UNIT 5
Sensory and Immune systems

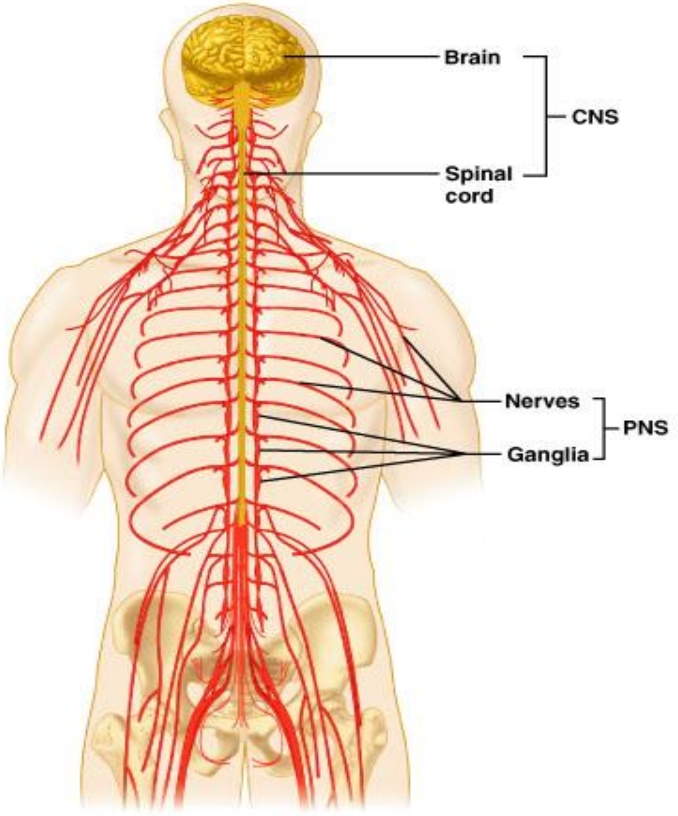
Nervous system

- The task of nervous system is to coordinate the mental processes by which we perceive, act, learn and remember.

- The human brain is a network of billions of individual nerve cells interconnected in systems that construct our perceptions of the external world, fix our attention, and control the machinery of our actions.

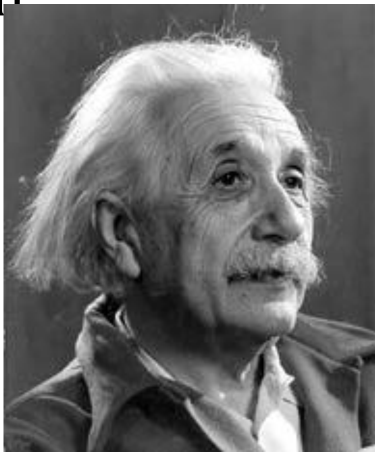
- The nervous system has two classes of cells: *nerve cells (neurons) and glial cells (glia).*

Neurotransmitters
Neuropeptides



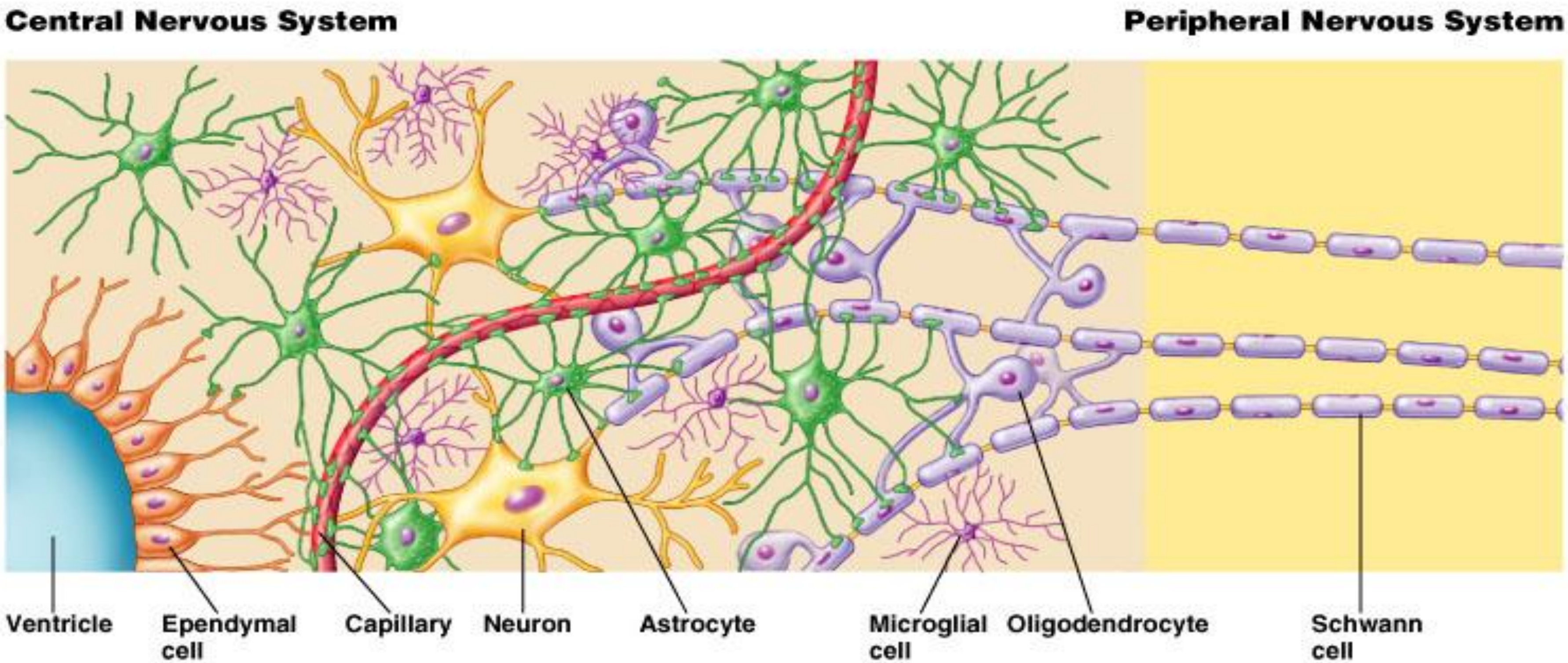
Supporting Cells (Neuroglial Cells) in the Central Nervous System (CNS)

- Neuroglia – usually only refers to supporting cells in the CNS, but can be used for Peripheral Nervous System (PNS)
  - Glial cells have branching processes and a central cell body
  - Outnumber neurons 10 to 1 (the guy on the right had an inordinate amount of them).
  - Make up half the mass of the brain
  - Can divide throughout life
  - Responsible for maintaining homeostatic control and immune surveillance in nervous system



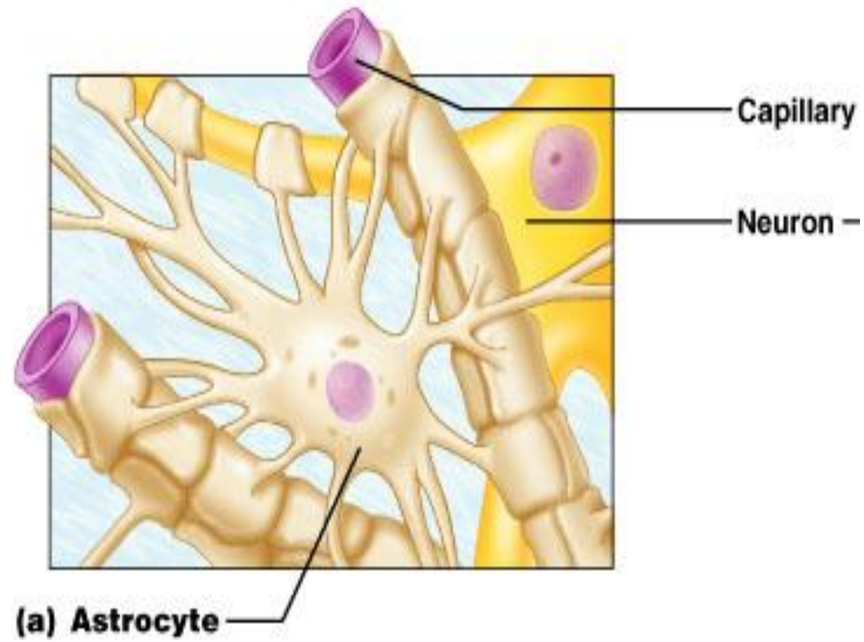
Glial cells

- **Glial cells are support cells.**
- **They are more in number than neurons.**
- **There are between 10 and 50 times more glia than neurons in the brain of humans.**
- **The name for these cells derives from the Greek word for glue. In actual terms, the glia do not commonly hold nerve cells together but surround the neurons.**

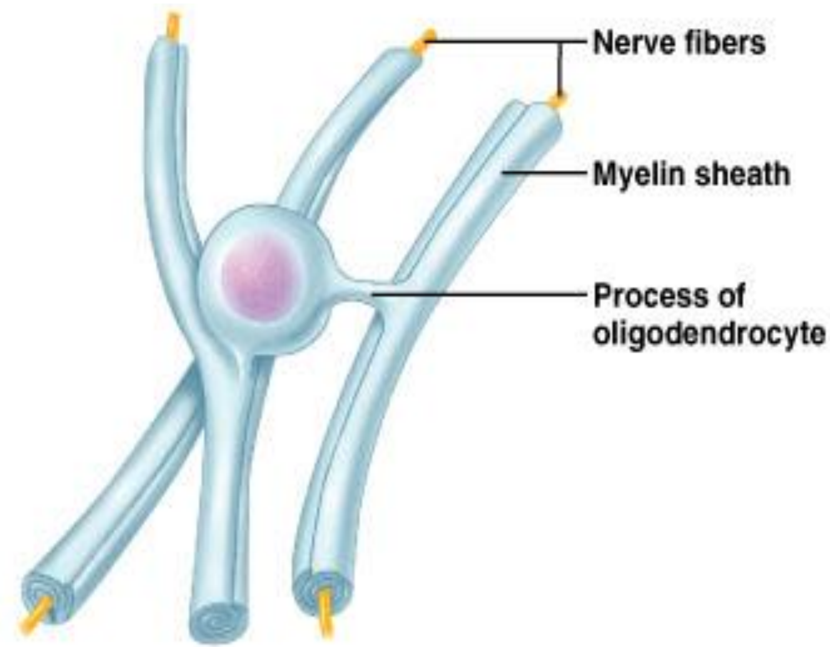


Types of Glial Cells in the CNS: **Astrocytes, Oligodendrocytes, and Microglia**

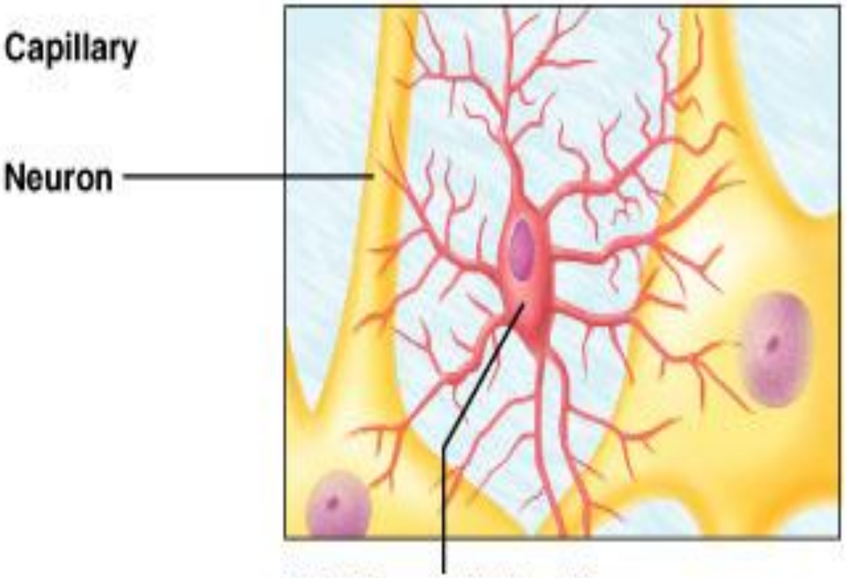
- ***Astrocytes*: Most abundant glial cell type, irregular star-shaped cell bodies .**
  - **Take up and release ions to control the environment around neurons**
  - **Recapture and recycle neurotransmitters (chemical messengers that carry chemical signals from one neuron to next target cells)**
  - **Involved with synapse formation in developing neural tissue**
  - **Produce molecules necessary for neural growth**
  - **Propagate calcium signals that may be involved in memory**



- *Oligodendrocytes*: Have few branches.
- Wrap their cell processes around axons in CNS
- Produce myelin sheaths for rapid conduction of nerve impulses
- Provide nutritional support
- *Schwann* cells: help in repair of damaged neurons outside CNS.



- *Microglia*: Smallest and least abundant.
- Derived from blood cells called monocytes
- Engulf invading microorganisms and dead neurons
- Phagocytes – the macrophages of the CNS
- Also produces immune molecules and growth factors to aid recovery of damaged neurons

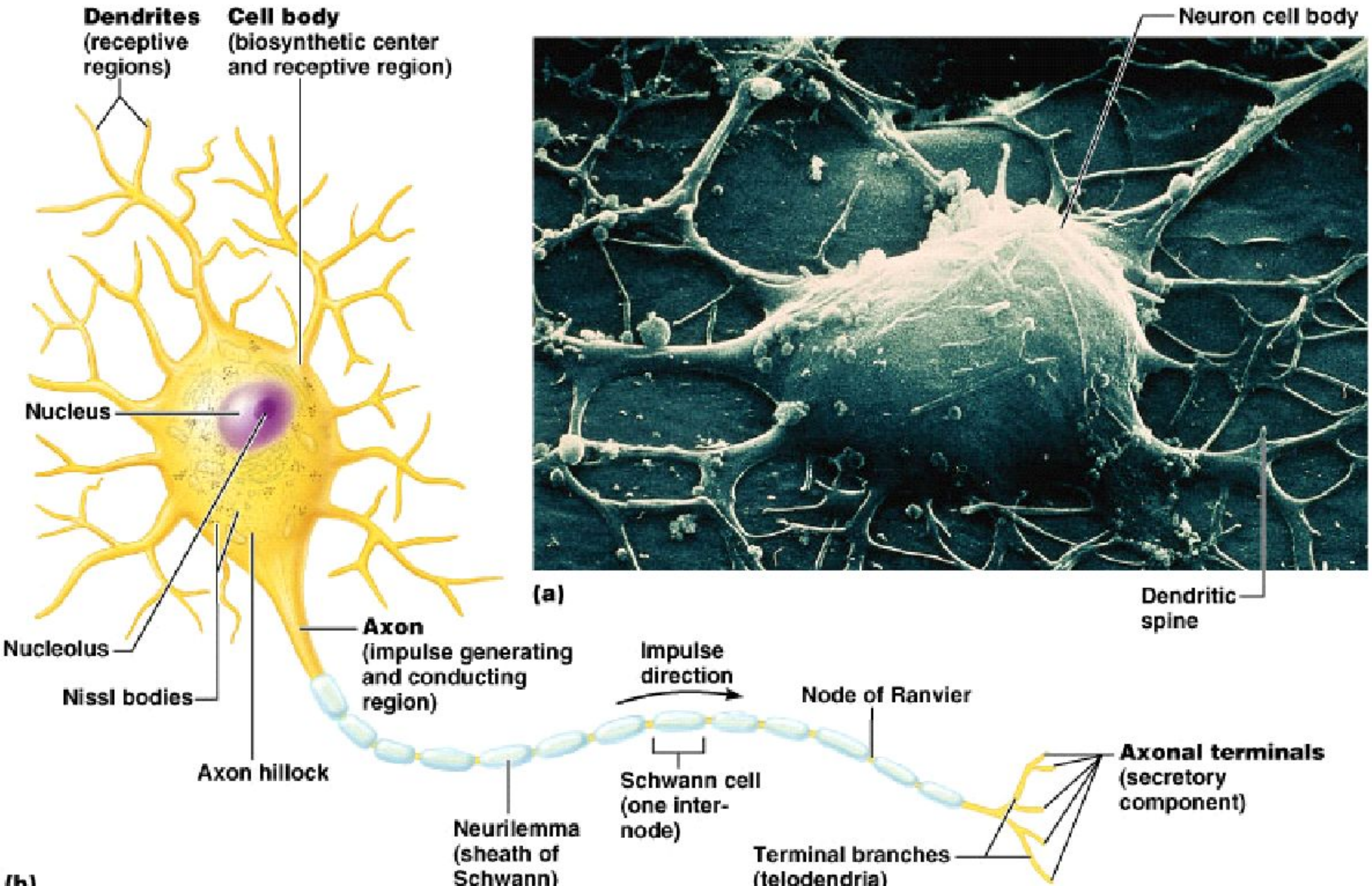


(b) Microglial cell

Nerve cells- Neurons

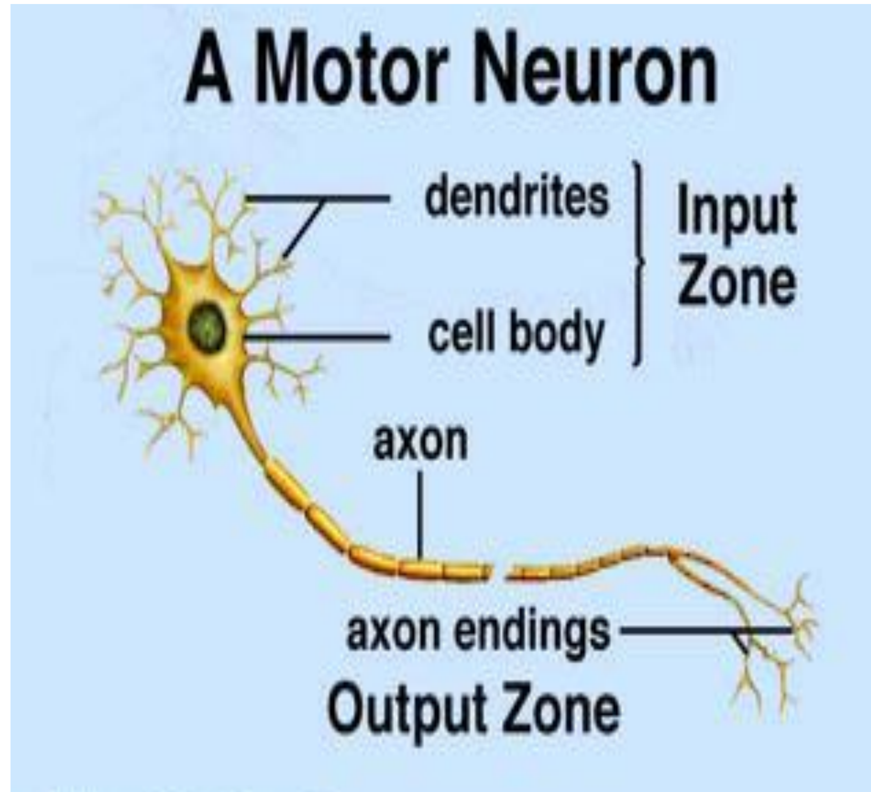
- **Nerve cells are the main signaling units of the nervous system.**
- **A typical neuron has four morphologically defined regions*: the cell body, dendrites, the axon, and presynaptic terminal***

