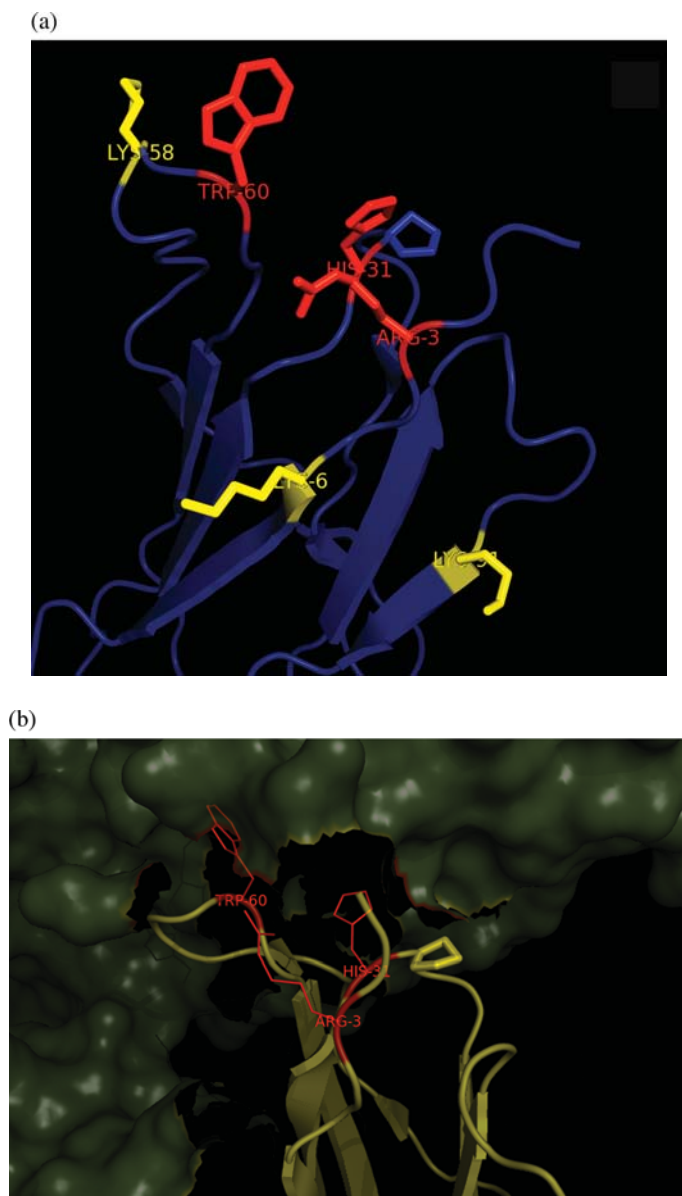
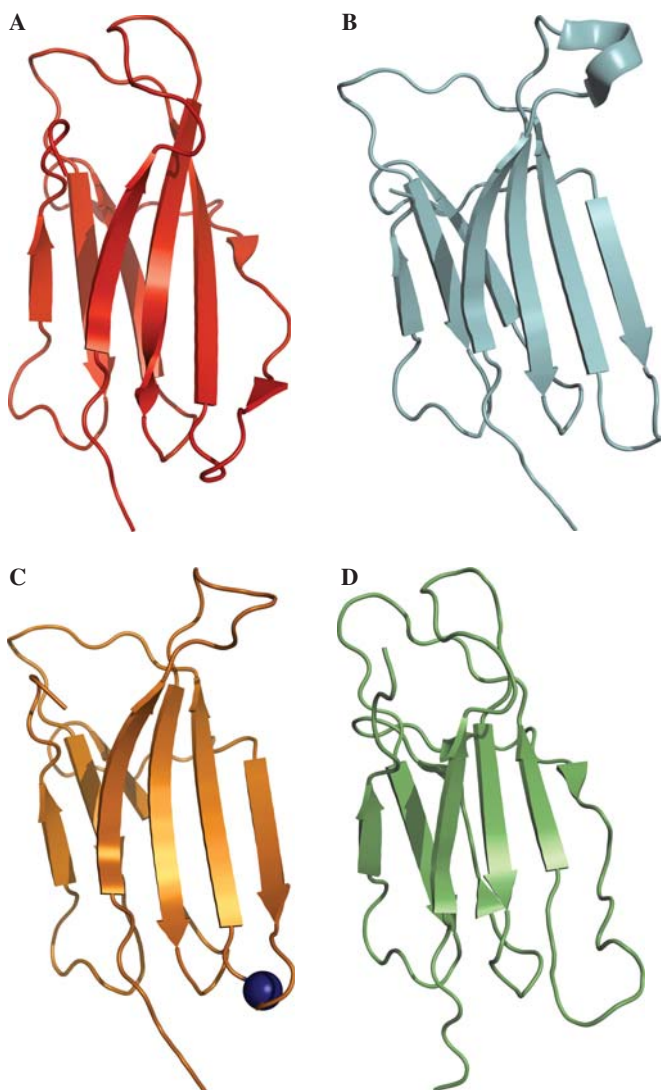


