Bulk transport

Endocytosis and exocytosis. Phagocytosis, pinocytosis, and receptor-mediated endocytosis.

Introduction

Imagine you are a macrophage: a merciless white blood cell that stalks, amoeba-like, through the tissues of the body, looking for pathogens, dead and dying cells, and other undesirables. When you encounter one of these, your task is not just to destroy it, but to *devour it whole*. (Chomp!)

This complete annihilation may seem a bit over the top, but it serves two useful purposes. First, it recovers valuable macromolecules for the body's use. Second, in the case of foreign pathogens, it allows the macrophage to present fragments of the pathogen on its surface. This display alerts other immune cells that the pathogen is present and triggers an immune response.

Let's take a step back, though. How does a macrophage "eat" a pathogen or a piece of cellular debris? In the past few sections, we've talked about ways that ions and small molecules, such as sugars and amino acids, can enter and exit the cell via channels and transporters. Channels and carrier proteins are great for letting specific small molecules cross the membrane, but they are too small (and too picky about what they transport) to let a cell take up something like an entire bacterium.

Instead, cells need **bulk transport mechanisms**, in which large particles (or large quantities of smaller particles) are moved across the cell membrane. These mechanisms involve enclosing the substances to be transported in their own small globes of membrane, which can then bud from or fuse with the membrane to move the substance across. For instance, a macrophage engulfs its pathogen dinner by extending membrane "arms" around it and enclosing it in a sphere of membrane called a food vacuole (where it is later digested).

Macrophages provide a dramatic example of bulk transport, and the majority of cells in your body don't engulf whole microorganisms. However, most cells do have bulk transport mechanisms of some kind. These mechanisms allow cells to obtain nutrients from the environment, selectively "grab" certain particles out of the extracellular fluid, or release signalling molecules to communicate with neighbours. Like the active transport processes that move ions and small molecules via carrier proteins, bulk transport is an energy-requiring (and, in fact, energy-intensive) process.

Here, we'll look at the different modes of bulk transport: phagocytosis, pinocytosis, receptor-mediated endocytosis, and exocytosis.

Endocytosis

Endocytosis (*endo* = internal, *cytosis* = transport mechanism) is a general term for the various types of active transport that move particles into a cell by enclosing them in vesicle made out of plasma membrane.

There are variations of endocytosis, but all follow the same basic process. First, the plasma membrane of the cell invaginates (folds inward), forming a pocket around the target particle or

particles. The pocket then pinches off with the help of specialized proteins, leaving the particle trapped in in a newly created vesicle or vacuole inside the cell.

Endocytosis can be further subdivided into the following categories: phagocytosis, pinocytosis, and receptor-mediated endocytosis.

Phagocytosis

Phagocytosis (literally, “cell eating”) is a form of endocytosis in which large particles, such as cells or cellular debris, are transported into the cell. We’ve already seen one example of phagocytosis, because this is the type of endocytosis used by the macrophage in the article opener to engulf a pathogen.

