

FIGURE 3.1 Aggregation competes with productive protein folding. Aggregation of nonnative protein chains as a side reaction of productive folding in the crowded environment of the cell. Enhancement of aggregation and chain compaction by macromolecular crowding and effects of chaperones are indicated. U, unfolded protein chain released from ribosome; I, partially folded intermediate; N, native, folded protein. Crowding is also predicted to enhance the formation of amyloid fibrils. (Adapted from [6], with permission of Science AAAS.)

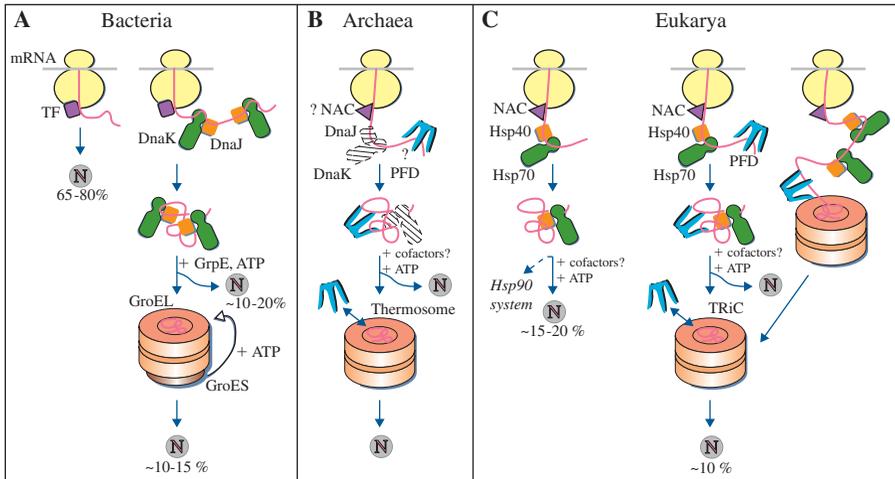


FIGURE 3.2 Chaperone pathways of protein folding in the cytosol. Models for the chaperone-assisted folding of newly synthesized polypeptides in the cytosol. (A) Bacteria. TF, trigger factor; N, native protein. Nascent chains probably interact generally with TF, and most small proteins (65 to 80% of total) may fold rapidly upon synthesis without further assistance. Longer chains (10 to 20% of total) interact subsequently with DnaK and DnaJ and fold upon one or several cycles of ATP-dependent binding and release. About 10 to 15% of chains transit the chaperonin system (GroEL and GroES) for folding. GroEL does not bind to nascent chains and is thus likely to receive a substantial fraction of its substrates after their interaction with DnaK. (B) Archaea. PFD, prefoldin; NAC, nascent chain-associated complex. Only some archaeal species contain DnaK/DnaJ. (C) Eukarya (the example of the mammalian cytosol). Like TF, NAC probably interacts generally with nascent chains. The majority of small chains may fold upon ribosome release without further assistance. About 15 to 20% of chains reach their native states in a reaction assisted by Hsp70 and Hsp40, and a fraction of these must be transferred to Hsp90 for folding. About 10% of chains are co- or posttranslationally passed on to the chaperonin TRiC in a reaction mediated by Hsp70 and PFD. (Adapted from [6], with permission of Science AAAS).

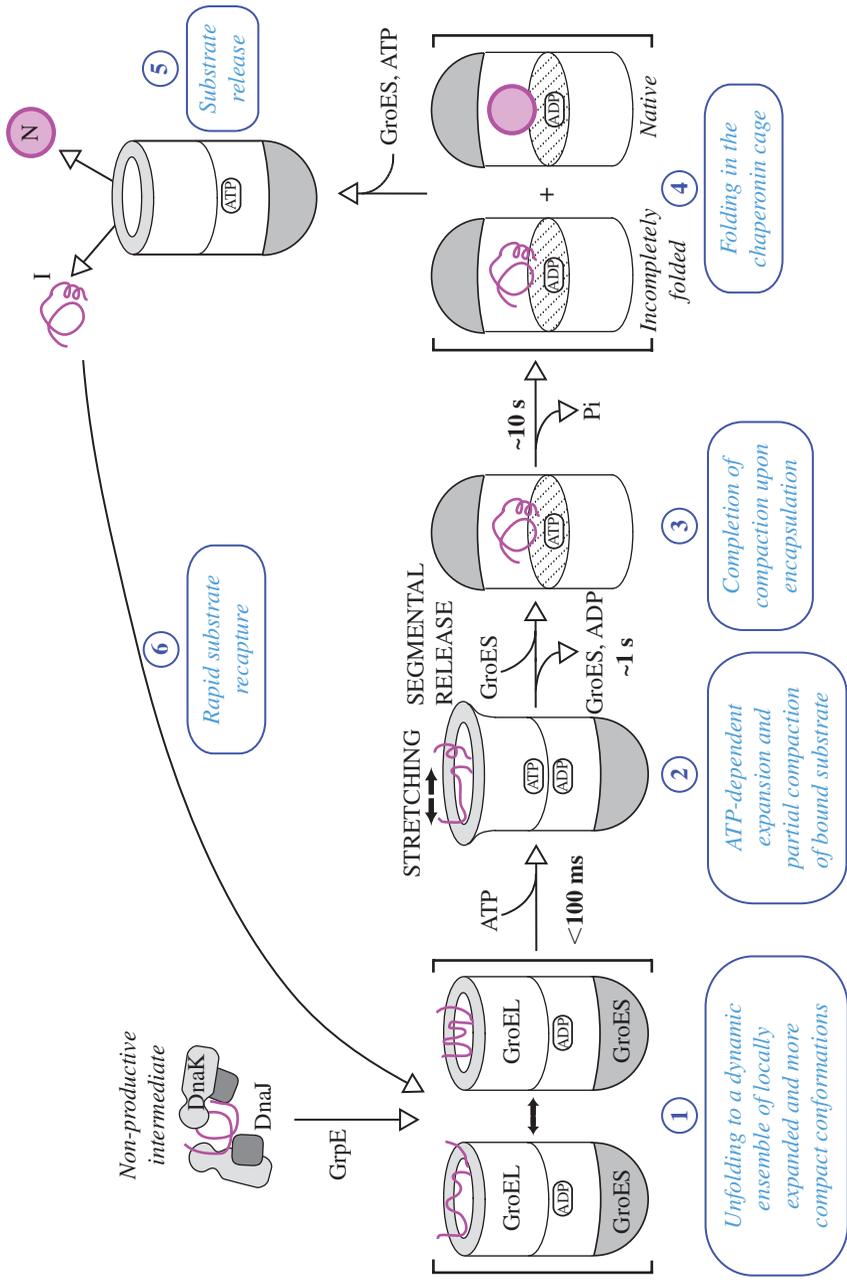


FIGURE 3.4 Protein folding with the GroEL–GroES chaperonin system. Working model summarizing the conformational changes in a substrate protein upon transfer from DnaK–DnaJ (Hsp70 system) to GroEL and during GroEL–GroES-mediated folding. Note that binding of a second substrate molecule to the open ring of GroEL in steps 4 and 5 is omitted for simplicity. N, native state; I, folding intermediate. (From [81], with permission of Elsevier).