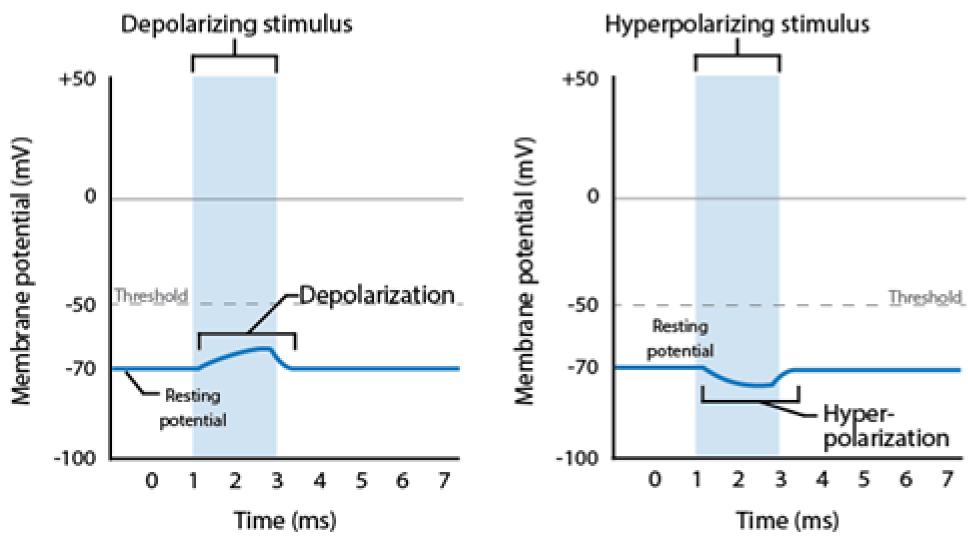
1.3.3

Graded Potential

Because we are dealing with charge differences and electrical currents, we use some unique terms to describe certain states of the membrane. At rest, the membrane is in a **polarized** state—polarized because of charge separation caused by the permeabilities and gradients of different ions. At steady state equilibrium, this polarized state is referred to as the **resting membrane potential**. As already emphasized, the inside of the cell membrane will be negative in relation to the outside of the membrane. We can show this graphically by using the units of mV on the y-axis and time on the x-axis (see figure below). Thus, any change in the membrane toward zero will be termed a **depolarization**. Note the prefix *de-,* meaning "away from." Any change in the membrane that moves back toward the resting potential would be a **repolarization** with the prefix *re-,* meaning "again." A change resulting in the movement away from the resting potential, but in a more negative direction, away from zero, will be termed **hyperpolarization** with the prefix *hyper,* meaning "excessive."



Graphical representation of graded potentials. On the left, it shows electrical movement away from rest or the "polarized state" and toward zero is called "depolarization". The graded potential returns to rest or polarized state again but never gets high enough to reach threshold. The representation on the right shows electrical movement away from rest. This movement is called hyperpolarization, and we see that hyperpolarization moves farther from the threshold rather than towards it.

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Now for some application. Opening channels for Na^+ or Ca2+ would cause a depolarization, while opening channels for K^+ or Cl^- (sometimes) would cause a repolarization or even a hyperpolarization. These changes in the resting potential come in two forms, **graded potentials** or **action potentials.** Graded potentials always precede action potentials, so we will address them first.

With graded potentials, the magnitude of the response is proportional to the strength of the stimulus. Hence, a strong stimulus might result in a 10 mV change in the membrane potentials, while a weaker stimulus may produce only a 5 mV change. Graded potentials result from the opening of mechanical or ligand-gated channels. Graded potentials can be summed (added) on top of one another to increase the change. Stated another way, if a stimulus is repeated over and over, it can result in an even larger deviation toward zero, from rest or away from rest to more negative values. This is the reason why the changes are called *graded*. The amplitude (change in the membrane potential) is determined by the number of channels activated, which, in turn, is determined by the number of stimuli, such as the concentration of chemicals or the number of channels opened. However, if a change in the depolarizing direction is really strong, the change may exceed the threshold for the cell and the graded potential changes into an action potential. Another characteristic of graded potentials is that they are conducted only short distances. As the signal spreads from the site of stimulation, it loses strength and eventually dies out completely; think of the ripples that spread in a pond when you throw a rock in.

For this reason, these signals are also sometimes referred to as **local potentials**, meaning that they happen locally but do not travel long distances. As stated, graded potentials can be induced intentionally by ligands or mechanical stimuli. In addition, graded potentials can occur because of changes in extracellular ion concentrations independent of ligands or mechanical stimuli. This is because protein voltage-gated channels are sensitive to the distribution of charge along the membrane. For example, the voltage-gated Na^+ channel gating mechanism is sensitive to the extracellular concentration of Ca^{2+}. If the extracellular Ca^{2+} ion concentration decreases below normal values (**hypocalcemia**) the gating mechanism will become hypersensitive, even opening spontaneously. In contrast, extracellular Ca^{2+} concentrations that increase above normal (**hypercalcemia**) will desensitize the gating mechanism, making the channel more difficult to open (effectively moving the threshold value further away from RMP). Thus, the Ca^{2+} ion has a direct effect on the Na^+ channel gating mechanism.

An indirect effect (not directly binding to the gating mechanism of the Na^+ channel) is observed with extracellular K^+ ion concentrations. Since K^+ is the main driver for membrane charge separation, any change in the extracellular concentration of K^+ will affect the K^+ concentration gradient such that the resting membrane potential will shift closer or further away from threshold. **Hyperkalemia** (extracellular K^+ above normal) will cause the RMP to be closer to threshold because of the weakened gradient (less K^+ leaves). **Hypokalemia** (extracellular K^+ below normal) will cause the RMP to move further away from threshold because of the increased gradient (more K^+ leaves). Changes in the membrane potential or the gating mechanisms of Na^+ channels can make the graded potential much more likely to cause or prevent an action potential. Thus, monitoring extracellular ion concentrations is important clinically because if the concentrations move outside of normal it can induce hyper excitability or hypo excitability in both muscle and neuronal cells.