Symmetry, Pseudo-symmetry and Evolution in Protein Structures

Don Vanselow, http://nativeproteins.blogspot.com
54 Greenways Road, Glen Waverley, VIC 3150, AUSTRALIA

Presented at BioPhysChem2011, 3-6 December 2011, University of Wollongong, NSW, Australia

The concept

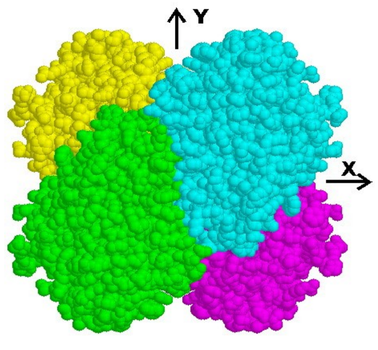
In the evolution of biological structures, natural selection chooses the best structure to perform a particular function in a particular environment.

It follows that, for structures of significant complexity, identical structures have probably been selected to perform the same function in the same environment.

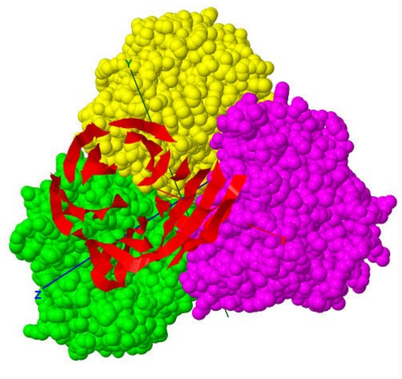
By widening our definitions of "identical" and "the same" we can say that similar structures have probably been selected for a similar function in a similar environment.

Spacial relationships in a protein complex are an important part of the environment in which a protein structure functions. It follows from the above propositions that we can expect symmetry and pseudo-symmetry in protein complexes made up of identical or similar structures respectively.

Neuraminidase from Avian Influenza Virus [1]

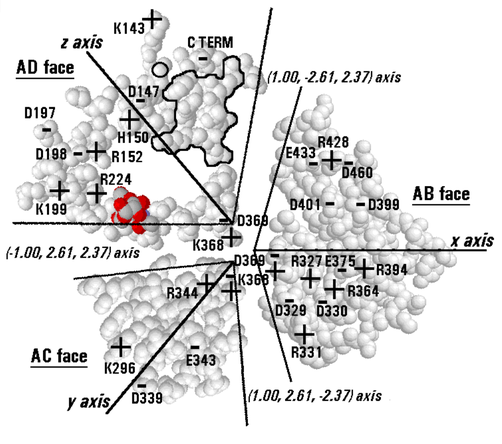


This homotetramer docks well with D2 symmetry, that is, with 2-fold rotational symmetry about x, y and z axes. All interfaces are complementary with their symmetry-related counterparts. There is almost no space left in the centre, as required by the physics [2].



This is the view down the axis of the "propeller" β-barrel of chain A which is shown transparent apart from ribbons representing β-sheet. Each "blade" of the "propeller" is pseudo-symmetric with the others and has approximately the same spatial relationship with the rest of the complex, i.e. they all point towards a point near the centre of the complex.

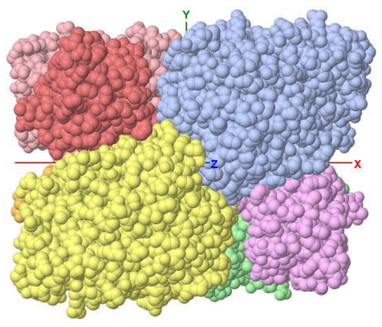
Each subunit has an interface with each of its symmetry-related neighbours. The 3 interfaces are mapped at right. The left side of each map is sterically and electrostatically complementary to the right side. The AD face has a raised area outlined in black that approx. fits into the mouth of the active site shown as empty space. Other faces are flat. Areas of surplus charge are matched by opposite charges on the other side, except one case where a long side chain has allowed a charge to wander.



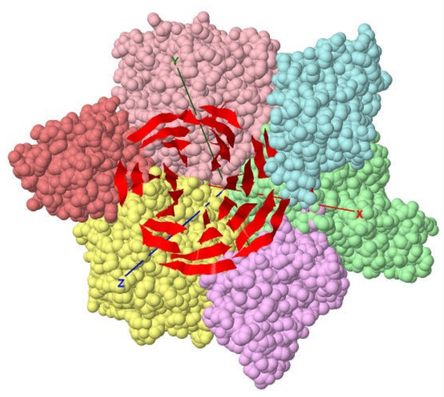
The same docking method has been used successfully on **10 other neuraminidases** of viral, bacterial or animal origin [1]. Basically they are very similar, even down to the location of the point to which the barrel axes are directed. They differ in their auxiliary domains, if present.

