'face-to-back, up–up' packing. SNQNNF, from the human prion protein, is thus far the only example of a class 2 zipper. In class 4, like class 2, the apposed, interdigitating faces of the sheets differ from each other ('face-to-back'). However, neighbouring sheets of class 4 are oriented with one sheet's edge facing 'up' and its neighbours' edges 'down'. GGVVIA, from the carboxy terminus of amyloid-β, adopts this orientation. The sheets of classes 7 and 8, like those of the 'parallel' classes 1–4, contain β-strands in register, but within each sheet, adjacent strands run in opposite directions. Antiparallel β-sheets in amyloid-like fibrils have been anticipated from previous

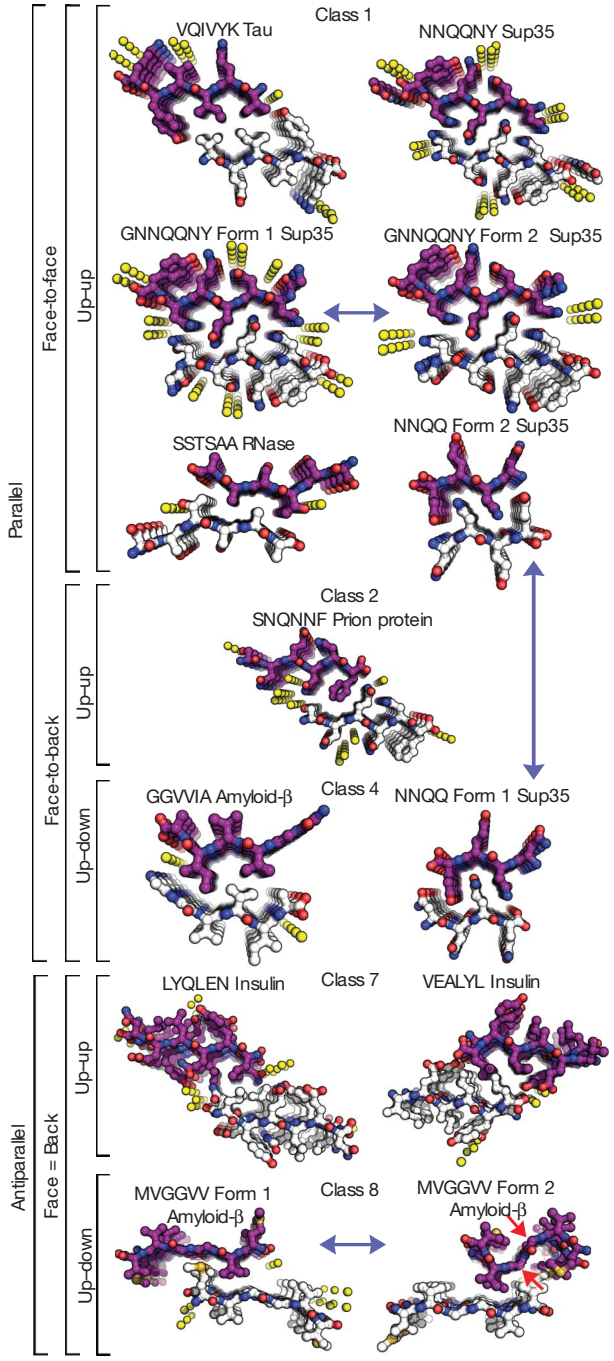

Figure 2 | Thirteen atomic-resolution structures for peptide segments of fibril-forming proteins. See text for details of nomenclature. A two-sheet motif of each structure is depicted in projection down the needle crystal axis, showing only the top members of ~10^5 stacked segments in each crystalline sheet. A dry, steric-zipper interaction is evidenced by the interdigitation of side chains between sheets. Carbon atoms are shown as purple or white, nitrogen as blue, and oxygen as red. Water molecules are shown as yellow spheres. NNQQNY also contains zinc acetate. Zippers are grouped by class (1, 2, 4, 7, 8); see text for details. Previously reported Sup35 zippers[22] belong to class 1. The three pairs of structures related by blue double-headed arrows are polymorphic pairs (forms 1 and 2; see text for details). The red arrows point to the 90° bend in the upper sheet of MVGGVV form 2.

