Supplemental Table S1

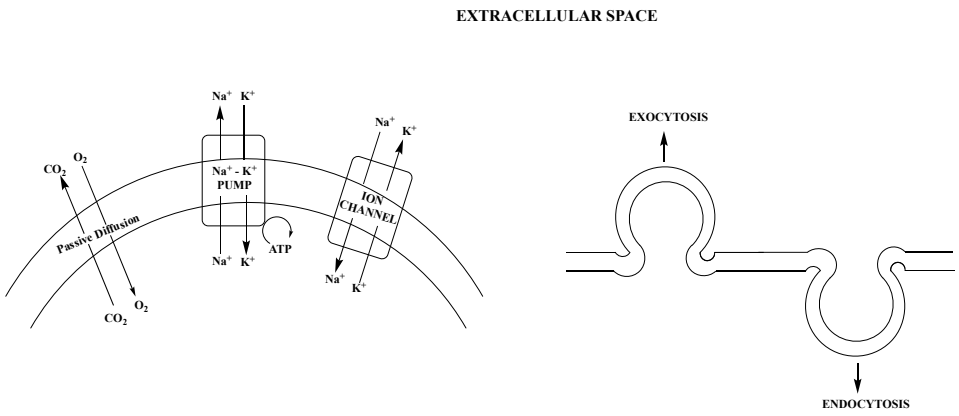
The table below shows the nine possible answers to the open-ended question. The relative complexity of the answers is signified by the instructor score, provided in the left column. While the answers below are arranged in the order of complexity (from the least complex answer to the most complex answer), the answers were randomised for the in-class activity.

Instructor Score	Answer
2	• The cell membrane allows some chemicals to cross easily, like O_2 and CO_2, by diffusion. • Other chemicals use proteins to help them to get across membranes. Usually the proteins help to get water soluble chemicals across the membrane and this is important for all sorts of cells in our bodies – like nerve and muscle cells. These proteins can be ion channels or transporters.

3	• The cell membrane transports fatty or non-polar substances but not ones that dissolve in water. This is because of the structure of the cell membrane.
	• Molecules like O_2 and CO_2 easily get across the cell membrane, so that we can get the substances into and out of our bodies. This is because they dissolve in the cell membrane very well.
	• Other compounds that cannot get across the membrane use proteins to get across the cell membrane, so we can get these important chemicals into our bodies. These sorts of chemicals include water and ions. Some examples of how compounds use proteins to get across membranes are:
	  o Channels for different sorts of ions like sodium. These substances move from a region of high concentration to a region of low concentration when the channels open up. It is important to have these ions in muscles and nerves and other cells.
	  o Other proteins in the cell membrane are transporters. These let in water soluble compounds and sometimes use energy from ATP.
	• Bulk transport across cell membranes can also by endocytosis and exocytosis – this is important for storage and release of chemicals in nerves.

4

- O_2 and CO_2 move across the membrane by passive diffusion. Na and K move against their concentration gradient by Na-K pump and ions move along their concentration gradient through ion channels. Exocytosis moves substances out while endocytosis brings things into the cell.