- **The *cell body (soma)* is the metabolic center of the cell. It contains the nucleus which stores the genes of the cell, as well as the endoplasmic reticulum, an extension of the nucleus where the cell's proteins are synthesized.**
- **The cell body gives rise to two kinds of processes: several short *dendrites* and one, long, tubular *axon*.**
- **These processes vary in number & relative length but always serve to conduct impulses (with dendrites conducting impulses toward the cell body and axons conducting impulses away from the cell body as shown in the figure).**


Dendrites
(receptive
regions)
Cell body
(biosynthetic center
and receptive region)
Neuron cell body
Nucleus
Nucleolus
Nissl bodies
Axon hillock
Axon
(impulse generating
and conducting
region)
Impulse
direction
Node of Ranvier
Schwann cell
(one inter-
node)
Neurilemma
(sheath of
Schwann)
Terminal branches
(telodendria)
Axonal terminals
(secretory
component)
Dendritic
spine
(a)
(b)

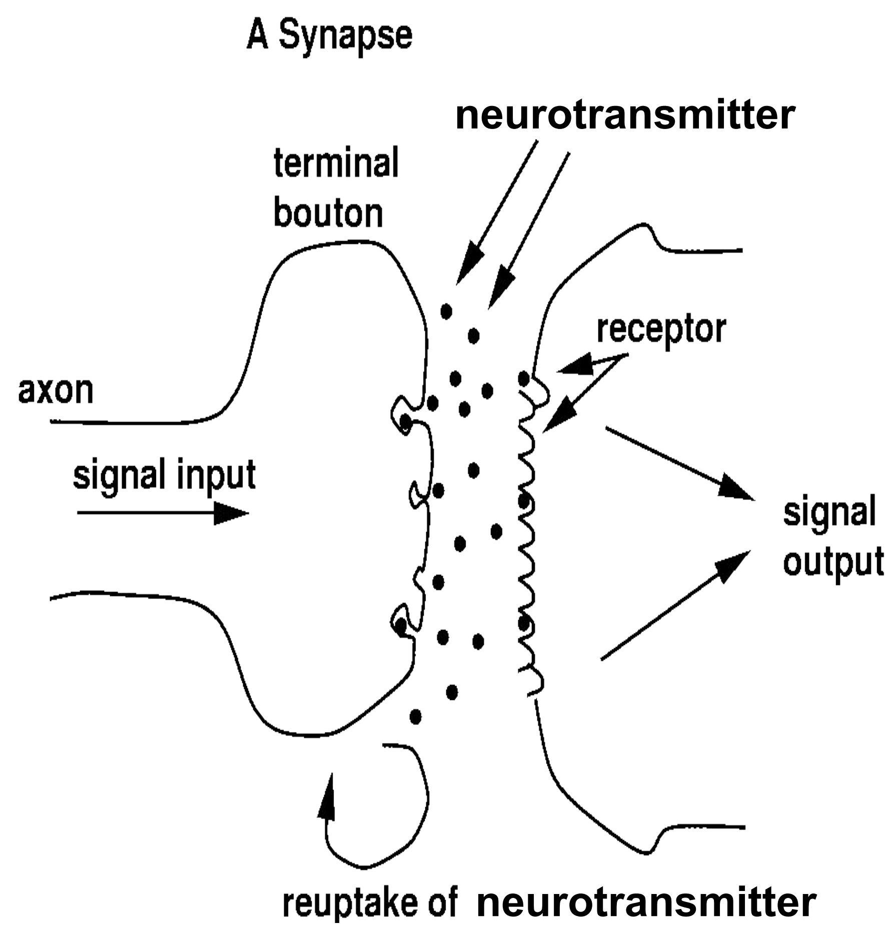
Action Potential

- Action potential: temporary shift in the neuron's membrane potential caused by movement of ion
- A neuron receives input from other neurons (typically many thousands). All the input signals are integrated. Once input exceeds a critical level, the neuron discharges a **spike** - an electrical pulse that travels from the body, down the axon, to the next neuron(s) (or other receptors). This spiking event is also called **depolarization**, and is followed by a **refractory period**, during which the neuron is unable to fire.

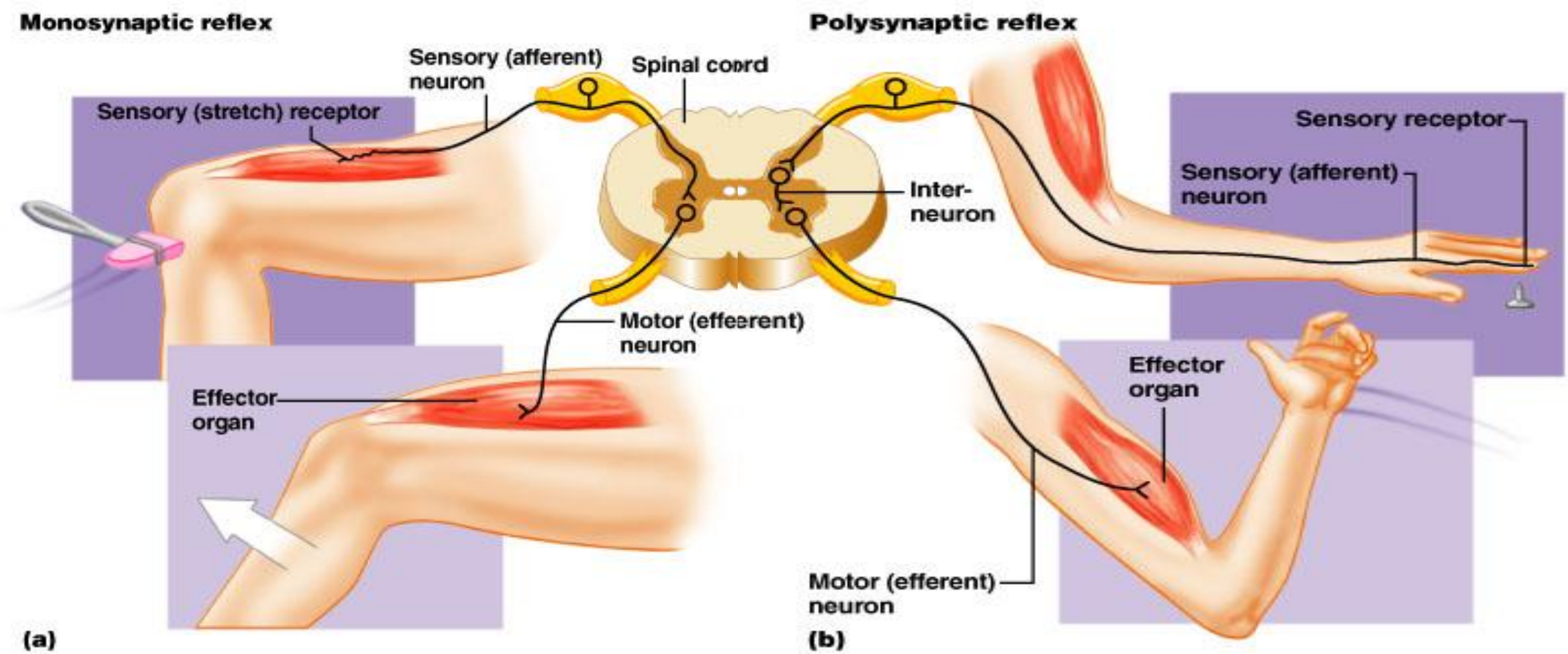


Synapse

- The axon endings (Output Zone) almost touch the dendrites or cell body of the next neuron.
- Transmission of an electrical signal from one neuron to the next is effected by neurotransmitters, chemicals which are released from the first neuron and which bind to receptors in the second. This link is called a synapse.
- The extent to which the signal from one neuron is passed on to the next depends on many factors, e.g. the amount of neurotransmitter available, the number and arrangement of receptors, amount of neurotransmitter reabsorbed, etc.

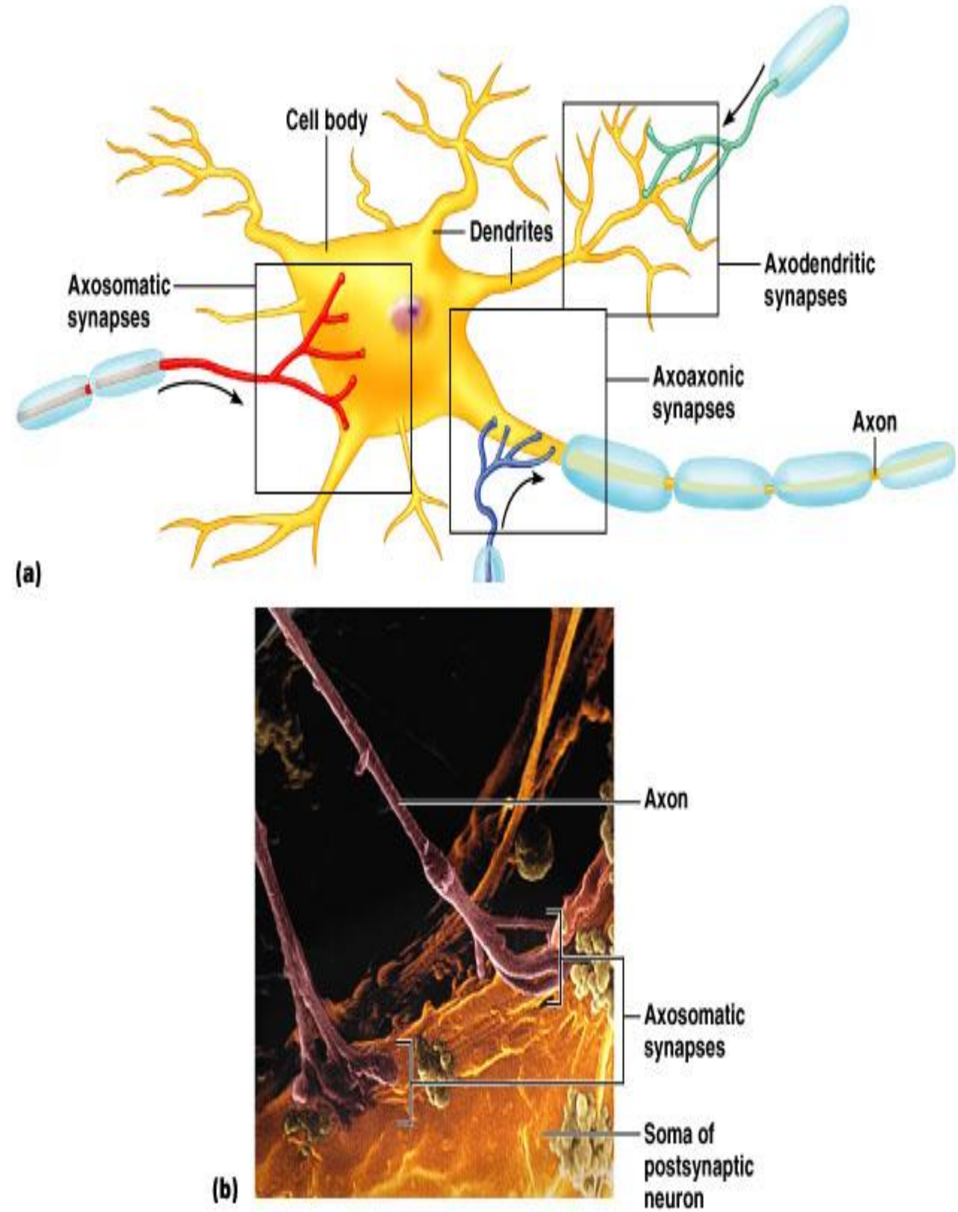


- Sensory signals picked up by sensory receptors
    - Carried by afferent nerve fibers of PNS to the CNS
- Motor signals are carried away from the CNS
    - Carried by efferent nerve fibers of PNS to effectors
    - Innervate muscles and glands



- The dendrites branch out in a tree-like fashion and are the main apparatus for receiving incoming signals from other nerve cells.

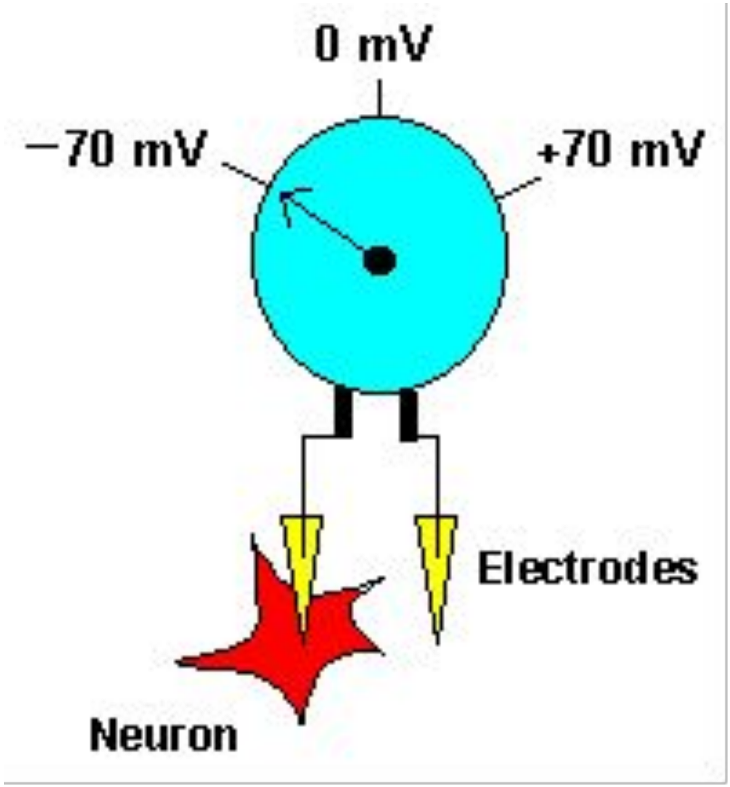
- In contrast, the axon extends away from the cell body and is the main conducting unit for carrying signals for other neurons.



