

Comparison of Protein Structures

Objective: To give a presentation of about 60 minutes at the end of the week covering the key aspects of the comparison of protein structures.

Comparing homologous objects are central to biology and the last decade has been dominated by this. The field of comparative genomics is an obvious example. However, many other objects than sequences in biology are homologous and can be subject to evolutionary study. Examples could be networks and structures. These objects are much more complex than sequences and there naturally is much more variation in the approaches used. Clearly the basic events are still at the sequence level that is then translated to the structure level by folding. However, only a very minor fraction of the sequence events changes into major structural changes. The nature of this relationship is elusive and it is very difficult to nail down the events that cause a structural change. Most methods of comparison would not be based on explicit evolutionary considerations, but would look for a maximal common substructure, how close in pace can atoms be placed if the complete structures were superimposed.

Both Big Questions and Possible Contents of Presentation are only meant as motivators that can be totally ignored.

The Big Questions Are:

How are structures represented?

How do structures evolve?

What are the basic events in structure change?

Can homology for different structures be ascertained?

Are all possible structures in evolution observed?

Structure alignment: local/global – pairwise/multiple – colinear/noncolinear – optimisation/model based.

Are observed structures representing all possible structures?

What is a random structure?

What is the relationship between sequence and structure evolution??

Is the present explosion in determined structures changing the situation??

How are larger sets of structures analyzed?

Possible Contents of Presentation

Description of Structure Knowledge now and possibly over time

Key example of structures and structure pairs

Major classes of comparison methods

Methods applicable to sets of structures

Tests of Homology

Interesting applications

Challenges for the Future

Starting pointers

http://en.wikipedia.org/wiki/Structural_alignment

Brown, N., C. Orengo and Taylor (1996) "A Protein Structure Comparison Methodology" *Computers Chem.* 20:359-380.

Chothia and Lesk (1986) The relationship between the divergence of sequence and structure in proteins. *EMBO J.*, 5, 823-826.

Holm L, Sander C (1996). Mapping the protein universe. *Science* 273: 595-603

Lin, K. and Taylor, W. R. and Klienjung, J. and Heringa, J. "Testing homology with (Cao et al.): A contact-based Markov model of protein evolution", *J. Compu. Biol. Chem.*, 27, 93--102, "2003"

Leonid Meyerguz, Jon Kleinberg, and Ron Elber (2007) "The network of sequence flow between protein structures" *PNAS*

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