

23. STRUCTURAL ANALYSIS AND CLASSIFICATION

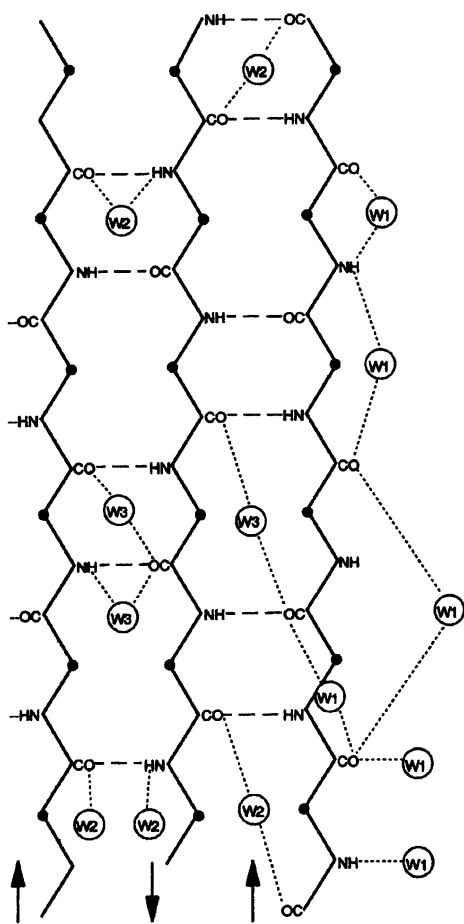


Fig. 23.4.3.3. Diagram of edge (W1), end (W2) and middle (W3) categories of interactions of water molecules with main-chain atoms in antiparallel β -sheets. Reprinted with permission from Thanki *et al.* (1991). Copyright (1991) Academic Press.

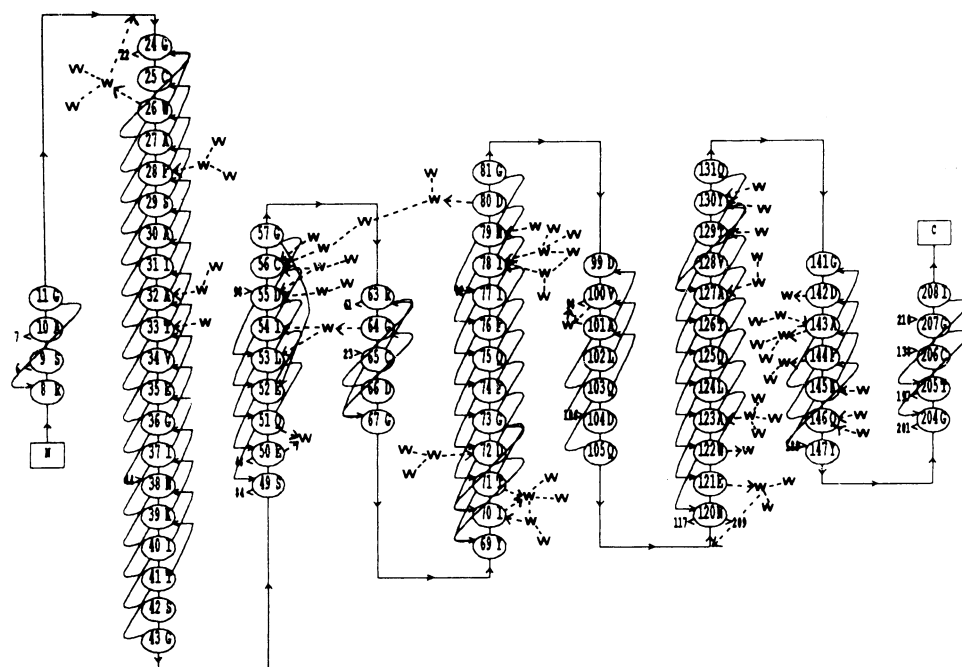


Fig. 23.4.3.4. Diagram of the hydrogen bonds in the α -helical structure in actinidin. Reprinted with permission from Thanki *et al.* (1991). Copyright (1991) Academic Press.

The analysis of main-chain hydration focused separately on hydration of β -sheets, α -helices and turns (Thanki *et al.*, 1991). In general, more water molecules were found to interact with carbonyl oxygens than with amide groups, due primarily to the fact that carbonyl oxygen atoms can accept two hydrogen bonds, whereas amide groups can donate a single one. Thus, free carbonyl oxygen atoms have the potential to interact with two water molecules, whereas those already involved in a secondary-structure interaction with the protein still have a lone pair of electrons that can accept a hydrogen bond from a water molecule. Of the free carbonyl oxygen atoms within secondary-structure elements, 45% of those in α -helices and 68% of those in β -sheets interact with water molecules. Of those that are involved in secondary-structure interactions within the protein, 21% of those in α -helices and 17% of those in β -sheets also interact with solvent. The free amide groups are well hydrated, with 38% of those in α -helices and 54% of those in β -sheets interacting with water molecules. However, virtually none (2% in helices and 6% in sheets) of the amides already involved in secondary-structure hydrogen bonding also interact with a water molecule.

Three types of interactions were observed for water molecules in the context of β -sheets (Fig. 23.4.3.3). Most (68%) of these interactions are with the edge of the β -sheet, in an extension of the secondary structure. The second most prominent type of interaction, comprising 23% of the total, is at the ends of the β -strands with either free amide or carboxyl groups. Finally, only 10% of the water molecules are found to bridge between two strands in the middle of the β -sheet.

Interactions of water molecules with α -helices are also found in three distinct positions relative to the secondary structure (Fig. 23.4.3.4): at the carbonyl terminus of the helix, at the amide terminal end and in the middle. Of those interacting at the carbonyl terminus, 48% interact with the carbonyl oxygen alone, 11% also interact with a nearby main-chain atom and 41% are involved in a water-mediated C cap, bridging a small polar side chain (Ser, Thr, Asp, or Asn) to a free carbonyl group at the end of the helix. Of water molecules interacting at the amide terminus of the helix, 25% interact with free amide groups alone, 45% bridge to local main-chain atoms and many of the remaining mediate in N-cap interactions with small polar side chains such as Ser and Asp.

In general, turns have a high exposure to solvent and therefore are found to be well hydrated. The pattern of hydration varies both with the type of turn and the location of the atoms within the turn. Not surprisingly, there are about twice as many hydrogen bonds to carbonyl groups as there are to amide groups in turns. Although the majority of the water interactions with turns are to single carbonyl oxygen or amide nitrogen atoms, bridging water molecules do appear, especially within more open turns. They occur in a variety of different patterns, bridging between two main-chain atoms in the turn or between a main chain and a small polar side chain.

Clearly, water molecules play a functional role in maintaining the integrity of the secondary-structure elements of proteins. They are often seen to extend α -helices or β -sheets, serving as an interface between these secondary-structure elements and the bulk solvent. Water molecules are also found to mediate the