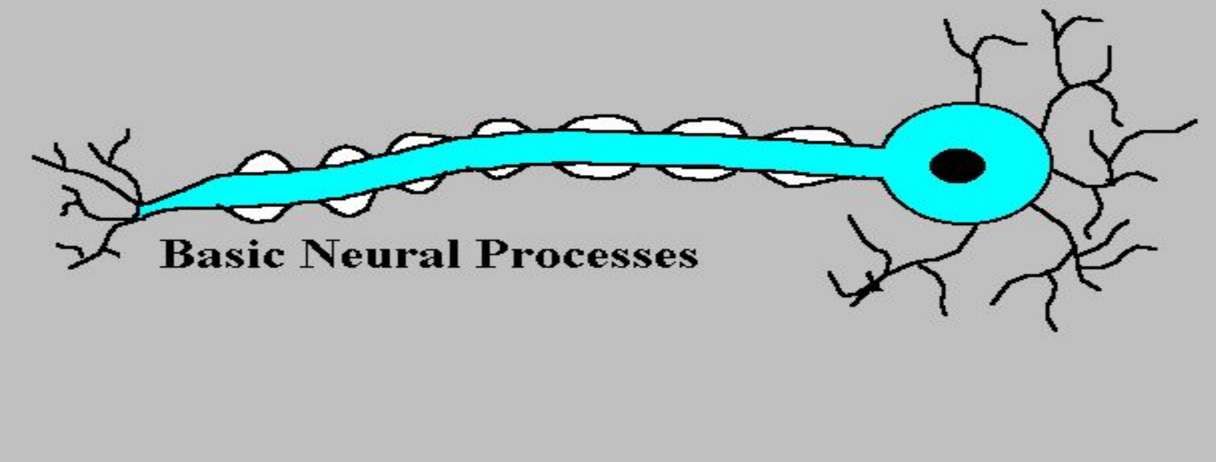
- **An axon can convey electrical signals along distances ranging from 0.1 mm to 3 m. These electrical signals called *action potentials* are rapid, transient with an amplitude of 100 mV and a duration of about 1ms.**

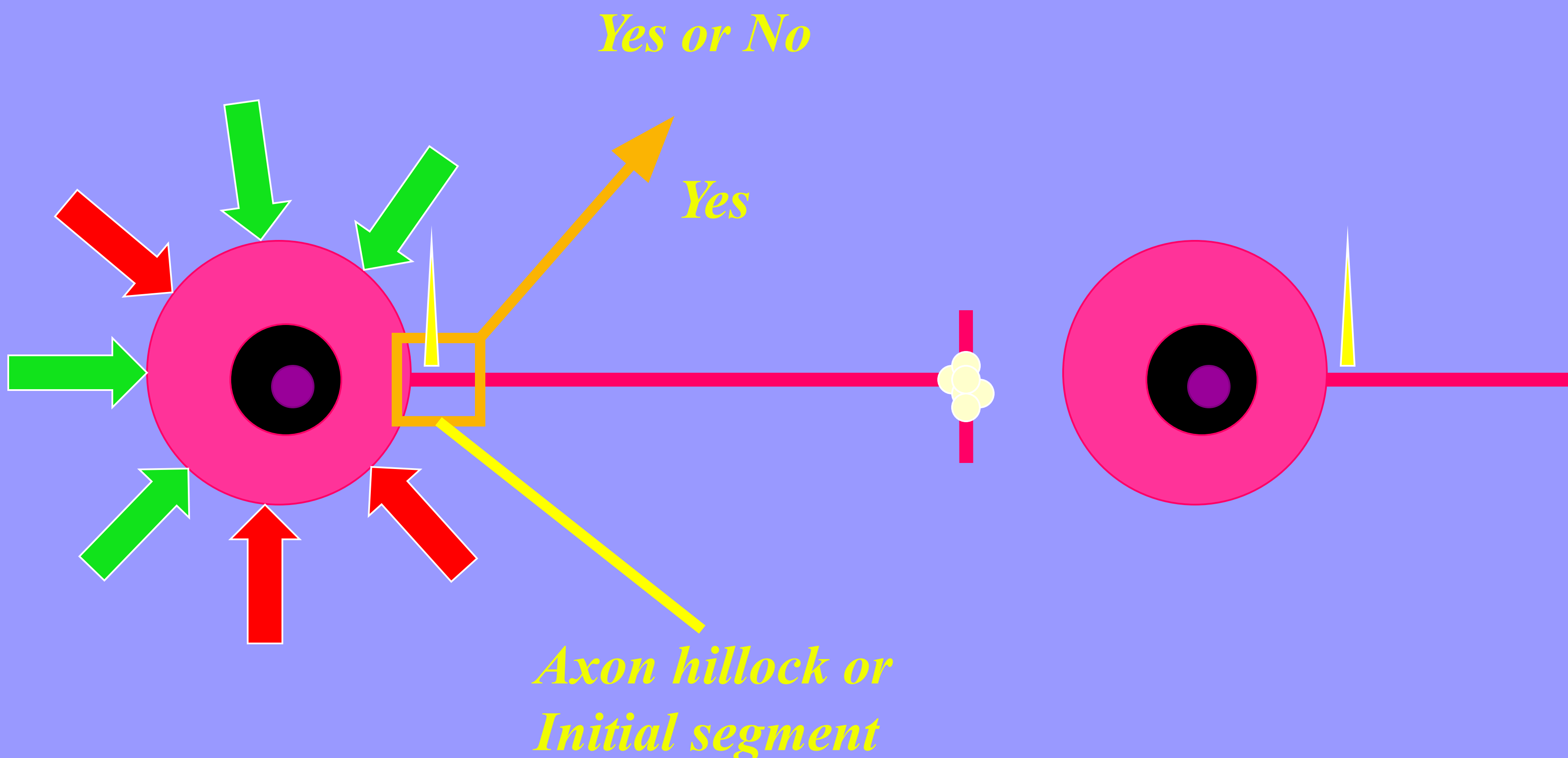
- **Neurons can respond to stimuli and conduct impulses because a membrane potential is established across the cell membrane. In other words, there is an unequal distribution of ions (charged atoms) on the two sides of a nerve cell membrane.**

- **This can be illustrated with a voltmeter: With one electrode placed inside a neuron and the other outside, the voltmeter is 'measuring' the difference in the distribution of ions on the inside versus the outside (see the adjoining figure). And, in this example, the voltmeter reads -70 mV (mV = millivolts). In other words, the inside of the neuron is slightly negative relative to the outside. This difference is referred to as the Resting Membrane Potential. It is called a RESTING potential because it occurs when a membrane is not being stimulated or conducting impulses (in other words, it's resting).**



Nerve Conduction

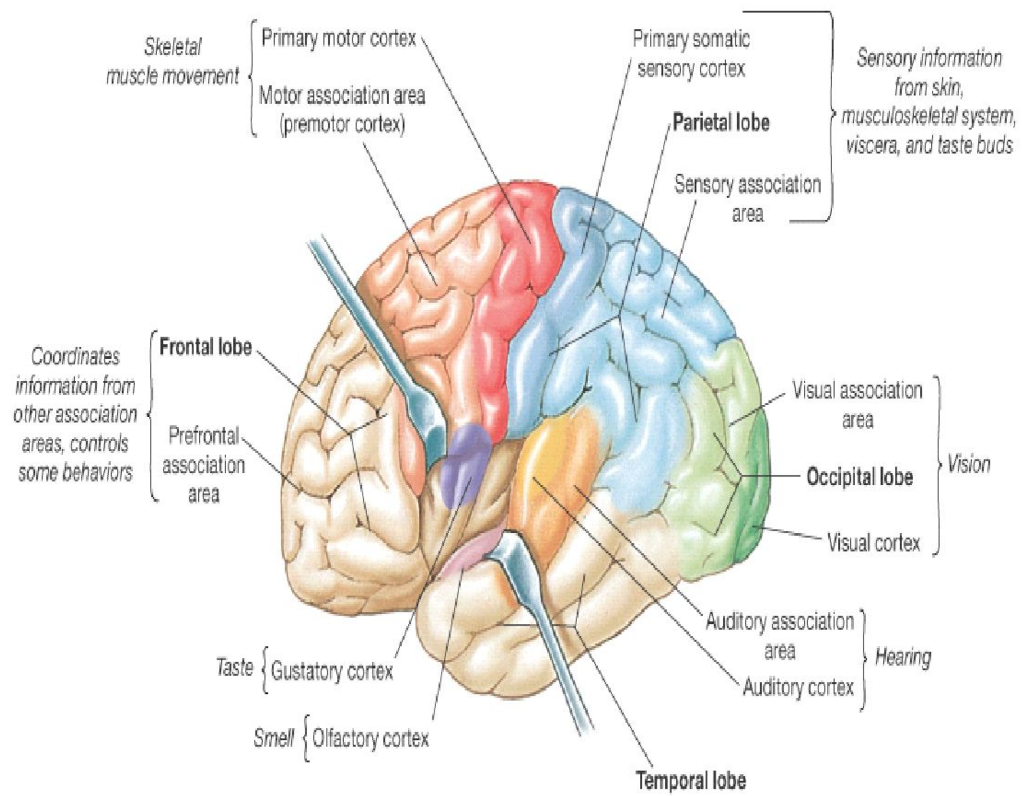




Neural Networks in the Brain

- The brain is not a homogeneous organ. At the largest anatomical scale, we distinguish **cortex**, **midbrain**, **brainstem**, and **cerebellum**. Each of these can be hierarchically subdivided into many **regions**, and **areas** within each region, either according to the anatomical structure of the neural networks within it, or according to the function performed by them.

- In addition to these long-range connections, neurons also link up with many thousands of their neighbors. In this way they form very dense, complex local networks:



Computer-based Neural Networks

- The brain's network of neurons forms a massively parallel information processing system. This contrasts with conventional computers, in which a single processor executes a single series of instructions.

- Despite of being built with very slow hardware, the brain has quite remarkable capabilities:
  - its performance tends to degrade gracefully under partial damage. In contrast, most programs and engineered systems are brittle: if you remove some arbitrary parts, very likely the whole will cease to function.
  - it can learn (reorganize itself) from experience.
  - this means that partial recovery from damage is possible if healthy units can learn to take over the functions previously carried out by the damaged areas.
  - it performs massively parallel computations extremely efficiently. For example, complex visual perception occurs within less than 100 ms, that is, 10 processing steps!
  - it supports our intelligence and self-awareness. (Nobody knows yet how this occurs.)

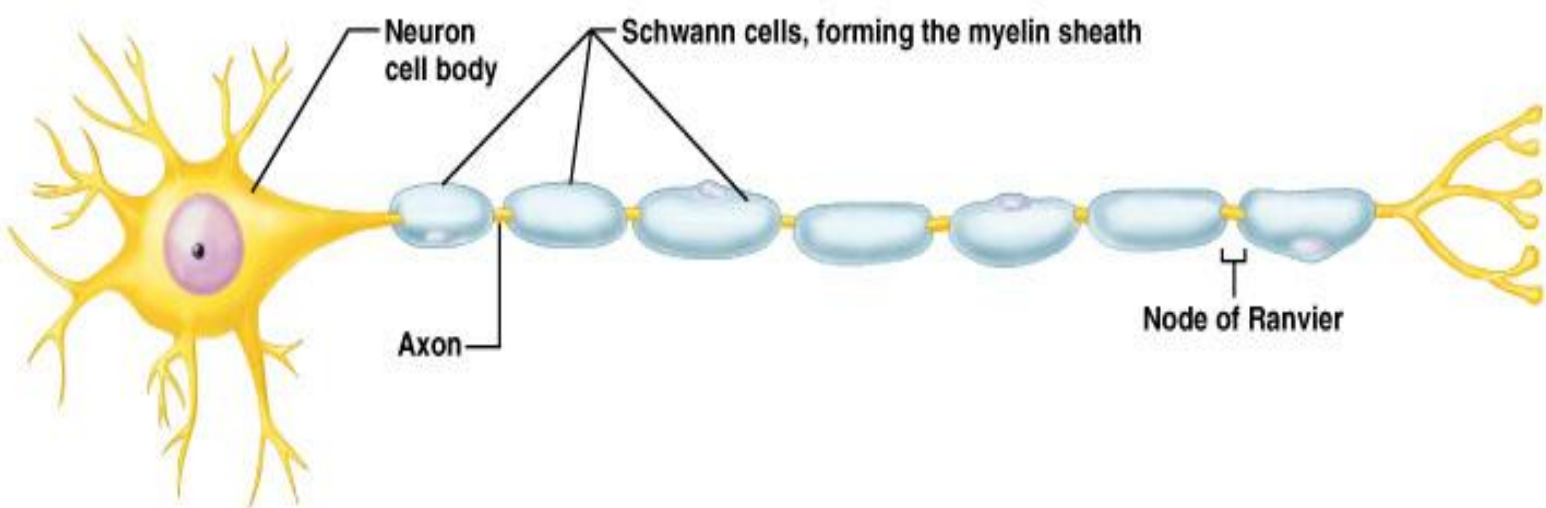
Applications of Neural Networks

- **Aerospace:** High performance aircraft autopilots, flight path simulations, aircraft control systems, autopilot enhancements, aircraft component simulations, aircraft component fault detectors
- **Automotive:** Automobile automatic guidance systems, warranty activity analyzers
- **Banking:** Check and other document readers, credit application evaluators
- **Cognitive science:** Modeling higher level reasoning, language, problem solving, Modeling lower level reasoning, vision, audition speech recognition, speech generation
- **Defense:** Weapon steering, target tracking, object discrimination, facial recognition, new kinds of sensors, sonar, radar and image signal processing including data compression, feature extraction and noise suppression, signal/image identification
- **Electronics:** Code sequence prediction, integrated circuit chip layout, process control, chip failure analysis, machine vision, voice synthesis, nonlinear modeling
- **Entertainment:** Animation, special effects, market forecasting
- **Financial:** Real estate appraisal, loan advisor, mortgage screening, corporate bond rating, credit line use analysis, portfolio trading program, corporate financial analysis, currency price prediction
- **Insurance:** Policy application evaluation, product optimization
- **Manufacturing:** Manufacturing process control, product design and analysis, process and machine diagnosis, real-time particle identification, visual quality inspection systems, beer testing, welding quality analysis, paper quality prediction, computer chip quality analysis, analysis of grinding operations, chemical product design analysis, machine maintenance analysis, project bidding, planning and management, dynamic modeling of chemical process systems

- **Mathematics:** Nonparametric statistical analysis and regression.
- **Medical:** Breast cancer cell analysis, EEG and ECG analysis, prosthesis design, optimization of transplant times, hospital expense reduction, hospital quality improvement, emergency room test advisement
- **Neurobiology:** Modeling models of how the brain works, neuron-level, higher levels: vision, hearing, etc. Overlaps with cognitive folks.
- **Oil and Gas:** Exploration
- **Philosophy:** Can human souls/behavior be explained in terms of symbols, or does it require something lower level, like a neurally based model?
- **Robotics:** Trajectory control, forklift robot, manipulator controllers, vision systems
- **Speech:** Speech recognition, speech compression, vowel classification, text to speech synthesis
- **Securities:** Market analysis, automatic bond rating, stock trading advisory systems
- **Telecommunications:** Image and data compression, automated information services, real-time translation of spoken language, customer payment processing systems
- **Transportation:** Truck brake diagnosis systems, vehicle scheduling, routing systems

Disorders of the Nervous System

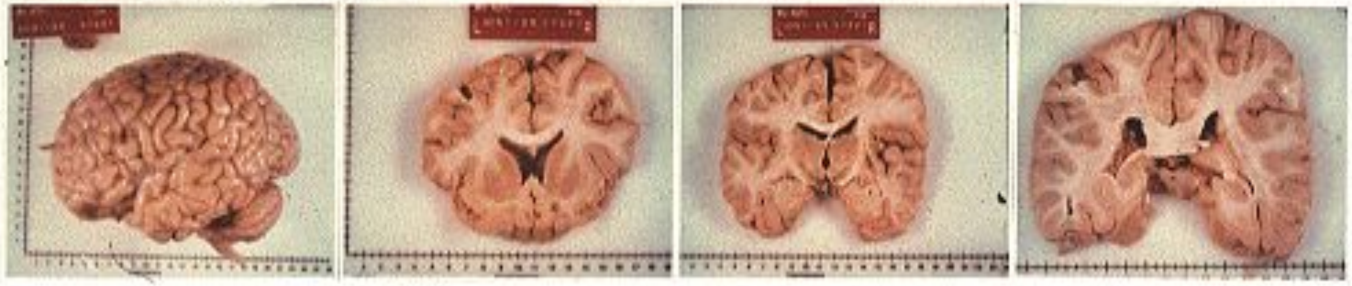
- Multiple sclerosis – common cause of neural disability
  - Varies widely in intensity among those affected
  - Cause is incompletely understood
  - An autoimmune disease
    - Immune system attacks the myelin around axons in the CNS



