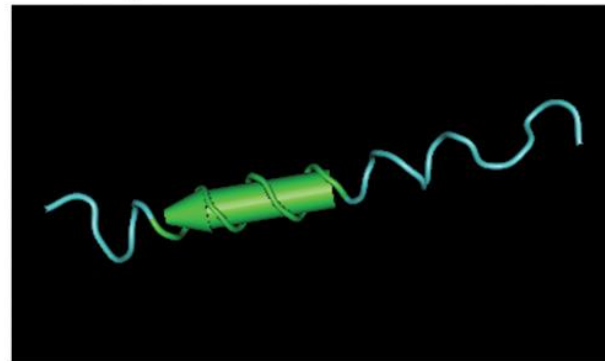
Regulation of Blood Glucose Concentration

- 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

A. Insulin

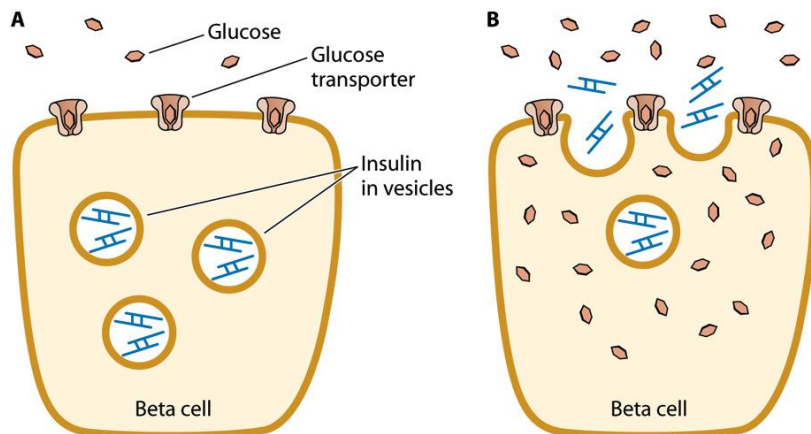


B. Glucagon

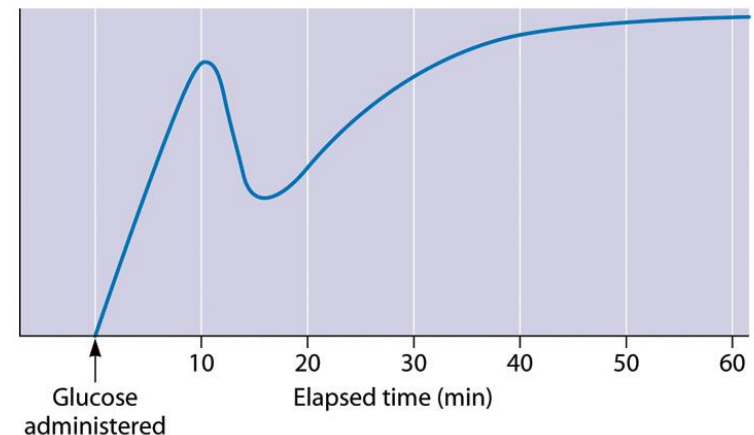


Insulin

- 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 fuse with cell membrane
 - Insulin is released to the blood stream
- Glucose stimulates the transcription of insulin gene.