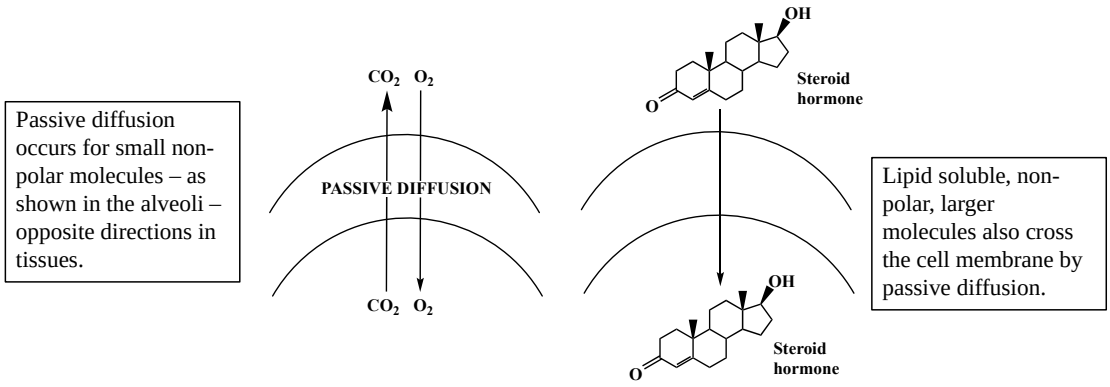


5

- The most important thing about transport of molecules across the cell membrane is that the cell membrane likes to dissolve lipid soluble molecules so it is not a good environment for allowing passage of compounds that are water soluble. This is because the lipid soluble molecules like to be in the middle of the membrane when they are being transferred across the cell membrane.
- Lipid soluble molecules like O_2, CO_2 and hormones are transferred around the body by easily diffusing across the cell membrane, so that we can get the substances into our cells at the correct concentrations. This is because their lipid solubility makes them like to be in the middle of the membrane where the fatty tails of the membrane are – so they dissolve in the cell membrane very well.
- Other compounds that cannot get across the membrane by dissolving in the fatty parts of the membrane use proteins in the cell membrane, so that they can move across the cell membrane when they need to cross into or out of cells. These sorts of chemicals will include water, ions and other polar molecules that prefer to be in an aqueous (watery) environment than in the fatty environment in the middle of the cell membrane. Now I will describe some of the examples of how compounds use proteins to allow the transport across membranes:
    - There are proteins called channels that allow molecules like water and a number of different sorts of biologically active ions to move through the cell membrane. The problem with this process is that it does not require any energy and therefore ATP is not involved in the process. This means that the substances can only move from a region of high concentration to a region of low concentration and cannot move against their concentration gradient. Some of the ions are important for things like the contraction of muscle cells and generating nerve signals, and also includes channels for water which is transferred across cell membranes during the process of osmosis.
    - Other proteins in the cell membrane work a different way and they are called transporters. The transporters can help the cell a lot with letting

5 cont.	some substances into the cell even though they are water soluble and not really able to move easily across the cell membrane. Using the energy from ATP, some of these processes are active transport and so they can accumulate against a concentration gradient, but others don't use this energy. o Co-transporters are also important and they involve processes like the sodium pump and also transfer of water soluble compounds that need the help of a protein to get across the membrane. This is important for some sugars that we eat in our diet and getting them into our blood, because the sugars are too water soluble to get across cell membranes without the help of proteins.
6	• The cell membrane consists of phospholipids and its structure allows the passage of some molecules across the membrane into or out of the cell, but does not allow other types of molecules to cross the membrane. • Small non-polar molecules cross the membrane easily because they have a similar chemical composition to the cell membrane. Example: O_2 and CO_2 are transferred around the body by this process of easily diffusing across the cell membrane, so is important when we breathe • Larger non-polar molecules also cross the cell membrane by diffusing – Example: some hormones dissolve in fat and because of that they can cross the cell membrane to reach their receptors. • Proteins also help the transport of a number of types of molecules across the cell membrane: o Water moves across cell membranes by osmosis. o There are also channels for a number of ions in cells, including sodium and potassium ions. These channels have different structures from each other. Examples include: Na^+ and K^+ channels which are both important in action potentials – e.g. neurones and muscle cells. o Transporters are other proteins that are involved in transfer of chemicals across cell membranes. Sometimes they need energy and then they are classified as being an active transport process.. Examples include: (i) The Na^+/K^+ pump that is important for establishing the resting membrane potential. (ii) Transporters for chemicals released form nerves. o There are also co-transporters where energy drives transport of polar molecules such as sugars into cells. Example is co-transport of Na^+ ions and glucose by linking with the sodium/potassium pump. • Bulk transport of liquids or particles can occur across cell membranes by the processes of pinocytosis and exocytosis. These processes can allow the release of chemicals from nerves.