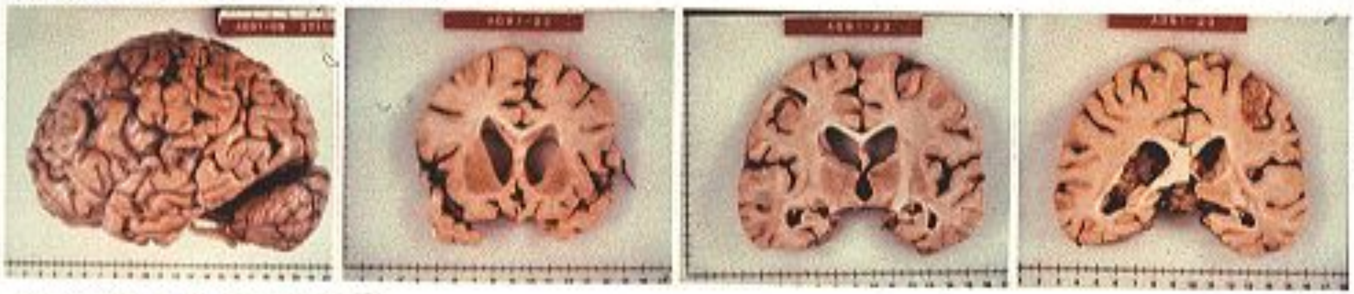
(a) PNS

BRAIN ATROPHY VISUAL STANDARDS

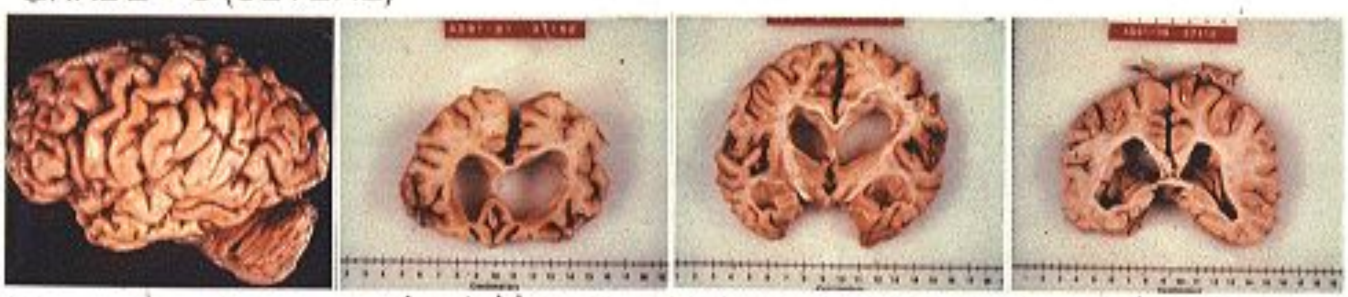
GRADE = 1 (NONE, NL FOR AGE)



GRADE = 2 (MODERATE)

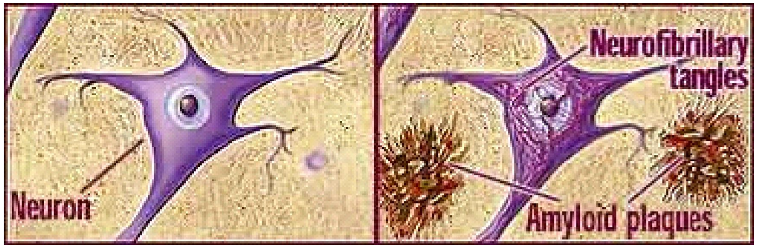


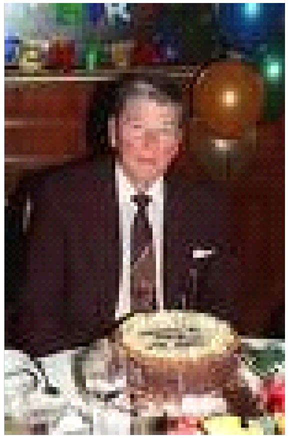
GRADE = 3 (SEVERE)



frontal horns body/temporal horns trigone

- **Alzheimer's Disease:**
  - **Age-associated disorder**
  - **Loss of memory, cognition, and executive performances**
    - **Deposits of amyloid plaques (Protein clumps)and neurofibrillary tangles (Abnormal accumulation of protein called 'tau") that interfere with neuronal functions**
    - **Loss of cholinergic neuronal functions (nerve functions activated by acetyl choline)**
- **Parkinson's Disease:**
  - **Age-associated disorder**
  - **Rigidity and incoordination interfering with mobility**
    - **Loss of dopaminergic neuronal functions**





Alzheimer's Disease

Parkinson's Disease

List of neurodegenerative diseases

- Alexander's disease
- Alper's disease
- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Ataxia telangiectasia
- Batten disease (also known as Spielmeyer-Vogt-Sjogren-Batten disease)
- Bovine spongiform encephalopathy (BSE)
- Canavan disease
- Cockayne syndrome
- Corticobasal degeneration
- Creutzfeldt-Jakob disease
- Huntington's disease
- HIV-associated dementia
- Kennedy's disease
- Krabbe's disease
- Lewy body dementia
- Machado-Joseph disease (Spinocerebellar ataxia type 3)
- Multiple sclerosis
- Multiple System Atrophy
- Narcolepsy
- Neuroborreliosis
- Parkinson's disease
- Pelizaeus-Merzbacher Disease
- Pick's disease
- Primary lateral sclerosis
- Prion diseases
- Refsum's disease
- Schilder's disease
- Subacute combined degeneration of spinal cord secondary to Pernicious Anaemia
- Schizophrenia
- Spielmeyer-Vogt-Sjogren-Batten disease (also known as Batten disease)
- Spinocerebellar ataxia (multiple types with varying characteristics)
- Spinal muscular atrophy
- Steele-Richardson-Olszewski disease
- Tabes dorsalis

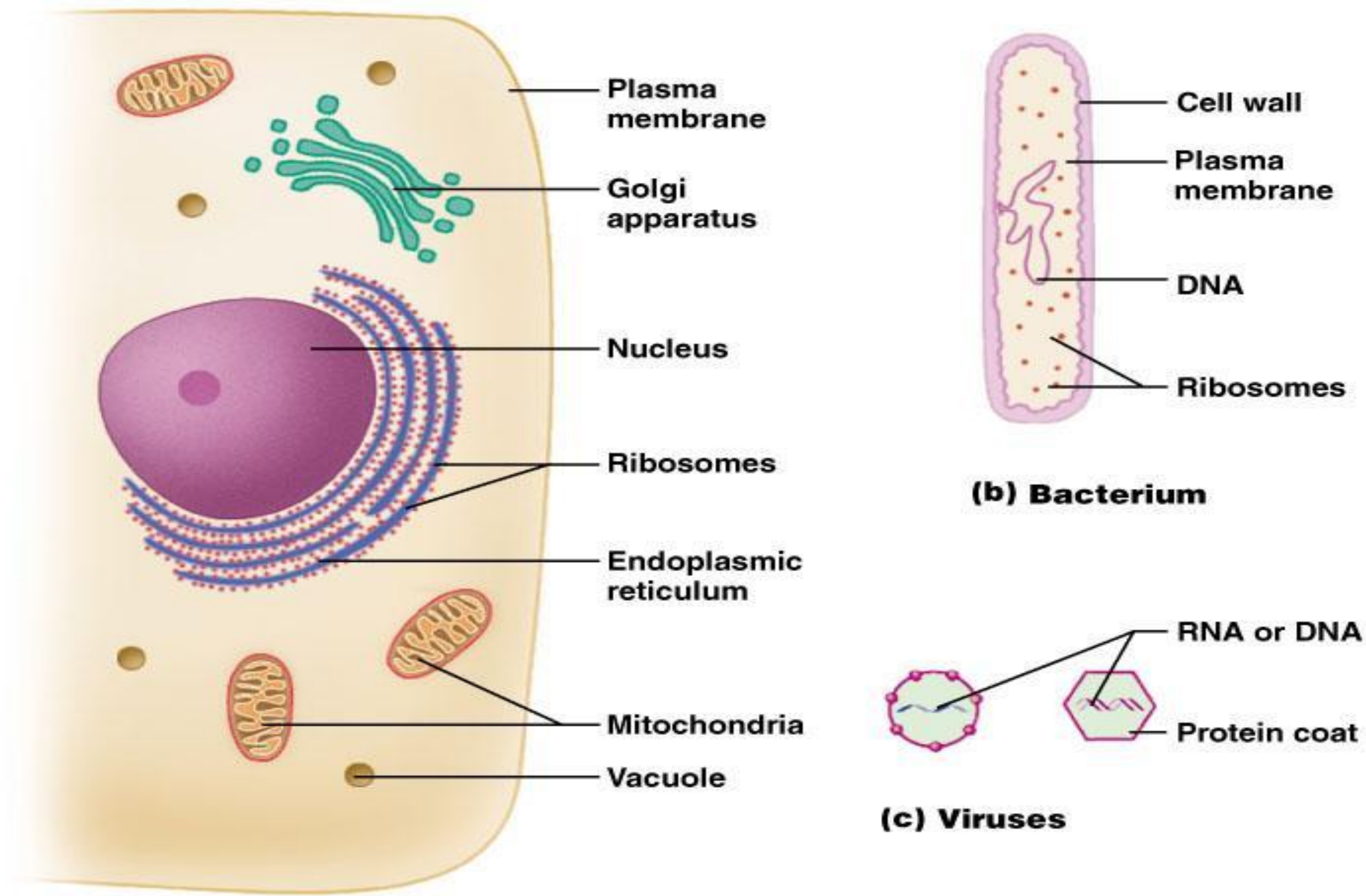
Immune System

Introduction
Fluid Systems of the Body
Innate Immunity
Adaptive or Acquired Immunity
- Cell-mediated immunity
- Humoral immunity

Immune Engineering

Cell Signaling

Eukaryotic Cells, Bacteria, and Viruses



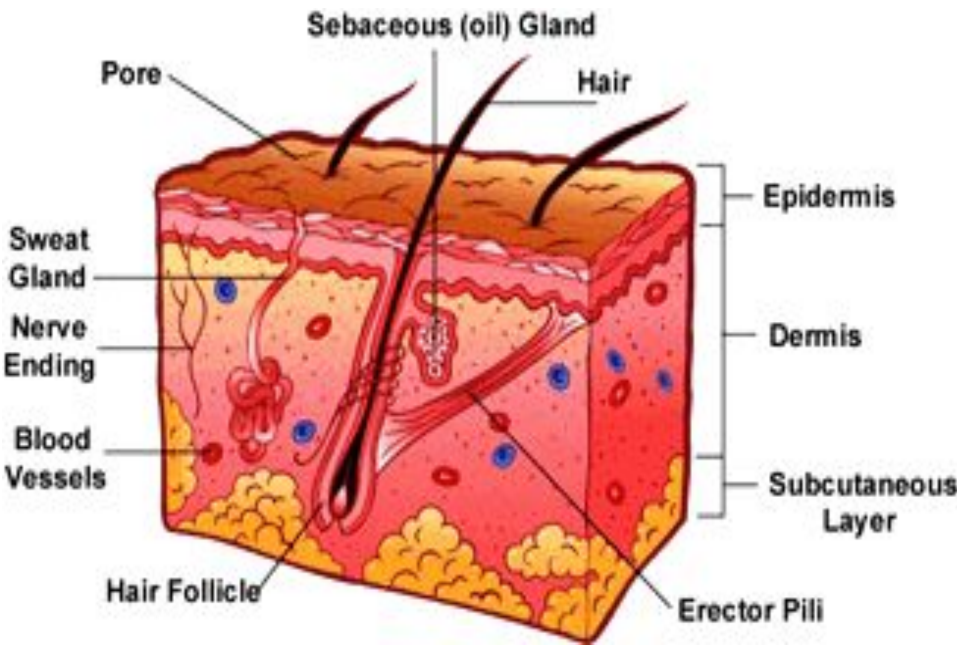
(a) Eukaryotic cell

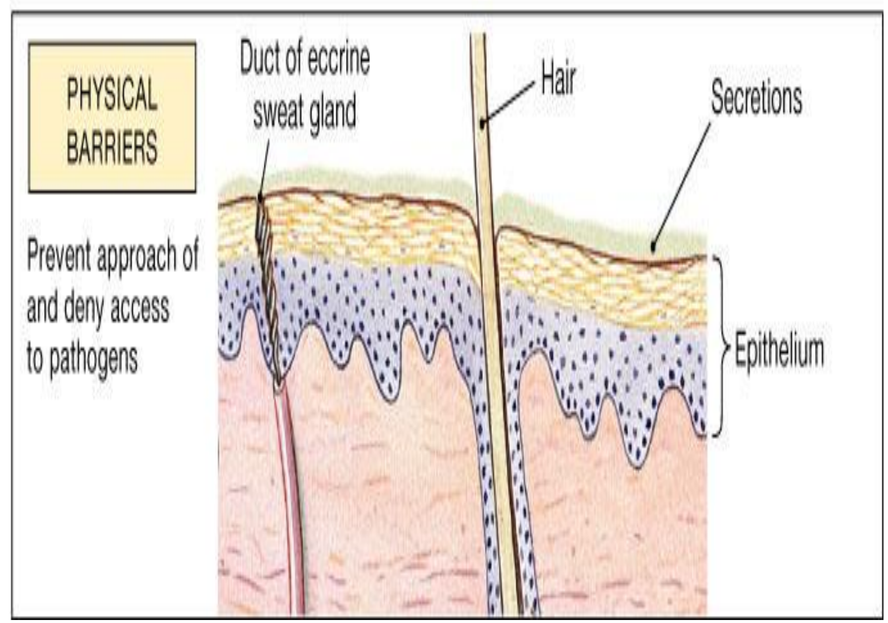
(b) Bacterium

(c) Viruses

Body Defenses: Overview

- **Physical barriers: skin & epithelial linings & cilia**
- **Chemical: acids, mucous & lysozymes**
- **Immune defenses – internal**
  - **Innate, non-specific, immediate response (min/hrs)**
  - **Acquired – attack a specific pathogen (antigen)**
- **Steps in Immune defense**
  - **Detect invader/foreign cells**
  - **Communicate alarm & recruit immune cells**
  - **Suppress or destroy invader**

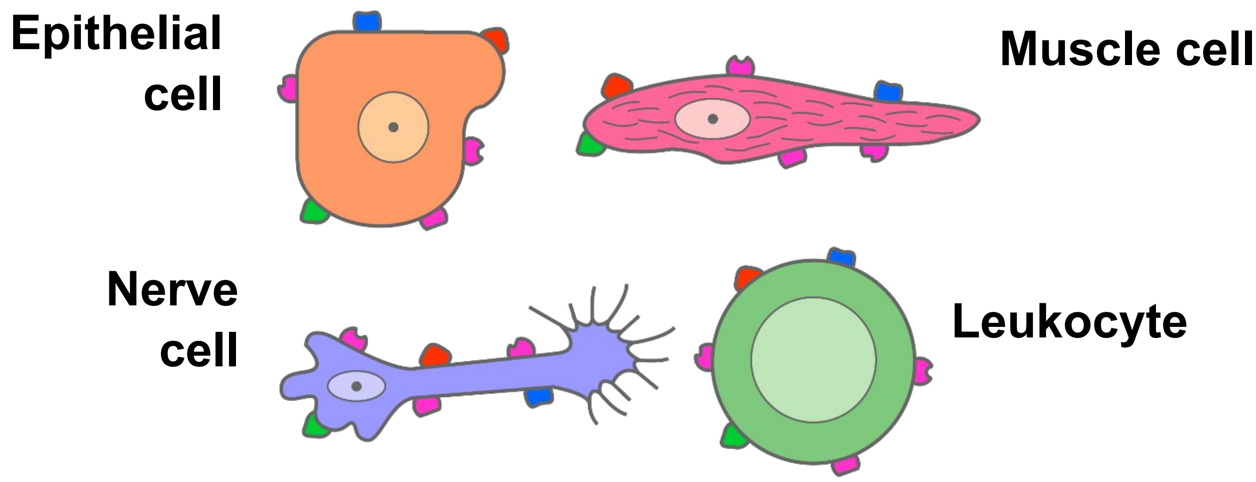




Discrimination of self from non-self

"The success of the immune system depends on its ability to discriminate between foreign (nonself) and host (self) cells. Survival requires both the ability to mount a destructive immune response against nonself and the inability to mount a destructive response against self."