The viral neuraminidases have known glycosylation sites serving as markers of surfaces that are truly external. Taken together, the locations of 14 sites show that this docking is **statistically highly significant (p< 0.001).** Of course, the locations are also consistent with the various crystallization patterns but this is inherent in the process of crystallization [3].

Galactose oxidase [4]

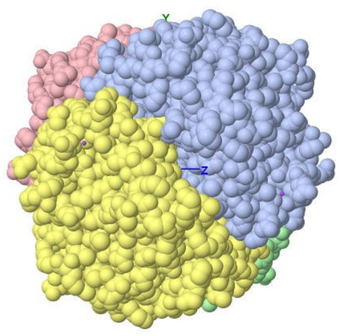


Homotetramer with D2 symmetry, each subunit with a "propeller" barrel domain and an auxilliary domain, all 8 domains coloured differently.

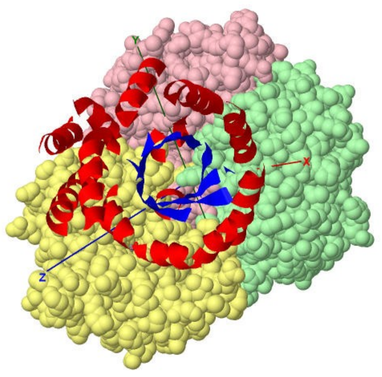


View down the axis of the "propeller" β-barrel of chain A. The barrel domain is shown transparent apart from ribbons representing the β-sheet barrel.

Dihydrodipicolinate synthase (DHDPS) [5]

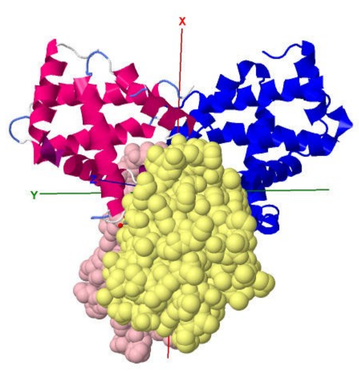


Homotetramer with D2 symmetry, each subunit being an α/β barrel. As with the other examples, there is almost no space left in the centre.



View down the axis of the α/β barrel of chain A, helices coloured red, β-sheet coloured blue. Chain A is shown transparent apart from ribbons representing helices and sheets.

Hemoglobin, R-State, from Homo sapiens [6]



Red and yellow are α subunits while blue and pink are β subunits. Each is a right-hand twisted barrel of 5 helices directed at the centre of the complex. There are short transverse helices at both ends of each barrel. Subunits are so similar that there is pseudosymmetry between them as well as in the arrangement of the helices. T-state is a "quaternary isomer", i.e. with the same structure but with the blue and yellow subunits changing places. Unlike the crystal structure, there is no hole in the centre as explained elsewhere [3].

Physical Meaning According to the constraint theory of protein function [2], even globular proteins are principally structural, transmitting compressive stress from the aqueous interface to the active site. It may be that β-sheet has a particularly low compressibility parallel to its backbone covalent bonds. The radial alignment of β-sheet in the centres of large barrels would allow transmission of surface-generated work to the active site with maximum efficiency, i.e. with the minimum used to compress the protein itself.

Helices may well be better at holding a large volume of protein into a coherent structure and could be useful in providing the necessary bulk to subunits. Apparently a small protein can get by with helices or β-sheet alone.

References

[1] Vanselow, D. G. (2007a) http://nativeproteins.blogspot.com, Post of 14 April 2007.
[2] Vanselow, D. G. (2002) Biophys. J., 82, 2293-2203.
[3] Vanselow, D. G. (2011) Paper to be presented at this meeting, Tues 6 December.
[4] Vanselow, D. G. (2007b) http://nativeproteins.blogspot.com, Post of 30 September 2007.
[5] Vanselow, D. G. (2011) http://nativeproteins.blogspot.com, Post of 5 May 2011.
[6] Vanselow, D. G. (2008) WATOC 2008 Poster No. 321. http://posters.f1000.com/P1181.

Further discussions, structures and links at http://nativeproteins.blogspot.com or the structure gallery can be directly accessed at www.nativeproteins.net76.net/gallery/index.htm