Concentration of insulin in blood



Roles of Insulin

- Binding to cell type-specific insulin receptors

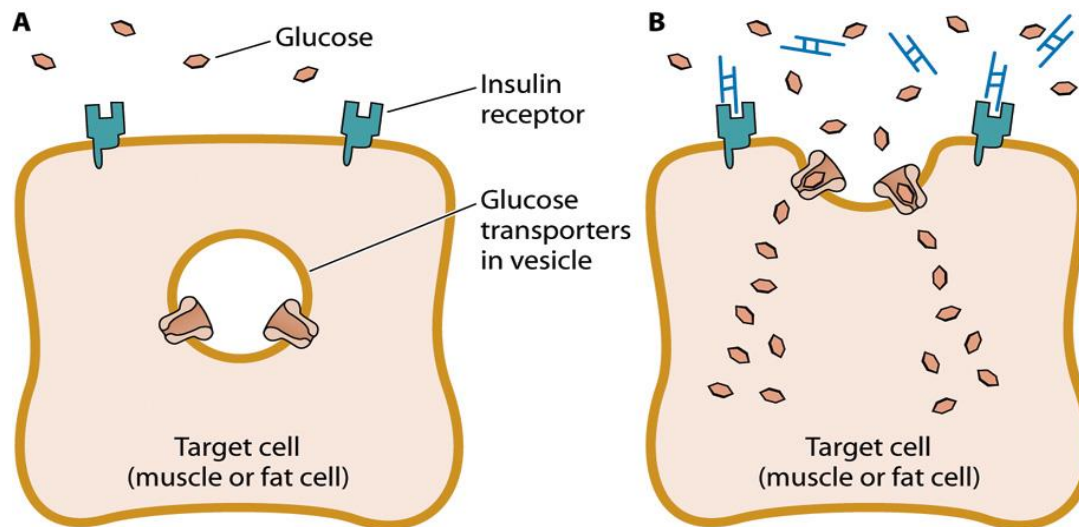
- e.g. Muscle and fat cells

Binding of insulin to insulin receptors

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

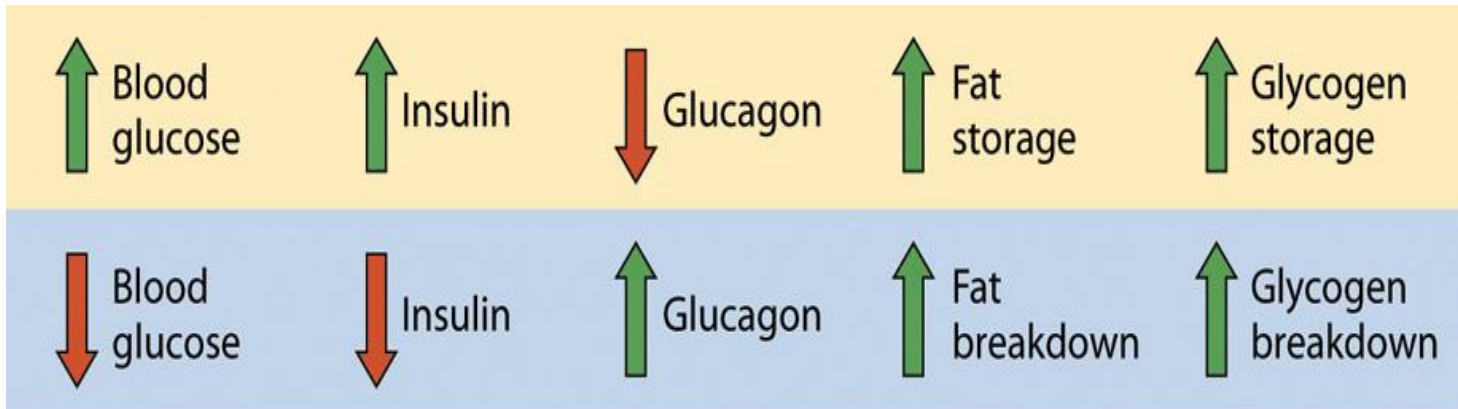
→ Stimulation of uptake of glucose from the blood

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



80-100 mg glucose / 100 ml of plasma is maintained.