Markers of Self

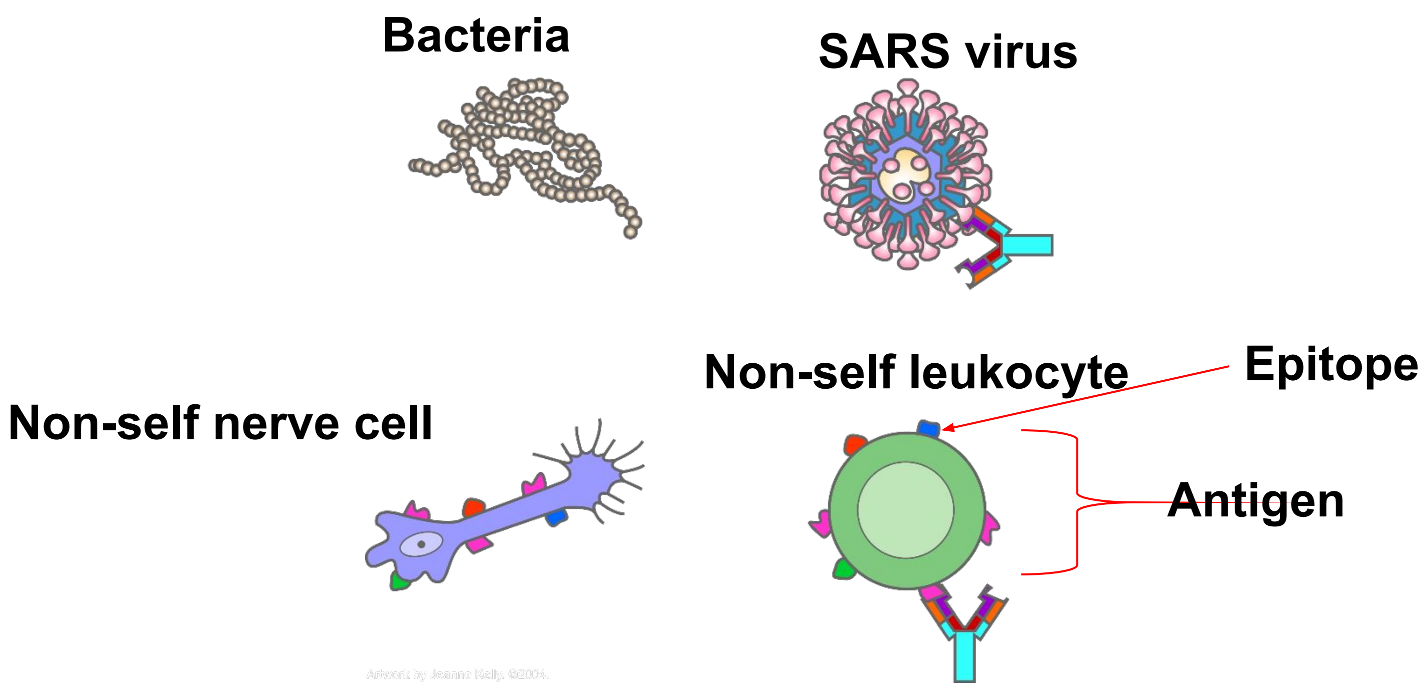


At the heart of the immune response is the ability to **distinguish between "self" and "non-self."**

- Every cell in your body carries the same set of distinctive surface proteins that distinguish you as "self."
- Normally your immune cells do not attack your own body tissues, which all carry the same pattern of self-markers; rather, your immune system coexists peaceably with your other body cells in a state known as self-tolerance.

This set of unique markers on human cells is called the **major histocompatibility complex (MHC) proteins**.

Markers of Non-self



Antigen = any non-self substance

- **Virus**
- **Bacteria**
- **Non-self cell (foreign cell)**

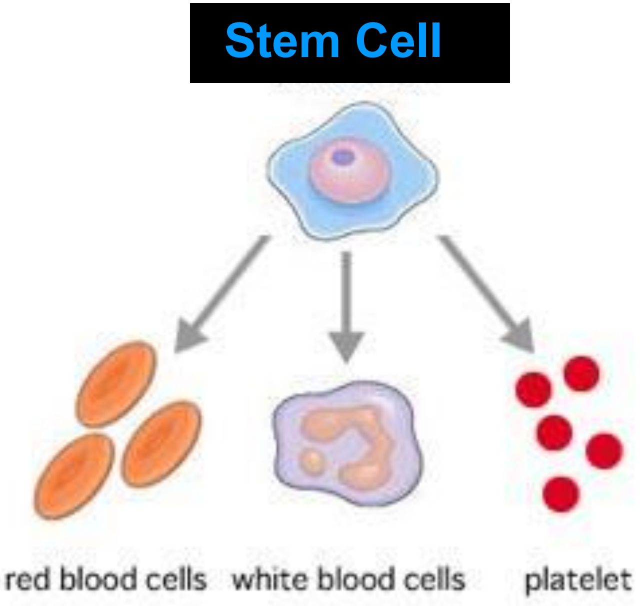
Epitope = The distinctive markers on antigens that trigger an immune response

Blood

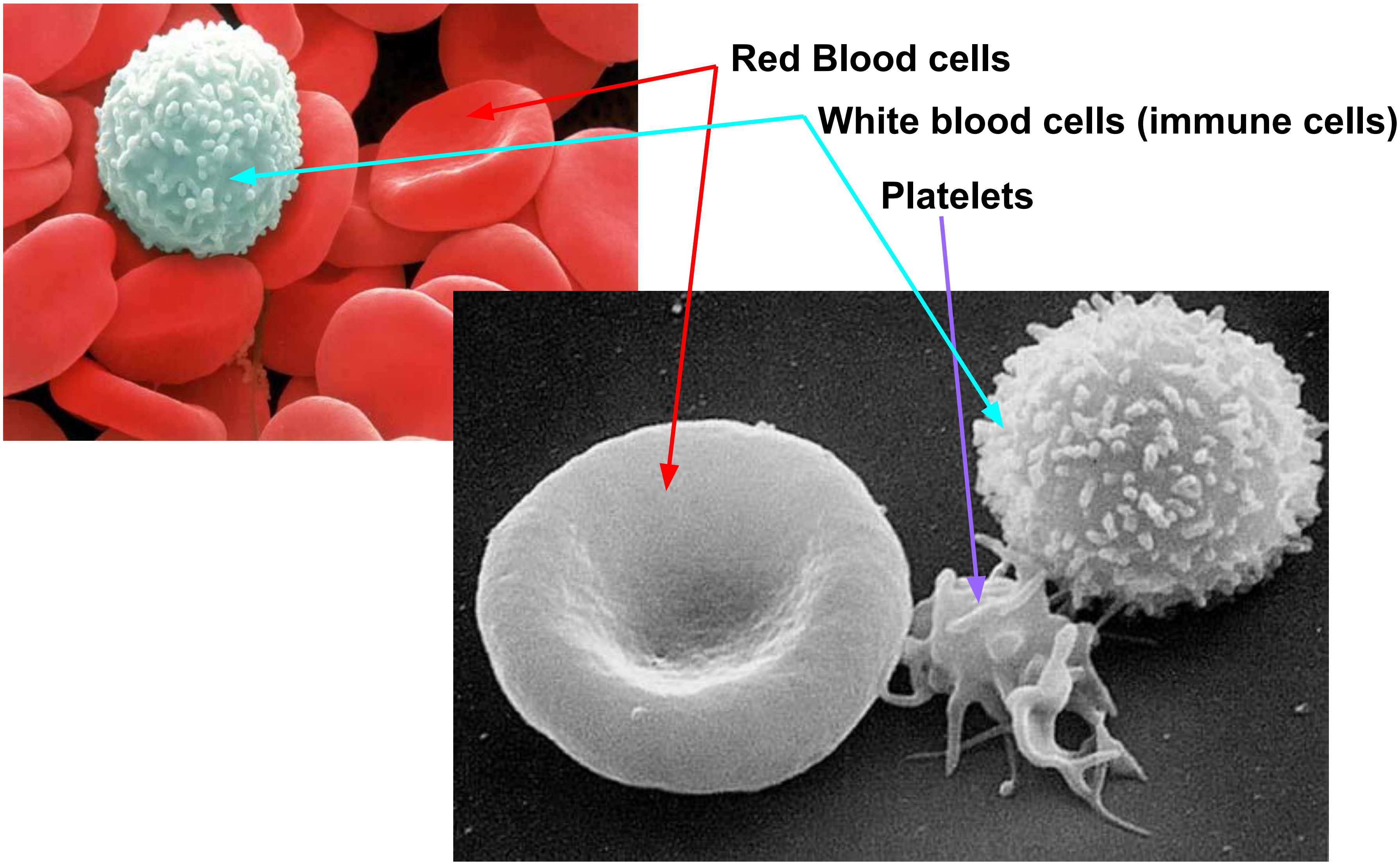
- Blood is 55% liquid (plasma) and 45% cellular

- Cellular component of blood:
  - Red blood cells = carry oxygen
  - White blood cells = immune system
  - Platelets = clot blood

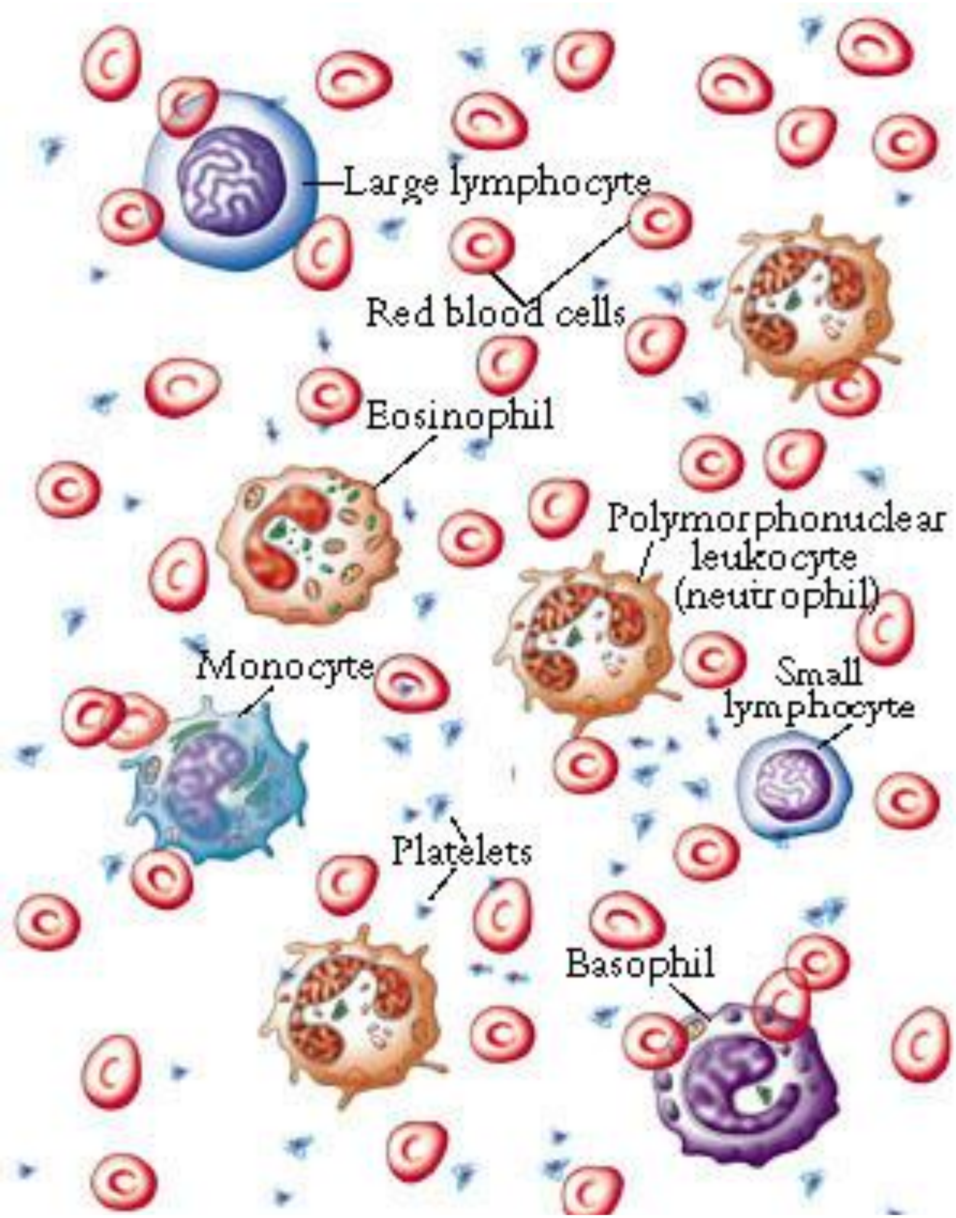
- All blood cells arise from a pluri-potent stem cell found in bone marrow



Blood cells

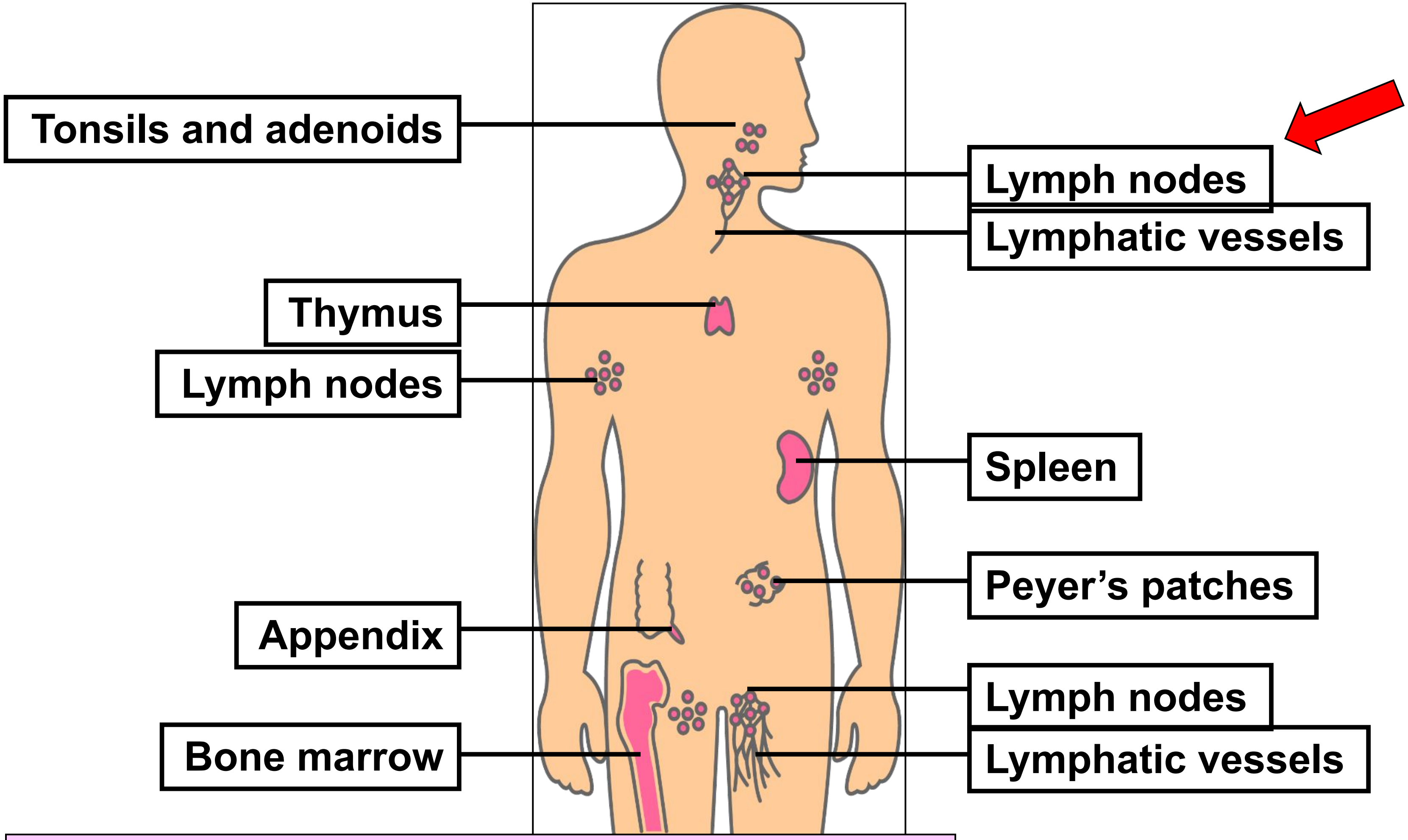


Leukocytes in the Blood



	Red Blood Cells	**5.0 X 10^6/mm^3**	
	Platelets	**2.5 X 10^5/mm^3**	
	Leukocytes	**7.3 X 10^3/mm^3**	
1	**Neutrophil**		**50-70%**
2	**Lymphocyte**		**20-40%**
3	**Monocyte**		**1-6%**
4	**Eosinophil**		**1-3%**
5	**Basophil**		**<1%**

Organs of the Immune System



Bone marrow, the soft tissue in the hollow center of bones, is the ultimate source of all blood cells, including the immune cells.

Lymphatic System

The organs of your immune system are connected with one another and with other organs of the body by a network of lymphatic vessels.