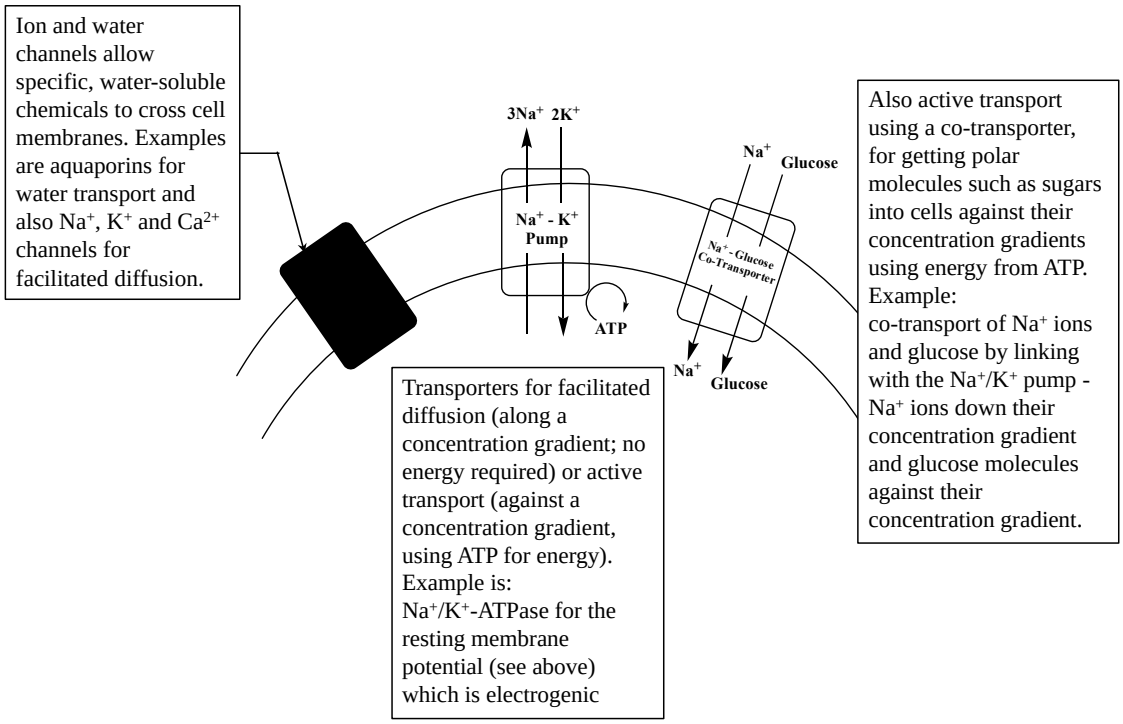
EXTRACELLULAR SPACE



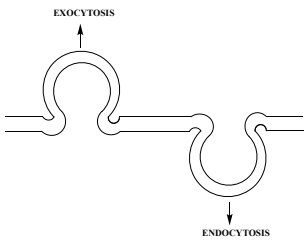
CYTOPLASM

Proteins traverse the cell membrane to transport other molecules.

7



Processes for bulk transport across cell membranes:
- Endocytosis pinching off membrane to envelope particles or solution
- Exocytosis – reverse of the above



8

- The bilayer selectively permeable phospholipid plasma membrane has the phospholipid tails inwards and the charged phosphates towards the inside and outside.
- Small non-polar or larger lipid soluble molecules cross membranes by passive diffusion, down the concentration gradient. Examples: O_2 and CO_2 transfer across the alveoli in the lungs and into / out of tissues in the systemic circulation; also steroid hormones diffuse into cells to act on their receptors.
- A membrane protein is used to allow transport of ions, water and other polar molecules across the membrane. These proteins include:
    - Aquaporins for transfer of water across the cell membrane to allow sufficient transfer of water, beyond that occurring by diffusion.
    - Ion channels for specific ions along their concentration gradient. Examples: voltage-gated Na^+ and K^+ channels – e.g. in neurones and muscle cells; voltage-gated Ca^{2+} channels at the neuronal synapse; also ligand-gated ion channels are the fastest responding superfamily of receptors – the ion channel-linked receptors.
    - Transporters mediate facilitated diffusion or active transport (against concentration gradient, using ATP). Examples include: (i) Na^+/K^+-ATPase allows active transport of 3 Na^+ out and 2 K^+ in and is hence electrogenic to set up the negative membrane potential; (ii) transporters for reuptake of neurotransmitters.
    - Co-transporters allow transport of polar molecules such as sugars into cells against their concentration gradients using a linked active process to provide energy from ATP. Example: co-transport of Na^+ ions and glucose linked to Na^+/K^+-ATPase.
    - Processes for bulk transport across cell membranes - e.g. pinocytosis, phagocytosis, receptor-mediated endocytosis, exocytosis – part of the cell membrane is pinched off. Example: release of neurotransmitter at the synapse.

