carried primarily by relatively slow, inward calcium currents instead of by fast sodium currents as observed in most other depolarizing cell types (e.g., nerve and muscle cell). Spontaneous depolarization (Phase 4) is due to a small increase in intracellular calcium, a decrease in intracellular potassium and a slow inward Na\(^+\) current. Once this spontaneous depolarization reaches a threshold, a new action potential is triggered. The rate of Phase 0 depolarization is much slower than that found in other cardiac cells (see Fig. 1.1).

An understanding of action potentials helps explain the effects of various stimuli on heart rate. Sympathetic activation releases norepinephrine which increases the slope of Phase 4 and thereby increases heart rate. Parasympathetic activation releases acetylcholine which decreases the slope of Phase 4 and hyperpolarizes the cell which in turn increases the time to reach threshold voltage. The effect of profound elevation in serum potassium concentrations can be predicted based on the action potential: severe hyperkalemia causes sinus arrest.

Non-pacemaker cells can change into pacemaker cells under certain conditions. For example, if a cell

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**Figure 1.1** Action potentials from different areas of the heart. The phases of the action potential are labeled.
becomes hypoxic, the membrane depolarizes which closes fast Na⁺ channels. When this occurs, action potentials can still be elicited but the inward current will be carried by Ca²⁺ (slow inward channels). These action potentials are similar to those found in pacemaker cells and display spontaneous depolarization and automaticity.

**Non-pacemaker cells**

The concentration of potassium ions inside a cardiac muscle cell greatly exceeds the concentration outside the cell. The reverse situation exists for sodium ions. The relative concentration of ions (and negatively charged intracellular proteins) determines membrane potential. The resting membrane potential (Phase 4; Fig. 1.2) in non-pacemaker cells remains near the equilibrium potential. When these cells are rapidly depolarized by a conducted action potential from another cell, this causes a transient increase in fast sodium channel conductance and a decrease in potassium influx (Phase 0). Subsequent repolarization is a three-phase process. Phase 1 is caused by the opening of potassium channels. Because of a (relatively) slow increase in calcium, repolarization reaches a plateau phase (Phase 2). Phase 3 occurs when potassium influx increases and calcium influx decreases.

The effective refractory period (ERP) refers to the time during Phases 0, 1, 2 and part of Phase 3, when the cell will not respond to action potentials transmitted from other cells. The ERP acts as a protective mechanism by preventing chaotic, irregular cellular depolarization. The length of the refractory period limits the frequency of action potentials (and therefore contractions) that can be generated by the heart.