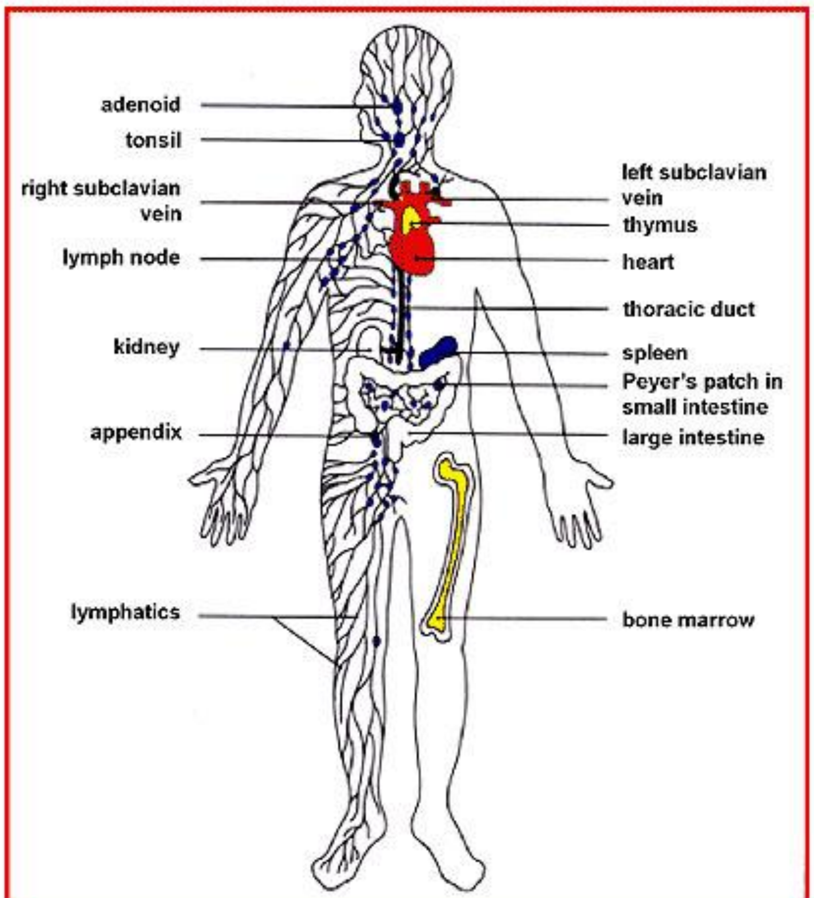
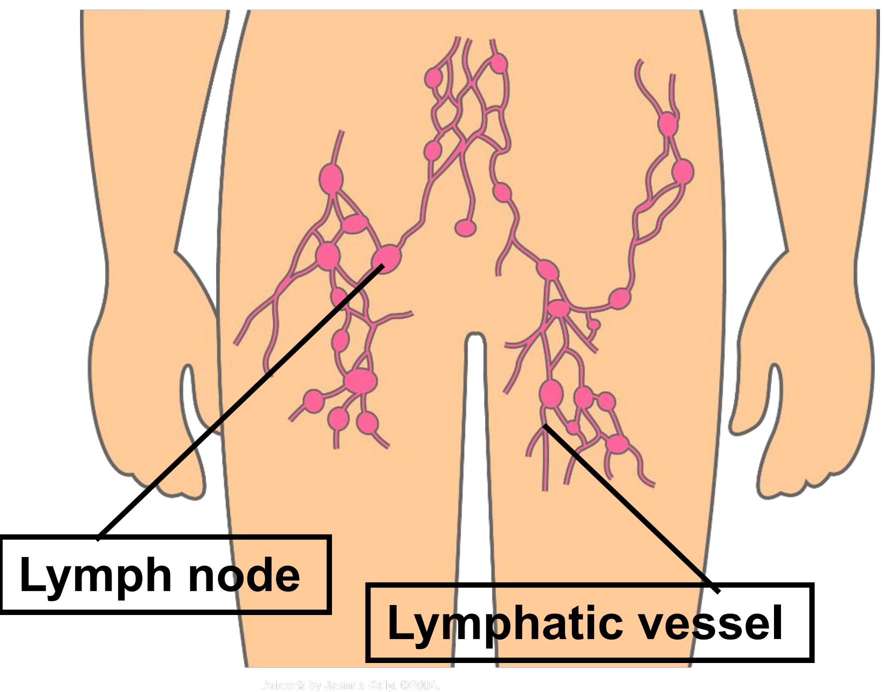


Figure 1. The immune system.

Lymphatic System

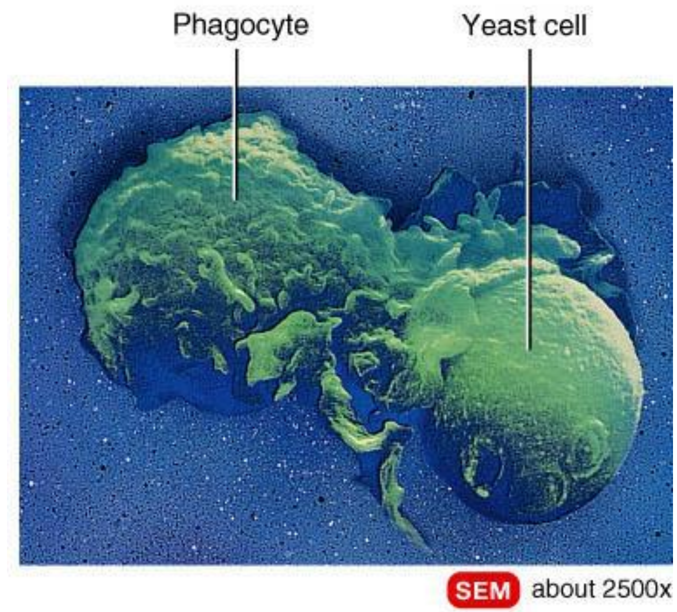
The organs of your immune system are connected with one another and with other organs of the body by a network of lymphatic vessels.



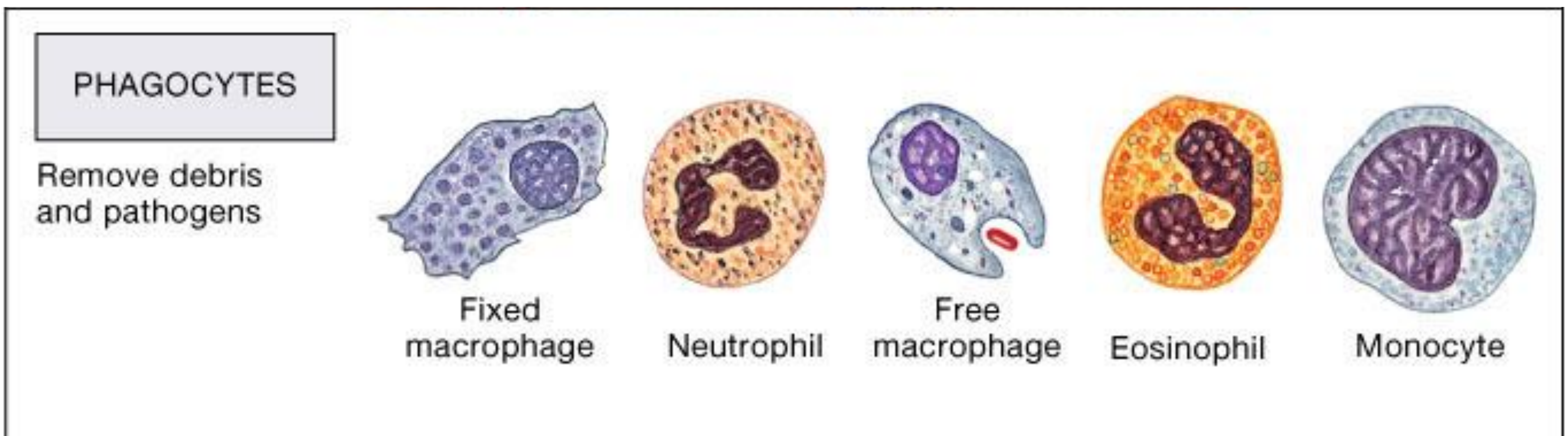
1. **Lymphatic vessels closely parallels the body's veins and arteries**
   - **Lymphatic vessels carry *lymph*, a clear fluid that bathes the body's tissues**
   - **Cells/fluids are exchanged between blood and lymphatic vessels, enabling the lymphatic system to monitor the body for invading microbes.**
2. **Lymph nodes contain high levels of immune cells**

Nonspecific Defenses, Phagocytes

- Remove cellular debris and respond to invasion by foreign pathogens
  - Monocyte-macrophage system - Fixed and free
  - Microphages – Neutrophils and eosinophils
  - Move by diapedesis
  - Exhibit chemotaxis

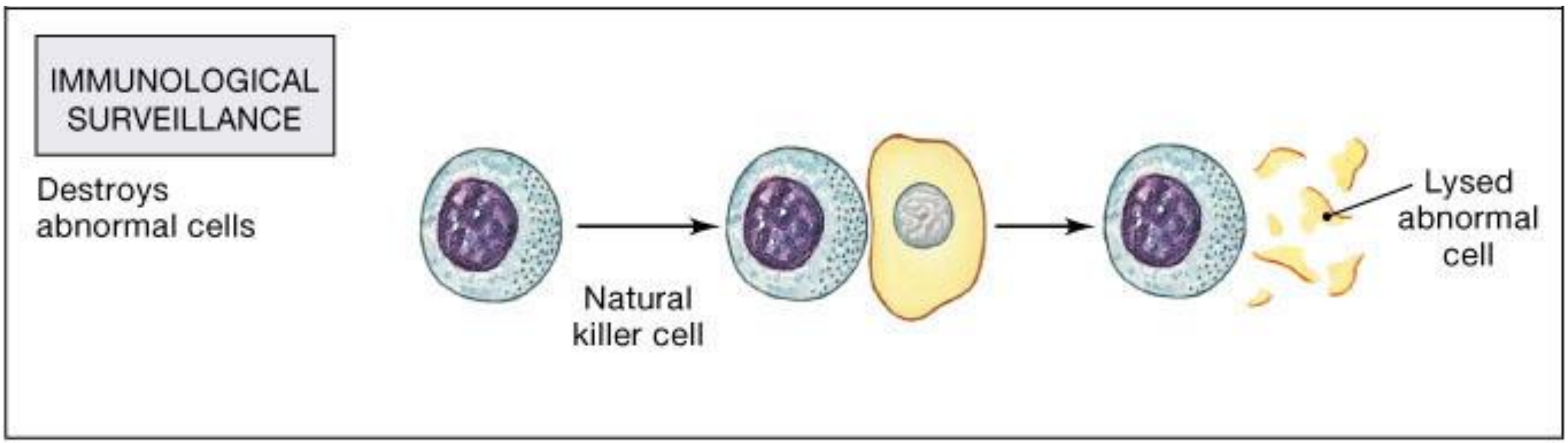


(b) Phagocyte engulfing a yeast cell

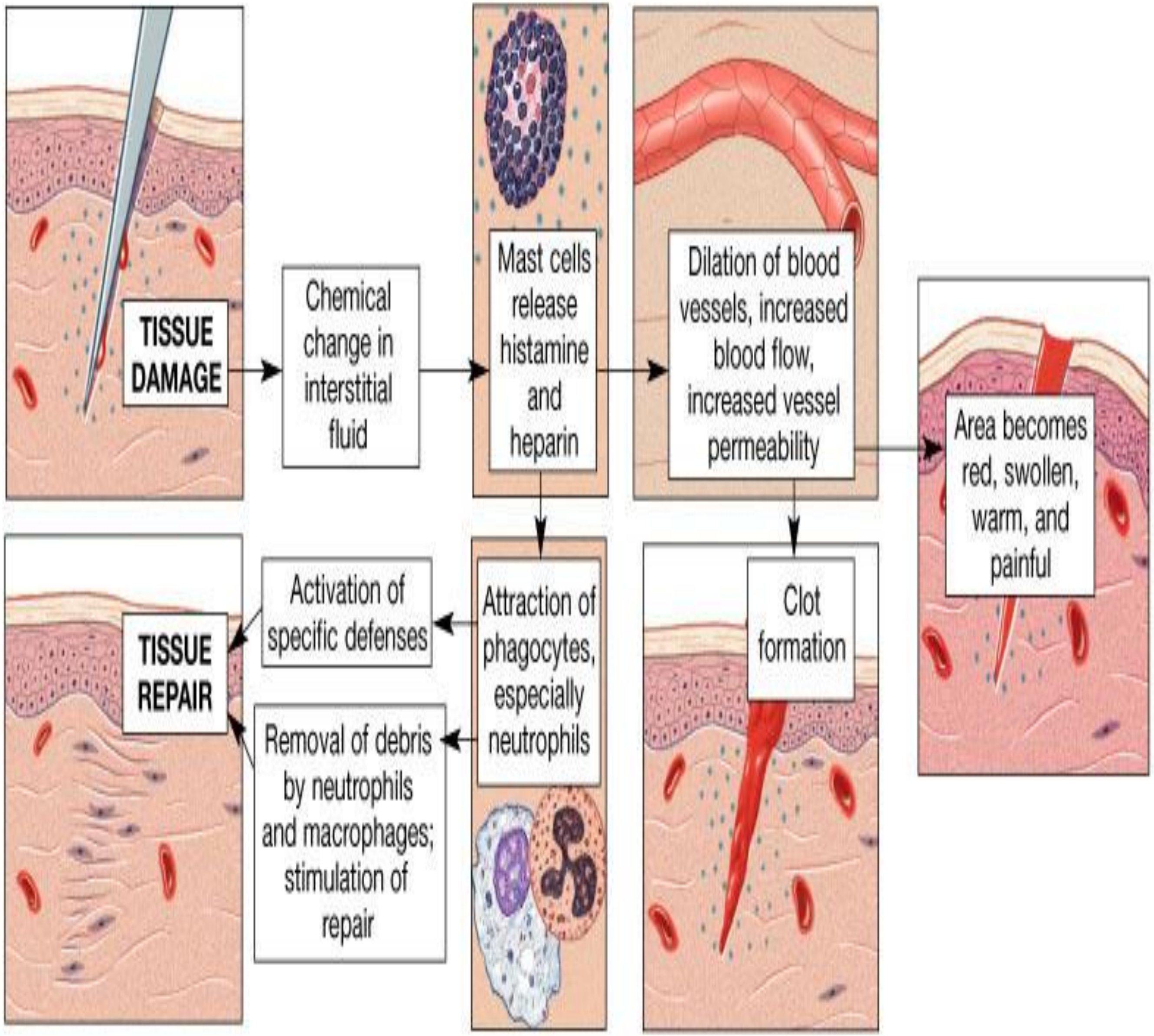


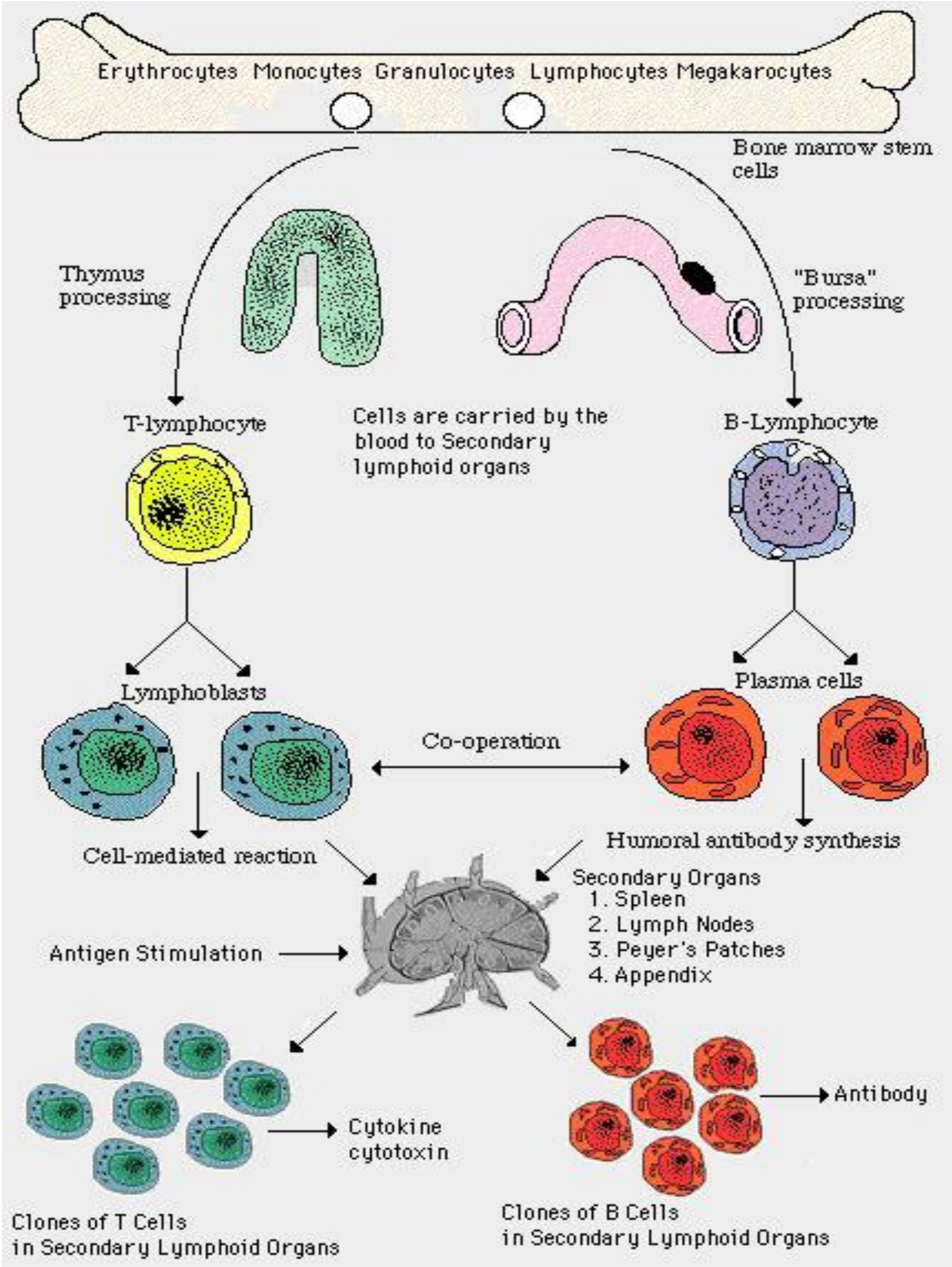
Nonspecific Defenses, Immunological surveillance

