

FIGURE 5.1 (A) Natively unfolded proteins or peptides can gain different secondary structure upon interaction with a charged or hydrophobic surface; in most cases, in the presence of phospholipid surfaces, β -sheet structure, followed by oligomerization, predominates when the peptide molecules remain at the surface, whereas monomeric α -helix results when the peptide penetrates the hydrophobic interior. (B) In close proximity to a charged or hydrophobic surface, folded proteins can undergo partial unfolding following weakening of intramolecular electrostatic or hydrophobic interactions; under these conditions, nonnative intermolecular interactions are favored with possible amyloid nucleation. In the case of phospholipid bilayers or biological membranes, partial unfolding can favor penetration into the hydrophobic interior, where secondary interactions are strengthened.

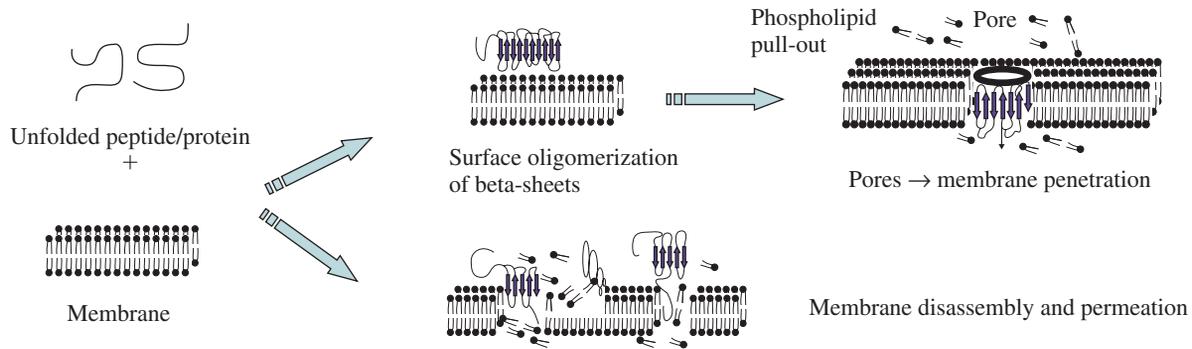


FIGURE 5.2 Protein–peptide oligomerization on a phospholipid bilayer or a cell membrane results in membrane permeabilization. This can follow peptide assembly onto the membrane into β -sheets subsequently organizing inside the membrane into amyloid pores; permeabilization can also be the result of preformed amyloid pore interaction with the membrane, or membrane disassembly by peptide monomers or oligomers. These possibilities could be not mutually exclusive. Most of the data on membrane permeabilization in cells exposed to amyloids highlight cytosolic-free Ca^{2+} increase.