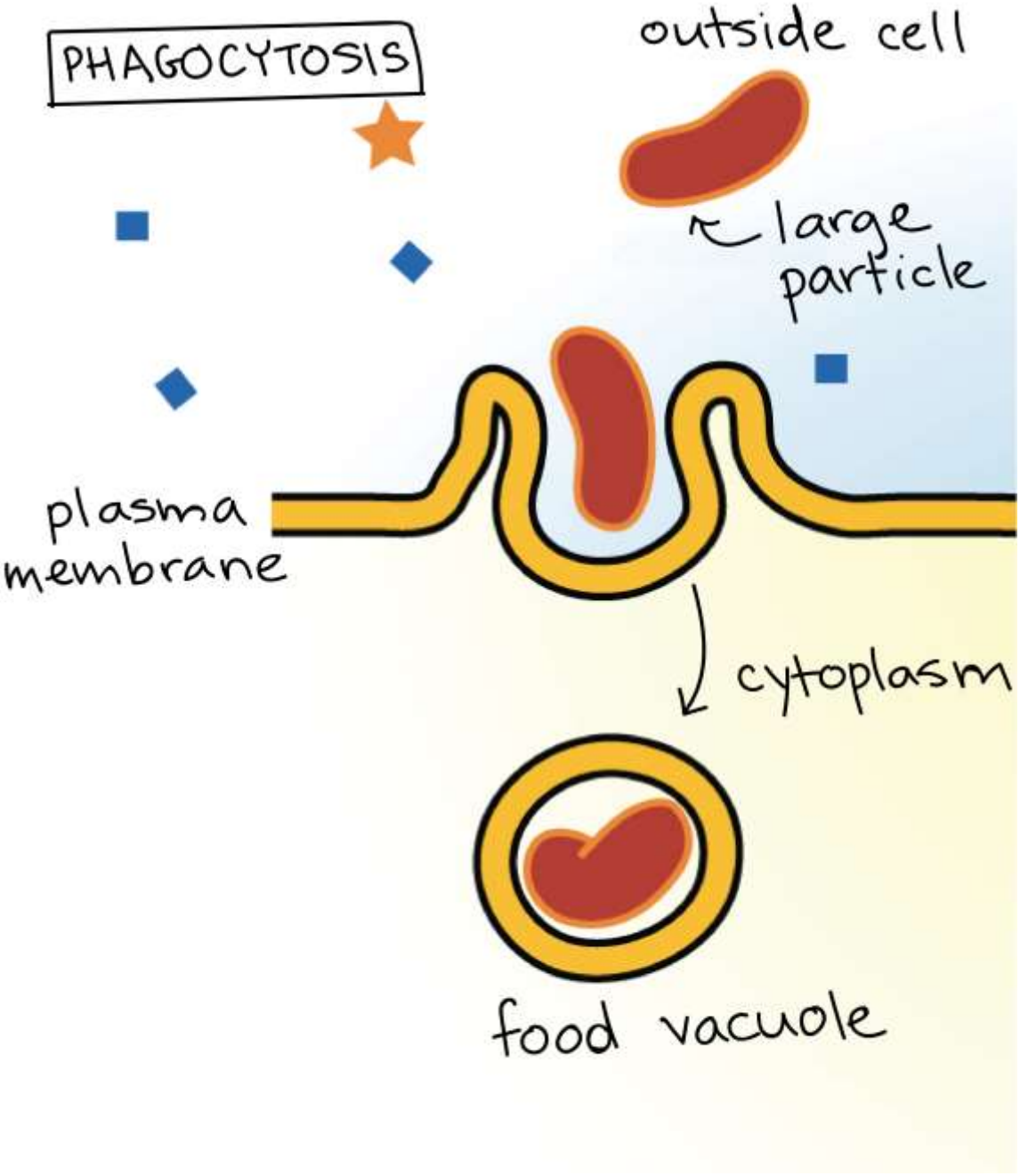


Diagram illustrating phagocytosis.

Image modified from Openstax (original work by Mariana Ruiz Villareal).

Single-celled eukaryotes called amoebas also use phagocytosis to hunt and consume their prey. Or at least, they try to – the image series below shows a frustrated amoeba trying to phagocytise a yeast cell that's just a tiny bit too big.

Once a cell has successfully engulfed a target particle, the pocket containing the particle will pinch off from the membrane, forming a membrane-bound compartment called a food vacuole. The food vacuole will later fuse with an organelle called a lysosome, the "recycling centre" of the cell. Lysosomes have enzymes that break the engulfed particle down into its basic components (such as amino acids and sugars), which can then be used by the cell.