- Constant monitoring of normal tissue by NK cells
- NK cells
  - Recognize cell surface markers on foreign cells
  - Destroy cells with foreign antigens



Inflammation





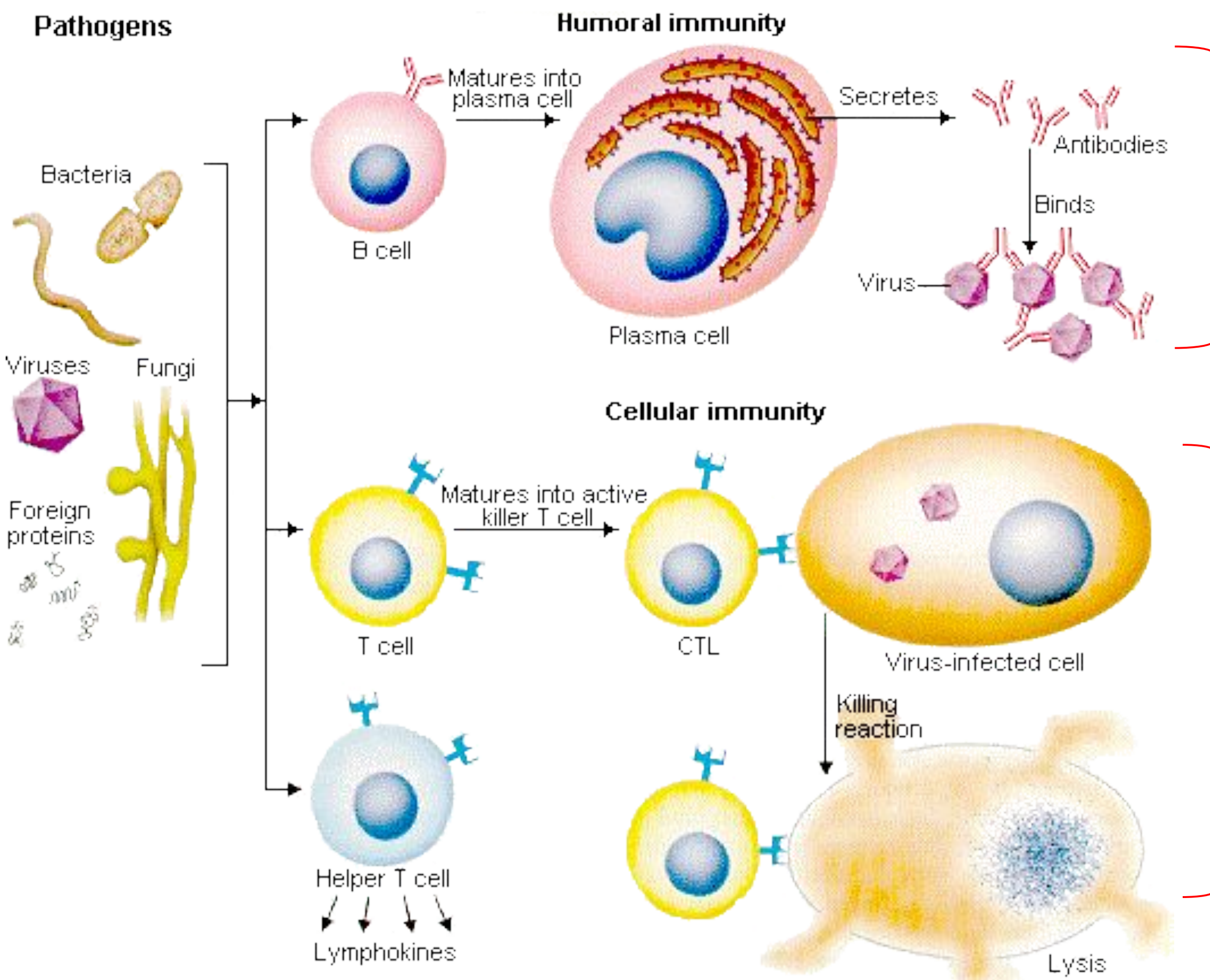
Adaptive or Acquired Immunity

- Acquired after birth
- Seen only in vertebrates
- Characteristic features are:
  - Diversity
  - Specificity
  - Self vs non-self
  - Memory

Immune Response System

Made up of two cellular systems (lymphocytes)

1. Humoral immunity - **B cells**
2. Cell-mediaed immunity - **T cells**

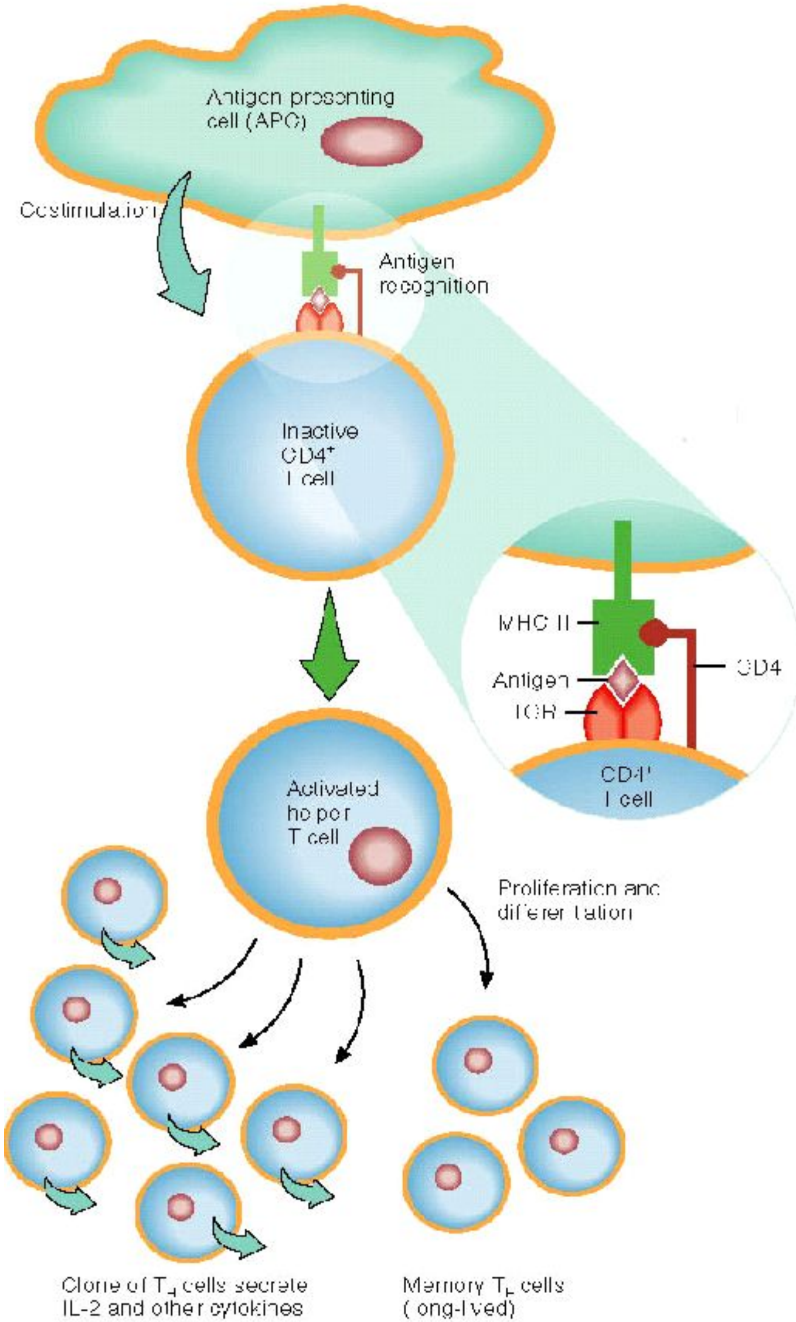


B cells make antibodies

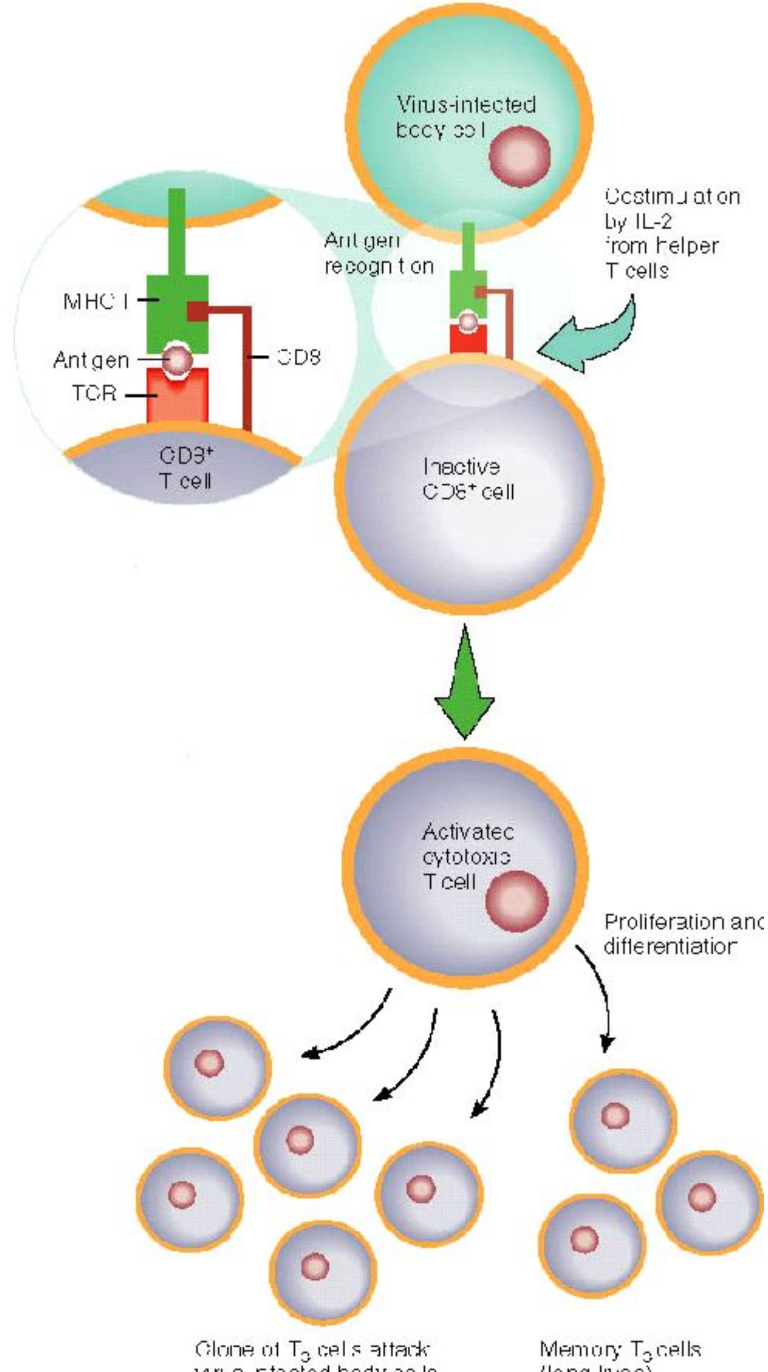
T cells mount direct attack on foreign/infected cell

Cell mediated immunity

- T cells must be activated
- Must have both surface antigen recognition and costimulation to activate
- T cell receptors recognise and bind to specific antigen presented with MHC complexes
  - T cell only activated if binds to antigen and receives costimulation
    - Co-stimulation provided by cytokines or membrane proteins
  - Need for co-stimulation prevents immune responses occurring accidentally
    - Recognition (binding to receptor) without costimulation results in anergy (prolonged state of inactivity) in both B and T cells
  - Once T cell co-stimulated it is activated
    - Proliferates
    - Differentiates (forms more highly specialised cells)
  - Activation, proliferation and differentiation occurs in secondary lymphatic organs and tissues

