

BCH222 :: Structure of Biological Macromolecules

alpha / beta Proteins

Assignment: α / β Proteins - Singly-wound Barrels

Reading

Richardson, Anatomy & Taxonomy, parts II.B. β Structure, and III.C. Parallel α / β Domains

Lesk, Branden, and Chothia (1989) Proteins **5**, 139-148
general introduction to singly-wound parallel α / β barrels

Edwards, Sternberg, and Thornton (1987) Protein Engineering **1**, 173-181
families of α / β loops

Graphics assignment

1. Kinemage file [abBarrel.kin](#) (52KB) :

Run through the animation of the triose P isomerase (TIM) barrel in Kin.1, to get a feeling for why it is described as "singly-wound". This is the first such barrel that was found, but by now there are many dozens of them known.

Compare that TIM barrel with the two alpha / beta barrel domains of IGPS-PRAI in Kin.2.

How many beta strands are in each of the barrels? _____, _____, _____

Are all the beta strands connected by +1x crossovers? _____

Does every crossover connection contain a helix? _____

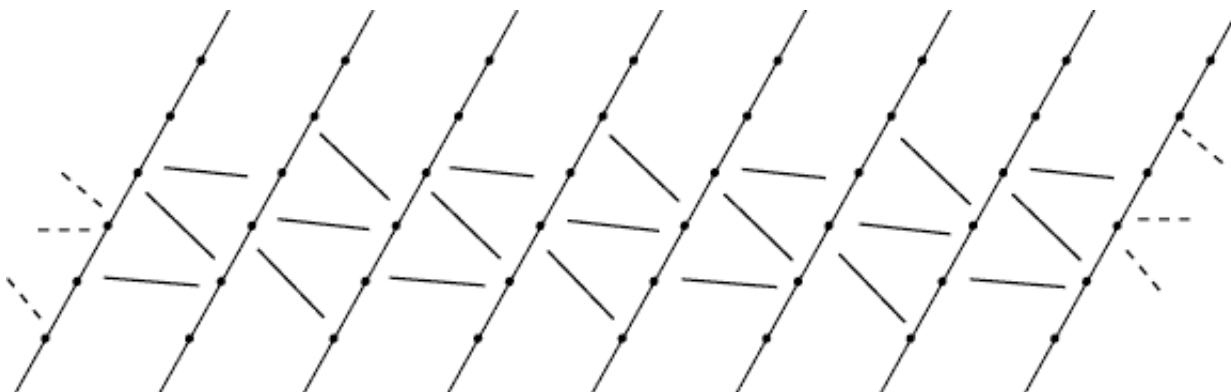
In file abBarrel.kin, kinemage 3 shows the type of interior packing typical of alpha / beta barrels. There are always at least three layers of hydrophobic sidechains, each layer perpendicular to the axis of the barrel, and sometimes there are additional hydrophilic layers on each end, as here.

What 4 residue types make up the central layer here? _____, _____, _____, _____

Why are there only 4 sidechains in each layer, rather than 8?

2. Kinemage file [babarel.kin](#) (44KB) :

Main chain, H-bonds, and sequence labels are shown. This is an idealized parallel alpha / beta-barrel modeled on TIM (triose P isomerase), PYK (pyruvate kinase), KGA (KDPG aldolase), TAA (taka-amylase), and GAO (glycolate oxidase). A very large number of parallel α / β -barrel proteins are known, all with 8 strands in the same singly-wound topology (with some minor exceptions). In this model structure all residues have the same phi, psi. (-114° , 124°). Strands were initially fit to a real barrel and then symmetrized as much as possible. (Departures from symmetry vary, some barrels being flattened and others round but conical.)



The above diagram shows the H-bonding pattern in babarel, as viewed from the outside and flattened into 2D. The H-bonds are, on average, perpendicular to the strands, so the strand twist gives the H-bond direction a twist, or effective offset from one strand to the next. Turn on & off "row perp." to see balls on the Cbetas for one row of 6 inward-pointing sidechains that are all adjacent in the direction perpendicular to the strands. What is the total offset or shear (in residues) if one follows the perpendicular average H-bond direction all the way around the barrel back to the starting strand? _____
What is the offset per strand? _____
Turn on the side chains. Why do they look so bristly?