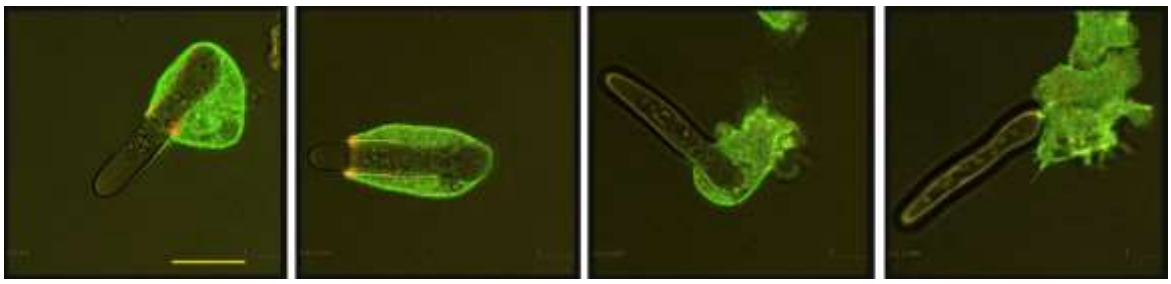
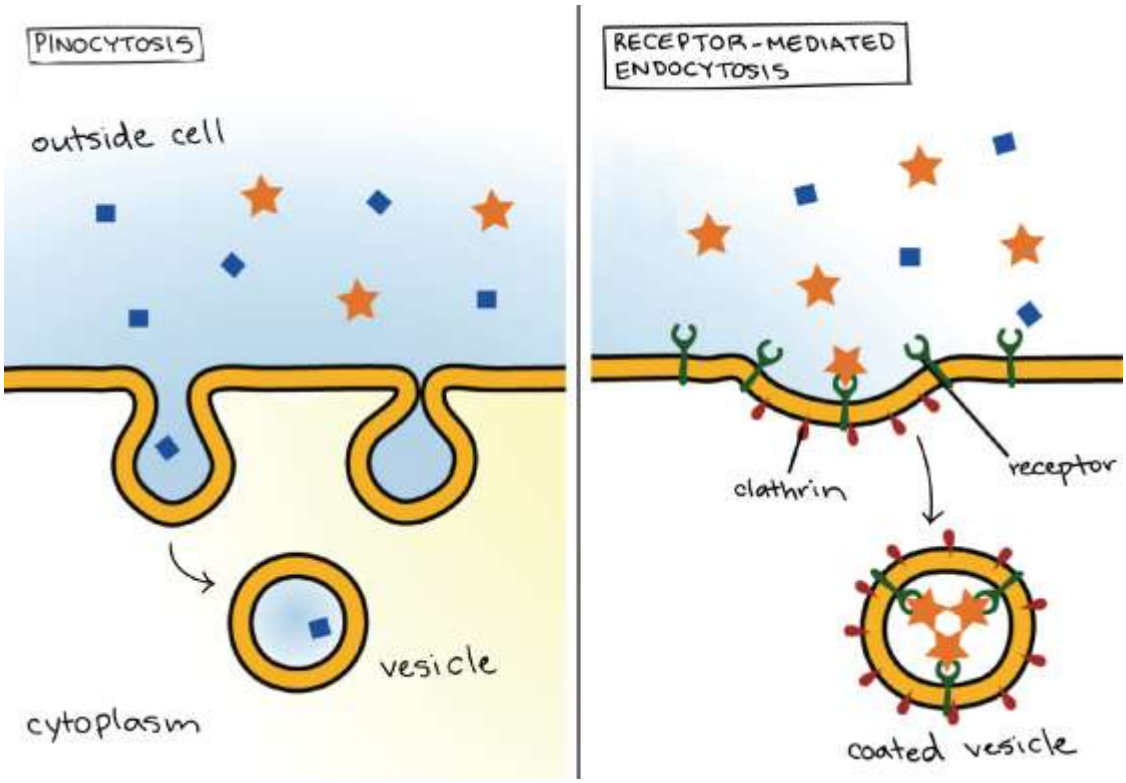


Image credit: series of stills from video by Margaret Clarke[1] (Cell Image Library, CIL: 12654; Clarke et al., 2010).

Pinocytosis

Pinocytosis (literally, "cell drinking") is a form of endocytosis in which a cell takes in small amounts of extracellular fluid. Pinocytosis occurs in many cell types and takes place continuously, with the cell sampling and re-sampling the surrounding fluid to get whatever nutrients and other molecules happen to be present. Pinocytosed material is held in small vesicles, much smaller than the large food vacuole produced by phagocytosis.



Diagrams depicting pinocytosis (left) and receptor-mediated endocytosis (right).

Images modified from OpenStax Biology (original work by Mariana Ruiz Villareal).

Receptor-mediated endocytosis

Receptor-mediated endocytosis is a form of endocytosis in which receptor proteins on the cell surface are used to capture a specific target molecule. The receptors, which are trans-membrane proteins, cluster in regions of the plasma membrane known as coated pits. This name comes from a layer of proteins, called coat proteins, that are found on the cytoplasmic side of the pit. Clathrin, shown in the diagram above, is the best-studied coat protein[2].

When the receptors bind to their specific target molecule, endocytosis is triggered, and the receptors and their attached molecules are taken into the cell in a vesicle. The coat proteins participate in this process by giving the vesicle its rounded shape and helping it bud off from the membrane. Receptor-mediated endocytosis allows cells to take up large amounts of molecules that are relatively rare (present in low concentrations) in the extracellular fluid[2,3].

Although receptor-mediated endocytosis is intended to bring useful substances into the cell, other, less friendly particles may gain entry by the same route. Flu viruses, diphtheria, and cholera toxin all use receptor-mediated endocytosis pathways to gain entry into cells.

Suppose a certain type of molecule were removed from the blood by receptor-mediated endocytosis. What would happen if the receptor protein for that molecule were missing or defective?

The target molecule would no longer be pulled out of the blood, so it might start building up to abnormally high levels. In fact, this is exactly what happens in the disease known as familial hypercholesterolemia.

In a normal person, the form of cholesterol called low-density lipoprotein or LDL ("bad" cholesterol) is removed from the blood by receptor-mediated endocytosis. In people who have familial hypercholesterolemia, the LDL receptors don't work right or may be missing entirely. People with this condition can have life-threateningly high levels of cholesterol in their blood because their cells cannot remove LDL particles from the bloodstream.

Exocytosis

Cells must take in certain molecules, such as nutrients, but they also need to release other molecules, such as signalling proteins and waste products, to the outside environment. **Exocytosis** (*exo* = external, *cytosis* = transport mechanism) is a form of bulk transport in which materials are transported from the inside to the outside of the cell in membrane-bound vesicles that fuse with the plasma membrane.