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*

Blood Pressure, Salt, and Water

■ Roles of blood circulation

- Capillaries: permeable cell wall, 60,000 miles in human body
- Provide nutrients to cells
 - O₂, nutrients, hormones
→ diffuse to interstitial fluid through capillary walls
- Elimination of waste products
 - Waste products → pass into capillaries

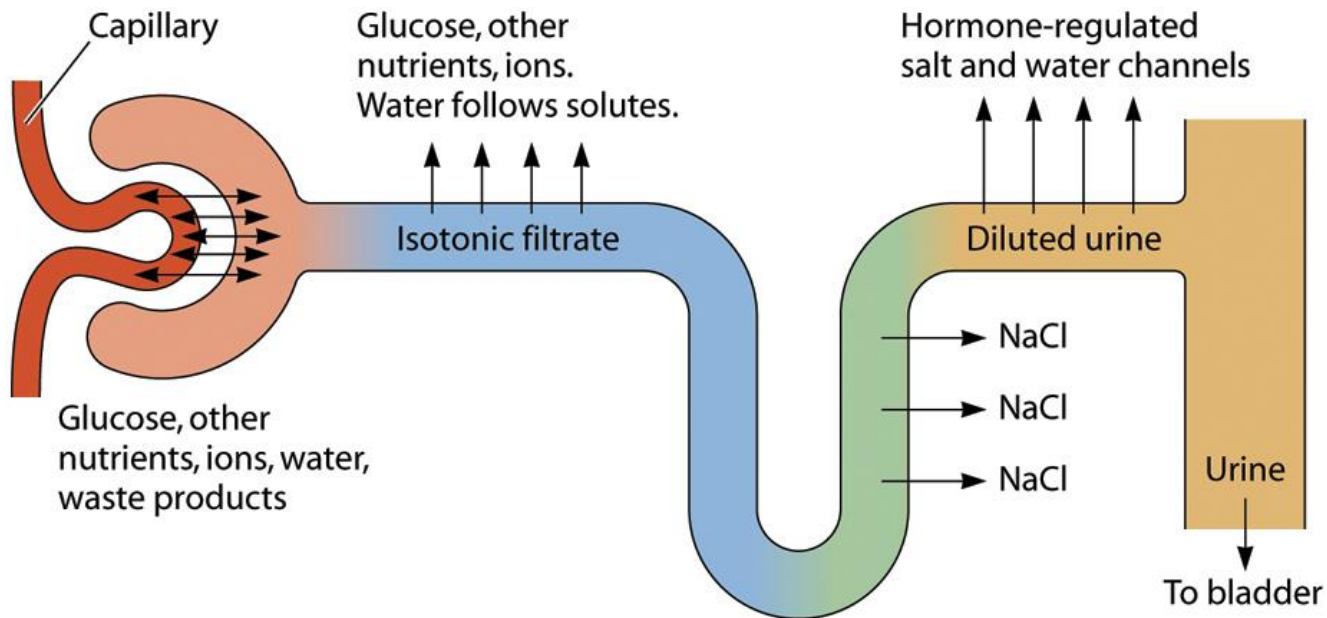
■ Blood pressure

- Low blood pressure:
 - problem in supplying nutrients to organs especially brain
- High blood pressure (Hypertension)
 - Weakening of blood vessel → burst and bleed : stroke, blindness
 - Stiffening of arteries: heart attack, heart failure
 - Kidney problem
- Affected by blood volume and muscle tone in the artery walls

How Kidneys Work

- Generation of urine during transport along the tubules of kidney
 1. Diffusion of small molecules from capillaries to tubules of kidney through very leaky walls
 - Filtrate: the fluid in the tubules
 2. Transporters to reabsorb nutrient
 - Tight junctions and microvilli
 - Isotonic filtrate: osmotic balance between filtrate and extracellular fluid
 3. Water impermeable, active transport of ions
 - Dilute urine
 4. Tubule with aquaporin channel and salt channels
 - Concentrated urine
 5. Bladder

Solute Transport in the Kidney



Capillary and kidney tubule walls are very leaky. Nutrients, salt, water, and waste products diffuse through interstitial fluid into kidney.

Tight junctions in the kidney epithelium permit water to pass through. Nutrients and salt are pumped out of filtrate. Water follows the solutes.

Tight junctions are impermeable to water. More ions are removed from filtrate.

Tight junctions are impermeable to water. Variable numbers of salt and water channels can be inserted into the epithelium, under hormone control.