On the H-bond diagram, the dots represent alpha-carbons. Circle the ones whose side chains extend toward the inside. As you saw in Kin.3 of abBarrel.kin, draw lines to connect the Calphas for each of the two central layers of 4 internal sidechains. Now find the two flanking layers of 4, and connect their Calphas. Choose "score & stay" to see how you did. The four layers are made up of sidechain types: _____, _____, _____, and _____. Considering conformation, H-bonding, and side chain direction, what is the rotational symmetry of this structure around the central axis of the barrel? (That is, is it 2-fold, 4-fold, 8-fold?) _____

3. Kinemage file  1tim_a.kin (90KB) :

To start with, turn on just main chain and H-bonds, to compare this real barrel with the idealized babarel. Check that there are really 8 strands, that each connection is righthanded, and that they each move over by a single strand and all in the same direction. Looking from the side of the barrel (view 2), estimate the angle (twist) between the strands in front and the ones in back. _____

Turn end-on to the barrel (view 1), so that in projection you see a central ellipse of beta strands surrounded by a ring of helices. The distance from one Calpha to the next is always a constant 3.8 Å, so that can be used as a yardstick to compare other distances. Measure the flattening of the barrel cross-section by estimating its major and minor axes in Calpha-Calpha units. _____ : _____

Turn on side chains. The table below gives the composition of residue types on the inside surfaces of 3 singly-wound parallel beta barrels. What are the five commonest residue types here? (circle them)

G	A	P	V	I	L	M	F	Y	W	S	T	N	D	Q	E	K	R	H	C
11	6	12	8	4	2	6	2	2	2	3	1	3	2	1	1	2	0	1	

Large hydrophobics predominate, of course; however, one curious feature is the large number of glycines, which in general are found in turns and loops rather than regular secondary structures. Turn off "non-gly" to see the glycines. Glycines have 3 unusual roles: 1) Flexibility; 2) Adoption of forbidden (usually positive phi) conformations; and 3) Smallest side chain to fit in tight positions. In this case, flexibility is unlikely, the Gly phi,psi values are more or less normal beta, and in many cases there are holes inside the barrel next to the Gly. Turn "non-gly" back on, and see if you can find one of these holes, next to Gly _____. From the babarel model building, we believe the function of these glycines is to relieve a bad contact between the internal Cbeta and a CO on the neighboring strand.

From the Thornton paper, locate the two alpha-beta connections in TIM that belong to the ab1 (at about residue _____) and ab3 (near _____) families, and find the defining conformational and sequence features in them. Why are none of the other connections in families? _____ . . .

4. Use a browser to visit the **SCOP** site, <http://scop.mrc-lmb.cam.ac.uk/scop/> Enter the classification at the top of the heirarchy, go to "alpha and beta, a/b" and then to the TIM barrel fold. Do one level of outline expansion, to view down to the "family" level. As of the October 2006 release 1.71, SCOP listed 32 superfamilies and 60 homologous families that have this fold. Most are enzymes and some entire metabolic pathways are populated with TIM barrels.

In the original 1981 Anatax, KDPG aldolase had a proposed but unconfirmed retracing as a classic TIM barrel. Find the E. coli KDPG aldolase structure in superfamily 11, under class I aldolases, and download the PDB file. What is its PDB code? _____ What is the resolution? _____ Å (look in the PDB file header) Import it into KiNG and make a ribbon kinemage of chain A (refer to the kinemage-construction tutorial if needed). How many β strands are in the barrel? ____ Do they all have +1x righthanded crossovers? ____ Does it match the ribbon schematic in Fig. 75 of Anatax? _____ (If not, in what way?)

Pick one of the specific TIM barrel PDB files in superfamilies 12-17 to download: what is its PDB code? _____ what is the protein's name? _____.

Use KiNG to create and look at a simple kinemage of it. What aspects of this structure are classic and what is atypical for a TIM barrel? _____

[If you don't find your initial structure choice interesting or tractable, try another one.]

Imagine that you are making a kinemage to add to this section of Anatax, to illustrate the idea of the more varied examples of TIM barrel folds now seen. Make a fairly simple kinemage of your chosen structure for this purpose (ribbon, ball&stick, or whatever, with at least one good view), and write a short explanatory caption into the kinemage text window.