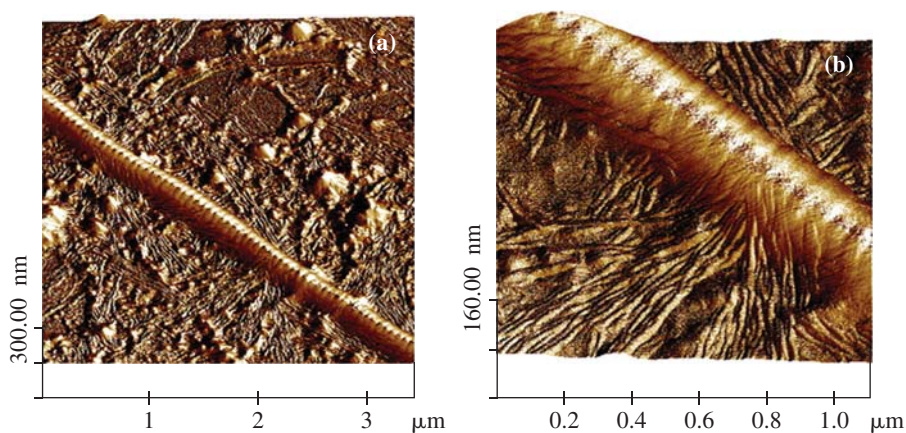
**FIGURE 38.1** Wild-type  $\beta_2m$  structure in MHC-I [20]. The strand segments are colored in yellow, the loop and bulge segments in green. The van der Waals surface of the molecule is shown in transparency. The strand naming scheme according to this representation is reported.



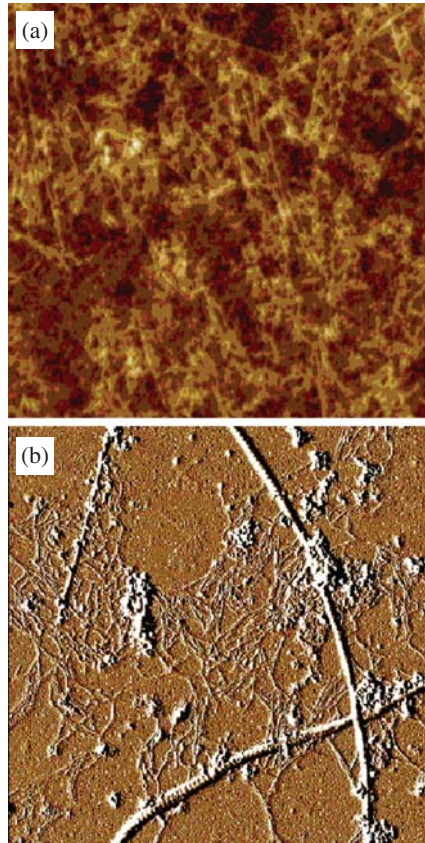
**FIGURE 38.2** (a) View of the functionally relevant apical region in  $\beta_2m$  solution structure. The backbone and side chain of Arg3, His31, and Trp60 are shown. The exposed and positively charged side chains of Lys6, Lys58, and Lys91, along with the corresponding backbone positions, are also shown. The side chain of Pro32 is also drawn. ( From [41].) (b) Same apical region of  $\beta_2m$  in MHC-I with Arg3, His31, and Trp60 highlighted. The heavy-chain binding surface is shown. (From [20].)



**FIGURE 38.3** Comparison between the crystal structures of (a) MHC-I-bound  $\beta_2\text{m}$  [20], (b) isolated  $\beta_2\text{m}$  [60], (c) Trp60Gly  $\beta_2\text{m}$  where the sphere indicates the mutation position [59], and (d) the solution structure of wild-type protein [41].  $\beta_2\text{m}$  strand D (the rightmost strand in all panels) is split into two substrands by a bulge centered at Asp53 in MHC-I (a), but only one of these substrands survives in solution (d). On the other hand, a regular and continuous  $\beta$ -strand D is observed when the protein is crystallized without the heavy chain (b), along with an outward orientation of the AB loop (refer to Fig. 1 for strand naming). Both features also occur in the crystal structure of the Trp60Gly mutant (c), which does not form fibrils when seeded in 20% TFE. Hence, a continuous D strand can not be considered the hallmark of  $\beta_2\text{m}$  fibril-competent conformation [60].



**FIGURE 38.4** Surface plots of a TM-AFM image (height data) of  $\beta_2$ m ex vivo amyloid material obtained from the femoral head of a patient affected by DRA: (a) amyloid fibrils surrounding a collagen fibril; (b) higher-resolution image of a portion of panel (a) showing amyloid fibrils crowding around the collagen fibril. (From [56], with permission.)



**FIGURE 38.5** TM-AFM images of  $\beta_2\text{m}$  incubated at  $37^\circ\text{C}$  and pH 6.4 in the presence of fibrillar collagen and heparin. (a) After 17 hours of incubation, thin filaments are clearly visible on a background of nonfibrillar material. Height data: scan size,  $1.2\text{ }\mu\text{m}$ ,  $Z$  range,  $8.0\text{ nm}$ . (b) Fibril network connecting isolated collagen fibrils, observed after 24 hours of incubation. Nonfibrillar aggregates are also present. Amplitude data: scan size,  $5.7\text{ }\mu\text{m}$ . (From [65], with permission.)