9

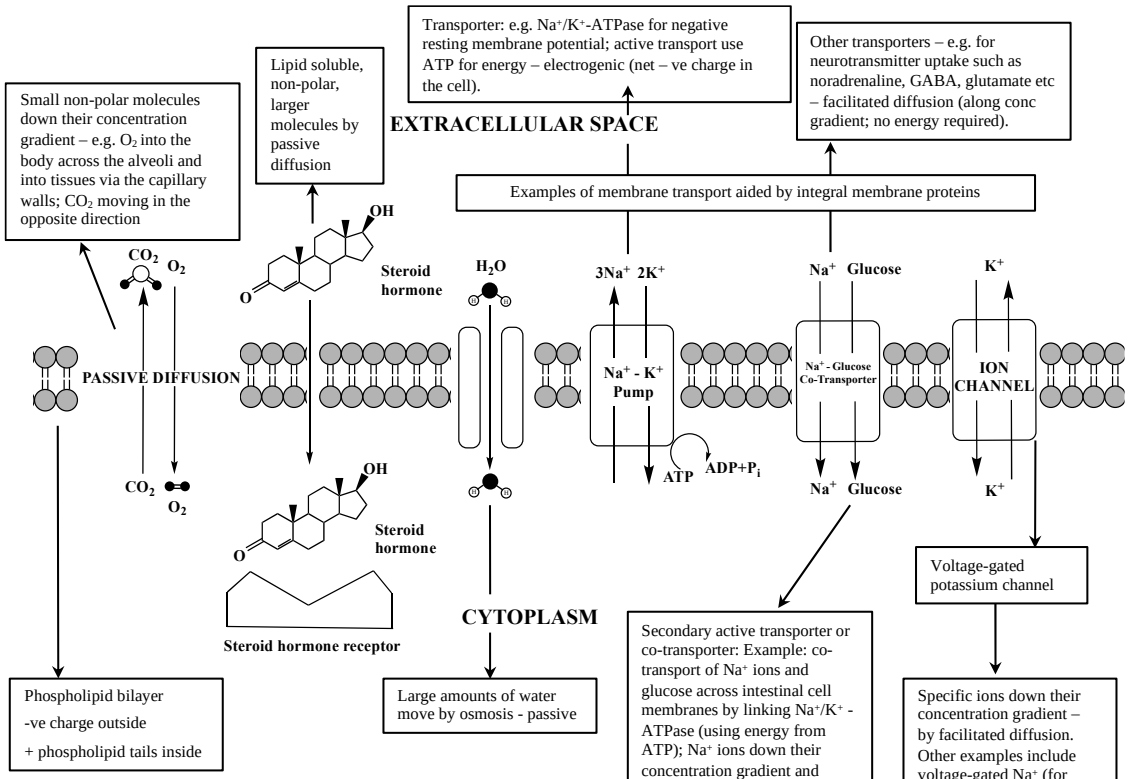
- The bilayer plasma membrane consists of non-polar phospholipid tails inwards and negatively charged phosphate groups oriented towards the extracellular space and the cytosol. A range of processes are available to allow passage of different types of molecules across the selectively permeable cell membranes.
- Small non-polar molecules can cross the cell membrane by passive diffusion, down their concentration gradient, because they are sufficiently lipid soluble to dissolve in the phospholipid part of the cell membrane. A large surface area and thin diffusion distances will maximise diffusion. Example: O_2 transfer across the alveoli from inspired air and into the pulmonary capillaries and also into tissues via the capillary walls in the systemic circulation; CO_2 moving in the opposite direction in both locations.
- Larger lipid soluble, non-polar molecules also cross the cell membrane by passive diffusion – Example: steroid hormones are sufficiently lipid soluble to cross the cell membrane to reach their intracellular receptors.

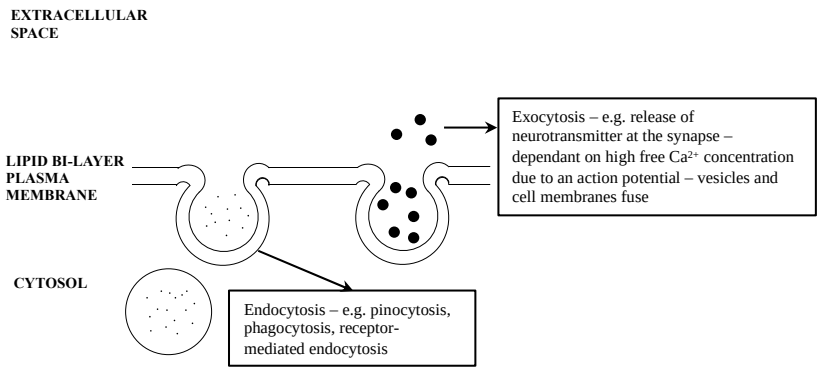
9 cont.

