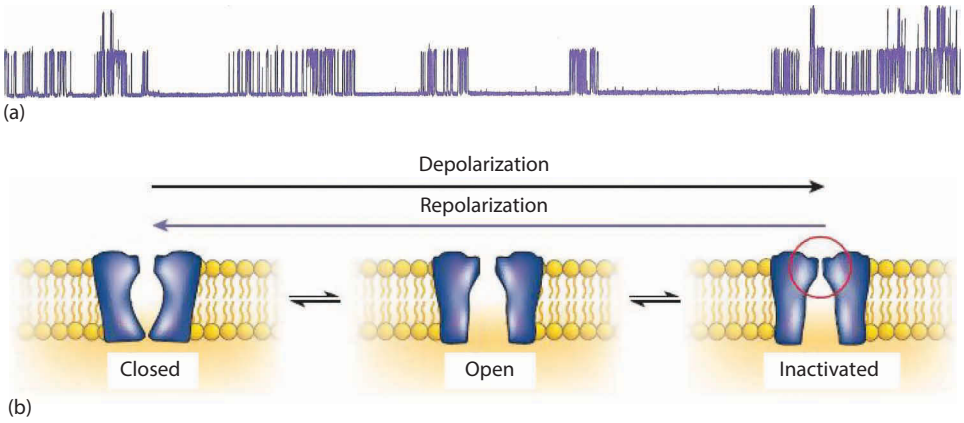

FIGURE 13.2 (a) Single channel recording of BK-type potassium channel. The baseline shows the closed state and the upward deflections are opening of single channels. The current through the channels is about 20 pA. (b) Opening, closing, and inactivation of ion channel. (From Sanguinetti, M.C. and Tristani-Firouzi, M., *Nature*, 440, 463, 2006.)

Patch–clamp studies of single ion channels have shown that the duration of channel opening ranges from a few μs to several hundred ms when exposed to a ligand or a voltage change (Figure 13.2). In the absence of a stimulus they either open less frequently or stay closed. The opening and closing of ion channels is called gating, and at the single channel level it is described by the distribution of open and closed times. Currents through all ion channels in the cell membrane can also be measured by ripping a hole in the cell which makes it possible to voltage-clamp the whole cell. This whole-cell current depicts the sum of hundreds of ion channels, and the kinetics of the current reflects the average open or closed times of the channels.

The gating is a dynamic process reflecting structural changes in the channel protein. The opening of a channel is preceded by conformational changes. Once the channel goes into the open state, the electrical current carried by ions through the channel can be recorded with a resolution of about 1 pA (10^{-12} A). The activation of single channels is a discrete event, and as seen from the recordings in Figure 13.2 the ion channels are either fully closed or fully open, although some channel types do show subconductance levels. Thus, it is possible to follow the movements between the two conformational states with an amazing time and current resolution.

The various ion channel types gate differently: some channels open only transiently whereas others stay open as long as the stimulus exists. Stimuli for ion channel activation are either (1) a change in the membrane potential, (2) a change in the concentration of extracellular ligands (neurotransmitters), (3) a change in the concentration of intracellular ligands (Ca^{2+}, H^+, cyclic nucleotides, or G-protein subunits), or (4) mechanical stimulation (e.g., stretch). Once the channels are exposed to the stimuli they open or activate, and when the stimulus is removed, the channels close in an opposite process called deactivation. A number of channel types do however also close in the presence of the stimulus. It is a general physiological phenomenon that continued stimulation of a signal process results in a decreasing output. This functional closure of ion channels in the presence of a stimulus is called inactivation and can occur either by parts of the channel protein plugging the open pore after a short delay, by collapse of the pore, or by decreased coupling between ligand binding and pore domains (Figure 13.2b).

13.1.4 Molecular Structures of Ion Channels

Ion channels are present in all cells, and they have been extensively characterized with respect to gating kinetics, voltage and ligand sensitivity, pharmacology, and other parameters. In addition, many ion channel types exhibit high affinity (pM or nM) to a number of toxins derived from scorpions,