What role does the cell membrane play in the body’s response to caffeine?

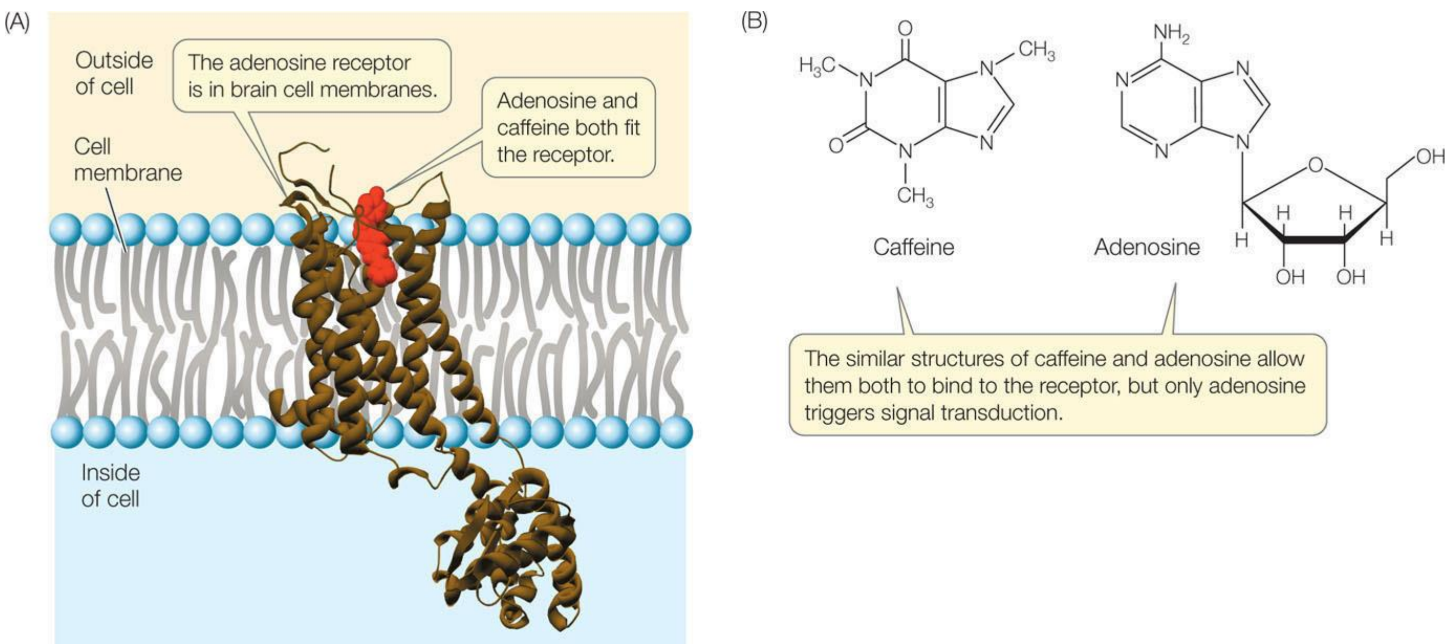
Caffeine has many effects on the body, but the most noticeable is that it keeps us awake. The caffeine molecule is somewhat larger and polar, and it is unlikely to diffuse through the nonpolar lipids of the cell membrane. Instead, it binds to receptors on the surfaces of nerve cells in the brain.

The nucleoside adenosine (attached to a 5-carbon sugar) accumulates in the brain when a person is under stress or has prolonged mental activity. When it binds to a specific receptor in the brain, adenosine sets in motion a signal transduction pathway that results in reduced brain activity, which actually means drowsiness. This membrane-associated signaling by adenosine has evolved as a protective mechanism against the adverse effects of stress.

Caffeine has a three-dimensional structure similar to that of adenosine and is able to bind to the adenosine receptor. Because its binding does not activate the receptor, caffeine functions as an antagonist of adenosine signaling, which results in the brain staying active and the person remains alert. With the caffeine molecule in place, adenosine is not able to bind and activate the receptor. The more caffeine in the system, the more receptors become blocked by caffeine molecules.

The interaction between a ligand and its receptor is reversible and noncovalent. In time, after drinking coffee or tea, the caffeine molecules disconnect from the adenosine receptors in the brain and allow for the adenosine molecules to bind once again and activate drowsiness.

In addition to competing with adenosine for a membrane receptor, caffeine blocks the enzyme cAMP phosphodiesterase. This enzyme acts in signal transduction to break down the second messenger cAMP. Can you explain how caffeine augments the fight-or-flight response, which includes an increase in blood sugar and increased heartrate?



5.19: Data from PDB 3EML. V. P. Jaakola et al., 2008. *Science* 322: 1211.

Hillis, D. Principles of Life (2015). Sinauer Associates.