- Integral membrane proteins in the cell membrane interrupt the phospholipid bilayer. These proteins include:
    - Aquaporins, which are channels through which H_2O can cross the cell membrane. Large amounts of water move across cell membranes by osmosis from areas of lower total solute concentration to higher solute concentration, partly by simple diffusion, but mainly by facilitated diffusion using aquaporins.
    - Ion channels which allow specific charged molecules (ions) to move down their concentration gradient by facilitated diffusion, depending on the type of channel. Examples include: voltage-gated Na^+ and K^+ channels which are both important in action potentials in excitable cells – e.g. neurones, muscle cells) and Ca^{2+} channels (e.g. required for neurotransmitter released at the neuronal synapse); ligand-gated Na^+ and Cl^- channels (e.g. direct synaptic transmission at the synapse by these ion-channel linked receptors for very fast neurotransmission or skeletal muscle contraction).
    - Transporters are proteins that can mediate facilitated diffusion (along a concentration gradient; no energy required) or active transport (against a concentration gradient, using ATP to provide the required energy). Examples include: (i) Na^+/K^+-ATPase (important for establishing the resting membrane potential. It involves active transport of 3 Na^+ out and 2 K^+ in, so it is an electrogenic pump resulting in a net negative charge in the cell compared with outside); (ii) transporters for neurotransmitters such as noradrenaline, GABA, glutamate, etc to recycle the transmitters back into the presynaptic neuron after release – usually facilitated diffusion along a concentration gradient.
    - There are also secondary active transport processes or co-transporters: e.g. transport of polar molecules such as sugars into cells against their concentration gradients (and hence requiring energy) using a linked active process. Examples: (i) co-transport of Na^+ ions and glucose across intestinal cell membranes by linking Na^+/K^+-ATPase (using energy from ATP) with co-transport of Na^+ ions down their concentration gradient and glucose molecules against their concentration gradient. (ii) Similarly, in plant cells linking H^+/K^+-ATPase (proton pump) with sucrose transport occurs by an analogous mechanism.
- Processes for bulk transport across cell membranes
    - Endocytosis – e.g. pinocytosis, phagocytosis, receptor-mediated endocytosis – part of the cell membrane is pinched off as a vesicle containing a solution (pinocytosis) or a particle (e.g. a bacterium or other particle; phagocytosis). Sometimes the process is controlled by a receptor.

Exocytosis – the reverse of the above, with the vesicle and cell membranes diffusing (after an influx of Ca^{2+} ions) – e.g. release of neurotransmitter at the synapse.

10


Transporter: e.g. Na+/K+-ATPase for negative resting membrane potential; active transport use ATP for energy – electrogenic (net – ve charge in the cell).
Other transporters – e.g. for neurotransmitter uptake such as noradrenaline, GABA, glutamate etc – facilitated diffusion (along conc gradient; no energy required).
Lipid soluble, non-polar, larger molecules by passive diffusion
Small non-polar molecules down their concentration gradient – e.g. O2 into the body across the alveoli and into tissues via the capillary walls; CO2 moving in the opposite direction
EXTRACELLULAR SPACE
Examples of membrane transport aided by integral membrane proteins
OH
O
Steroid hormone
CO2
O2
H2O
3Na+ 2K+
Na+ Glucose
K+
PASSIVE DIFFUSION
Na+ - K+ Pump
Na+ - Glucose Co-Transporter
ION CHANNEL
ATP
ADP+Pi
Steroid hormone receptor
CYTOPLASM
Voltage-gated potassium channel
Phospholipid bilayer
-ve charge outside
+ phospholipid tails inside
Large amounts of water move by osmosis - passive
Secondary active transporter or co-transporter: Example: co-transport of Na+ ions and glucose across intestinal cell membranes by linking Na+/K+ - ATPase (using energy from ATP); Na+ ions down their concentration gradient and glucose molecules against their concentration gradient. Same in plant cells for linking H+/K+ - ATPase (proton pump) with sucrose transport
Specific ions down their concentration gradient – by facilitated diffusion. Other examples include voltage-gated Na+ (for action potentials in excitable cells– e.g. neurones, muscle cells) and v-g Ca2+ channels (neurotransmitter released at the neuronal synapse); ligand-gated Na+ and Cl- channels (e.g. direct synaptic transmission at the synapse by very fast ion-channel linked receptors in nerves and skeletal muscle).


EXTRACELLULAR SPACE
LIPID BI-LAYER PLASMA MEMBRANE
CYTOSOL
Exocytosis – e.g. release of neurotransmitter at the synapse – dependant on high free Ca2+ concentration due to an action potential – vesicles and cell membranes fuse
Endocytosis – e.g. pinocytosis, phagocytosis, receptor-mediated endocytosis