

FIGURE 1.1 Folding and aggregation: two sides of the same coin. The multitude of conformational states available to a polypeptide chain is described as a combined energy landscape for protein folding (light gray) and aggregation (dark gray). In the folding landscape the intermediate, nativelylike, and fully native states are reported as different minima. The aggregation landscape shows mature amyloid fibrils as well as other ordered or amorphous aggregates. The unfolded, intermediate, and nativelylike states shown in the folding landscape are able to cross the barrier and form aggregates via multiple pathways. (Adapted from [30], with permission.)

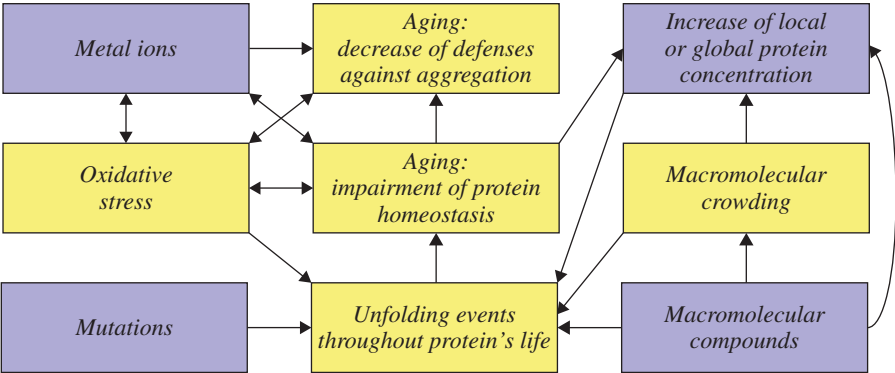


FIGURE 1.2 Some of the factors that are thought to influence the formation of misfolded aggregates in vivo. Some act directly on the protein undergoing aggregation, and their effects can be monitored and studied in vitro (dark gray boxes). Others act at the organism level, involving a further level of complexity (light gray boxes). Arrows indicate links between the various factors.