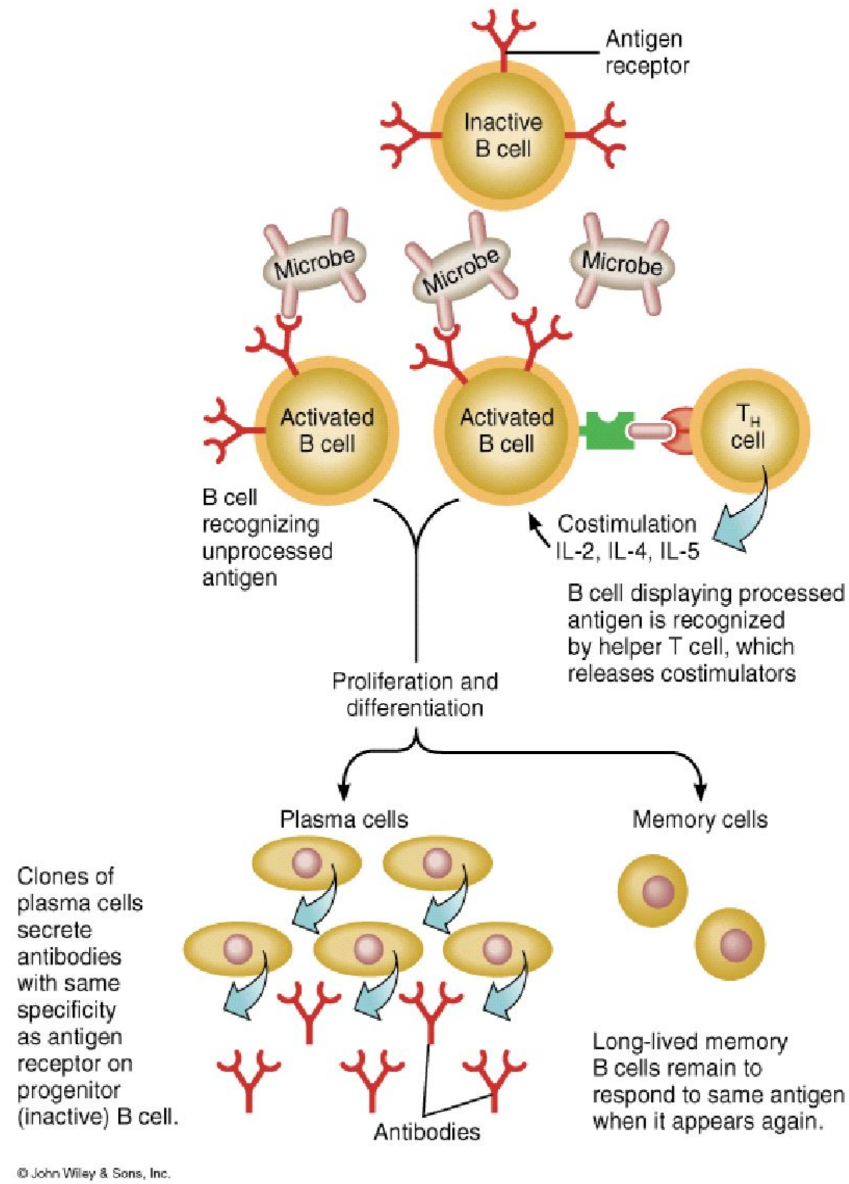


(a) Helper T (T_H) cells or CD4+ cells

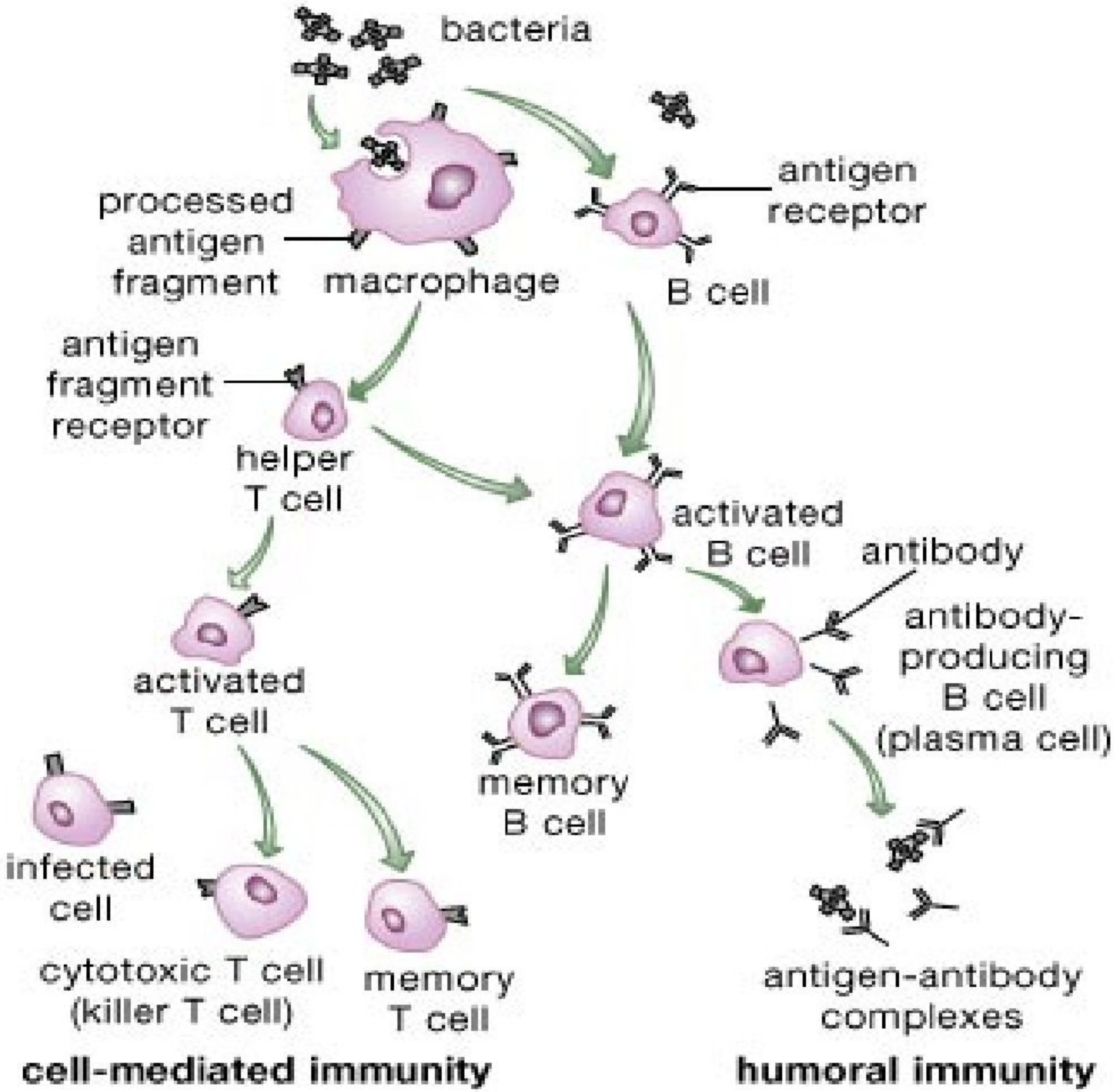


Humoral (Antibody-mediated) immunity

- **Mediated by B cells**
- **Antigen can activate B cell in two ways:**
  - **direct binding**
    - **provokes less vigorous response**
  - **B cells process antigen (act as APC) and display processed antigen with MHC proteins**
    - **T_H cells recognise processed antigen**
      - **T_H cells provide co-stimulation for B cell**
- **Activated B cell**
  - **proliferates and differentiates**
    - **plasma cells**
      - **secrete antibodies with same antigen binding properties as receptors**
    - **memory B cells**



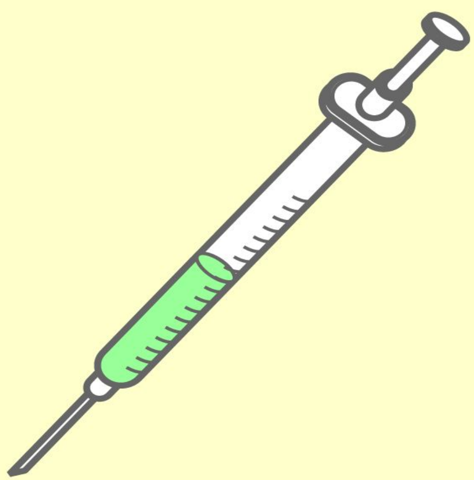
Summary of Acquired Immunity



Immunity: Active and Passive

Active immunity

Naturally acquired



Artificially acquired

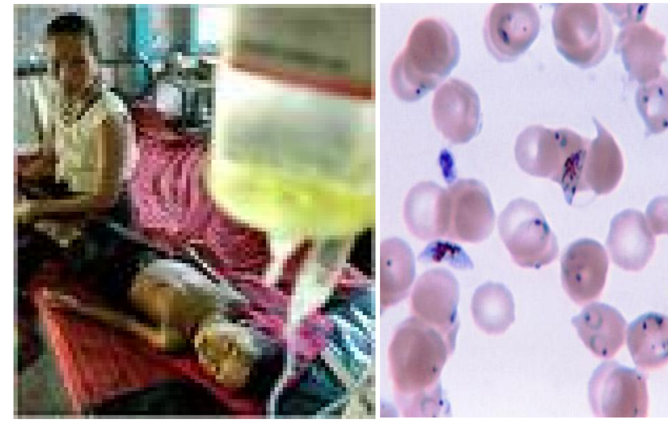
Passive immunity

Naturally acquired

Artificially acquired

HIV/AIDS Patient

Aging



Malaria-parasitic disease

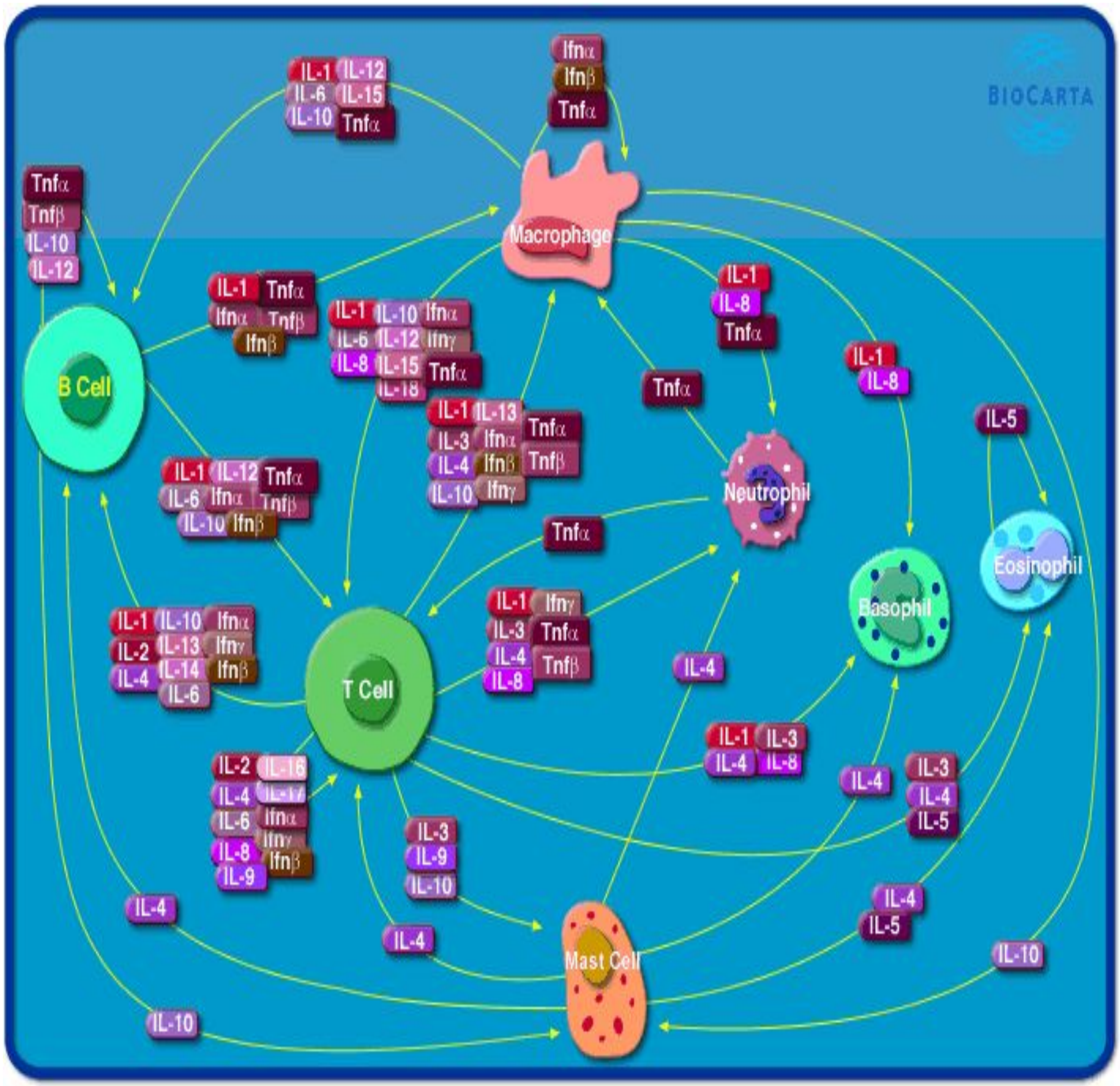
Smoking causes cancer

Diabetes

Rheumatoid arthritis

Immune Engineering

- The complexity of the immune system can be compared to that of the brain.
- There is a vast number of cells, molecules, and organs that compose the immune system, and these have to act in concert, and together with other vital systems, so as to promote and maintain life.
- Neither can the immune system act in isolation to maintain life, nor can a higher organism live without an immune system.



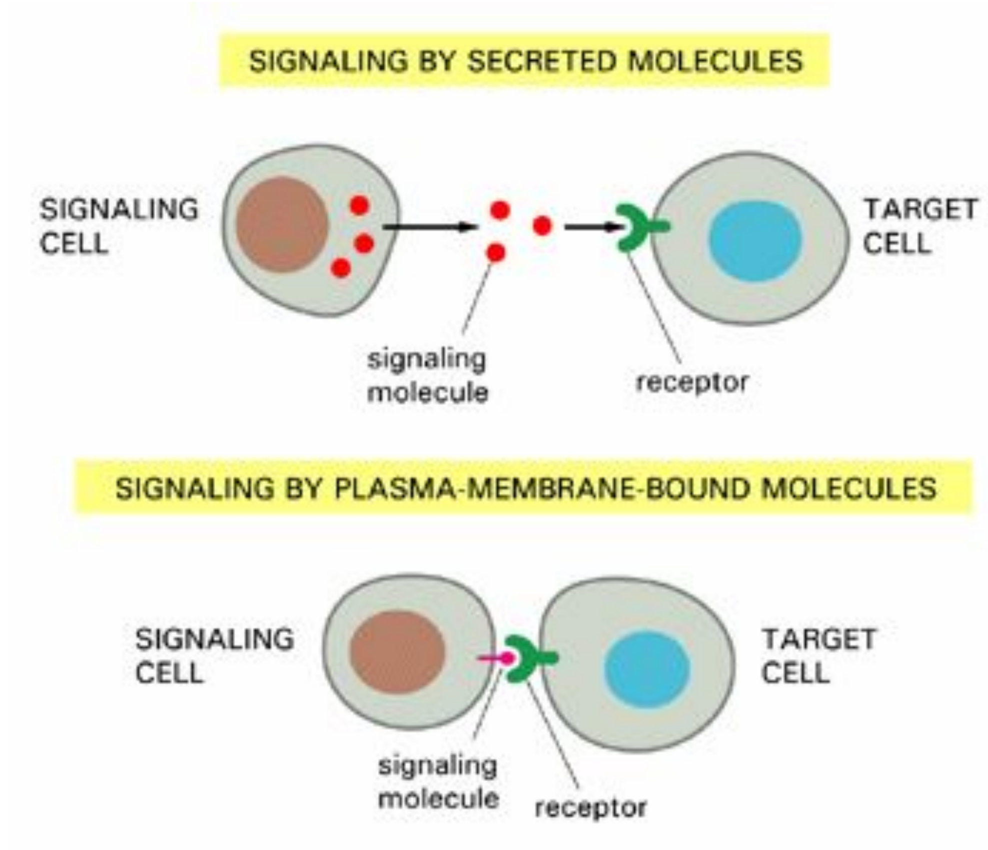
- **Artificial immune systems (AIS) compose a new computational intelligence approach inspired by theoretical and experimental immunology with applications to problem solving.**

- **Like all new approach, the field still lacks a more formal description and better theoretical foundations.**

- **The application of mathematical analysis and modeling to immunology may result in outcomes such as a deeper and more quantitative description of how the immune system works, a more critical analysis of hypothesis, it can assist in the prediction of behaviors and the design of experiments.**

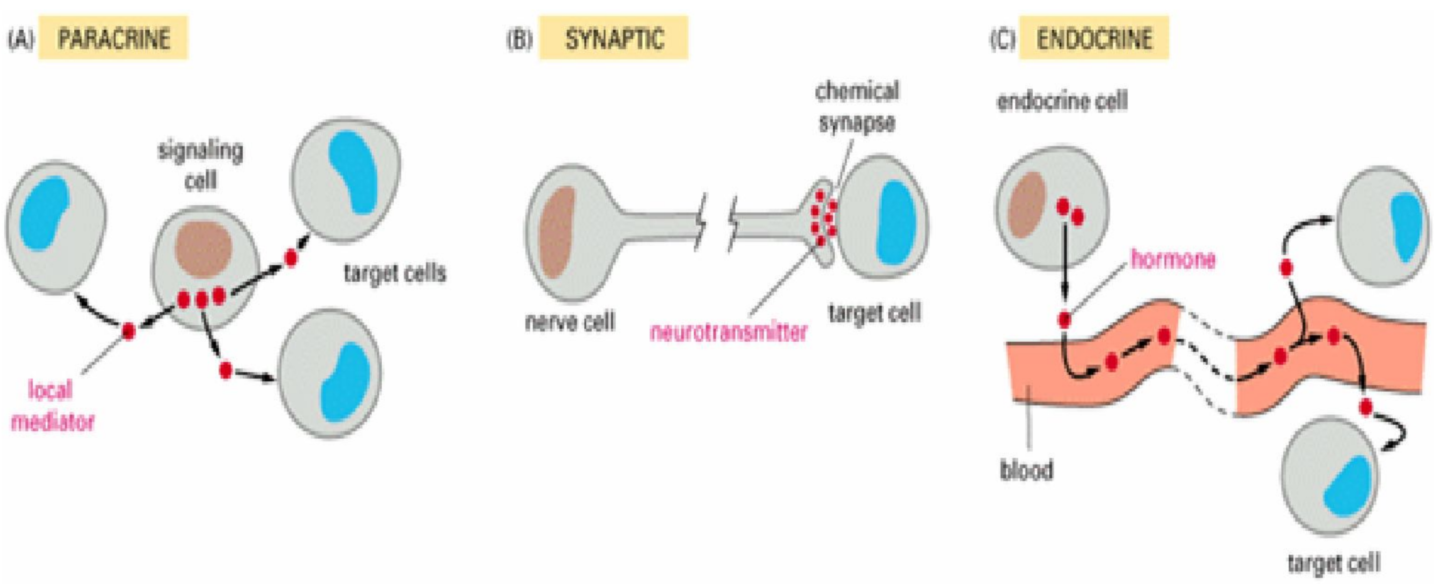
General Principles of Cell Signaling

- Unicellular organisms resembling present-day bacteria were present on Earth for about 2.5 billion years before the first multicellular organism appeared.
- One reason why multicellularity was so slow the evolve may have been related to the difficulty of developing the elaborate cell communication mechanisms that a multicellular organism needs.
- These communication mechanisms depend heavily on extracellular **signal molecules,** which are produced by the cells to signal to their neighbors or to cells further away.
- The signal molecules are mainly proteins.
- These proteins include cell-surface *receptor proteins*, which bind the signal molecule, plus a variety of *intracellular signaling proteins* that distribute the signal to appropriate parts of the cell.



Secreted Molecules Mediate Three Forms of Signaling: Paracrine, Synaptic, and Endocrine

- Paracrine signaling depends on signals that are released into the extracellular space and act locally on neighboring cells.
- Synaptic signaling is performed by neurons that transmit signals electrically along their axons and release neurotransmitters at synapses, which are often located far away from the body.
- Endocrine signaling depends on endocrine cells which secrete hormones into the bloodstream that are then distributed widely throughout the body



There Are Three Known Classes of Cell-Surface Receptor Proteins: Ion-Channel-linked, G-Protein-linked, and Enzyme-linked