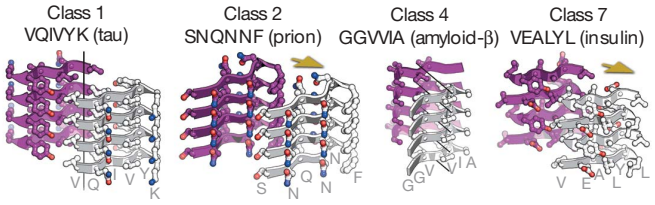

Figure 3 | 3D views of representative steric zipper structures of classes 1, 2, 4 and 7, showing the front sheet in silver and the rear sheet in purple. Oxygen atoms are red; nitrogen atoms are blue. Black lines show crystallographic 2_1 symmetry axes, and the yellow arrows show translational symmetry. The value of the shape complementarity parameter[46], S_C, for GGVVIA ($S_C = 0.92$) is the largest value we have found for any protein interface, consistent with the higher toxicity and lower solubility of amyloid-β(1−42) than (1–40).

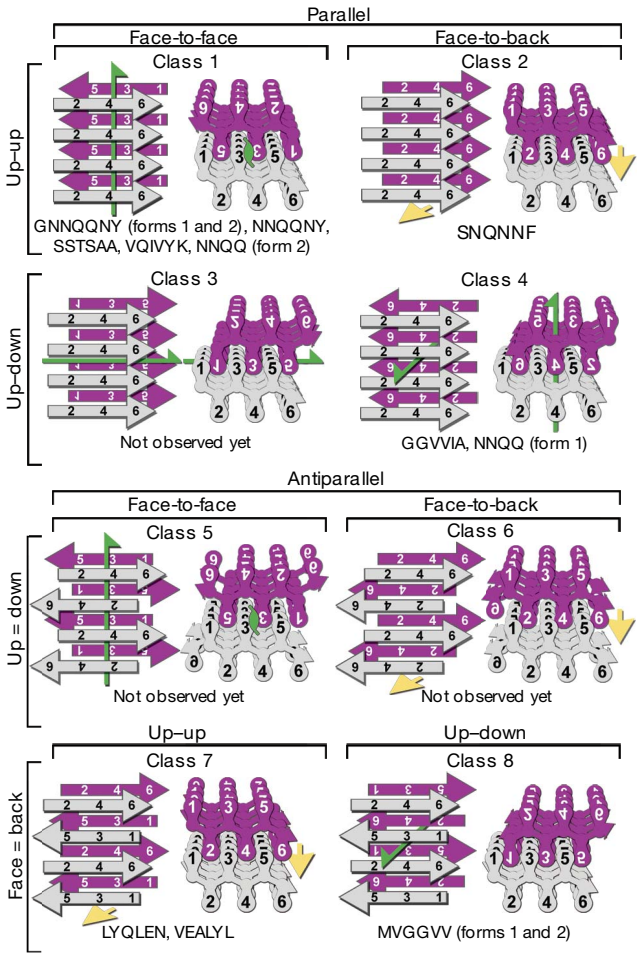

Figure 4 | The eight classes of steric zippers. Two identical sheets can be classified by: the orientation of their faces (either 'face-to-face' or 'face-to-back'), the orientation of their strands (with both sheets having the same edge of the strand 'up', or one 'up' and the other 'down'), and whether the strands within the sheets are parallel or antiparallel. Both side views (left) and top views (right) show which of the six residues of the segment point into the zipper and which point outward. Green arrows show two-fold screw axes, and yellow arrows show translational symmetry. Below each class are listed protein segments that belong to that class.