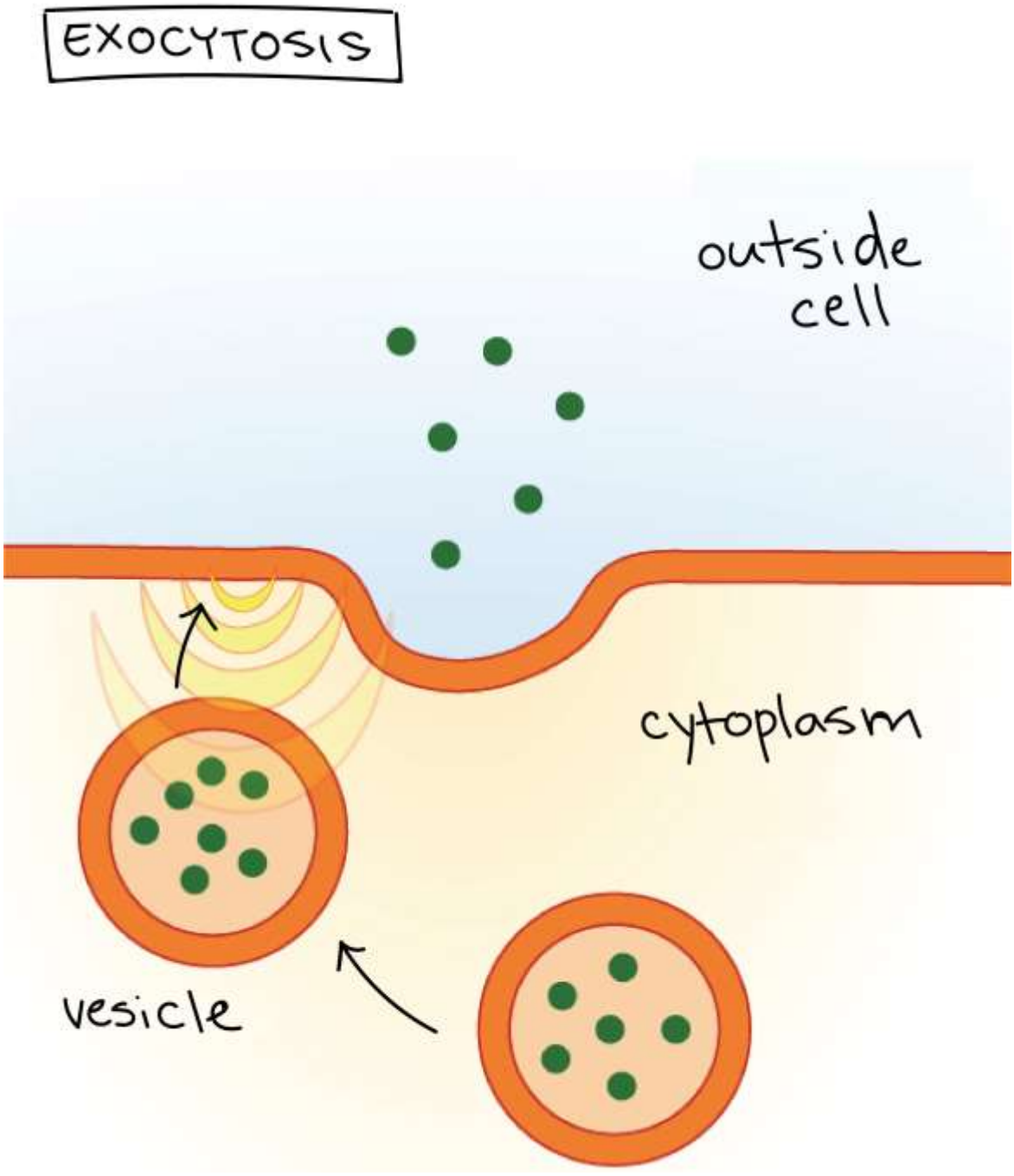


Diagram illustrating the process of exocytosis.

Image modified from OpenStax Biology (original work by Mariana Ruiz Villareal).

Some of these vesicles come from the Golgi apparatus and contain proteins made specifically by the cell for release outside, such as signalling molecules. Other vesicles contain wastes that the cell needs to dispose of, such as the leftovers that remain after a phagocytised particle has been digested.

These vesicles are transported to the edge of the cell, where they can fuse with the plasma membrane and release their contents into the extracellular space. Some vesicles fuse completely with the membrane and are incorporated into it, while others follow the “kiss-and-run” model,

fusing just enough to release their contents (“kissing” the membrane) before pinching off again and returning to the cell interior[4].