Clustal W

Introduction

- Clustal W is a general purpose multiple sequence alignment program for DNA or proteins.
- It produces biologically meaningful multiple sequence alignments of divergent sequence.
- It calculate the best match for the selected sequence ,and lines them up so that the identiies.

Algorithm

- Clustal W is a matrix-based algorithm, whereas tools like T-coffee are consistency-based.
- Clustal W has a fairly efficient algorithm that competes well against in other software.
- The first step to the algorithm is computing a rough distance matrix between each pair of sequence, also known as pairwise sequence alignment.

Accuracy and Results

- The algorithm ClustalW uses provides a close –to-optimal result almost every time.
- However, it does exceptionally well when the data set contains sequences with varied degrees of divergence.

Clustal Omega

- Clustal omega is a new multiple sequence alignment program that uses seeded guide trees and HMM profile –profile technique to generate alignment between three or more sequence.
- Ideally, might think to build up multiple alignments through weighted sum of pairs (pairwise scores)
- But this is too computationally intensive
  - And doesn't make much biological sense

Basic Steps

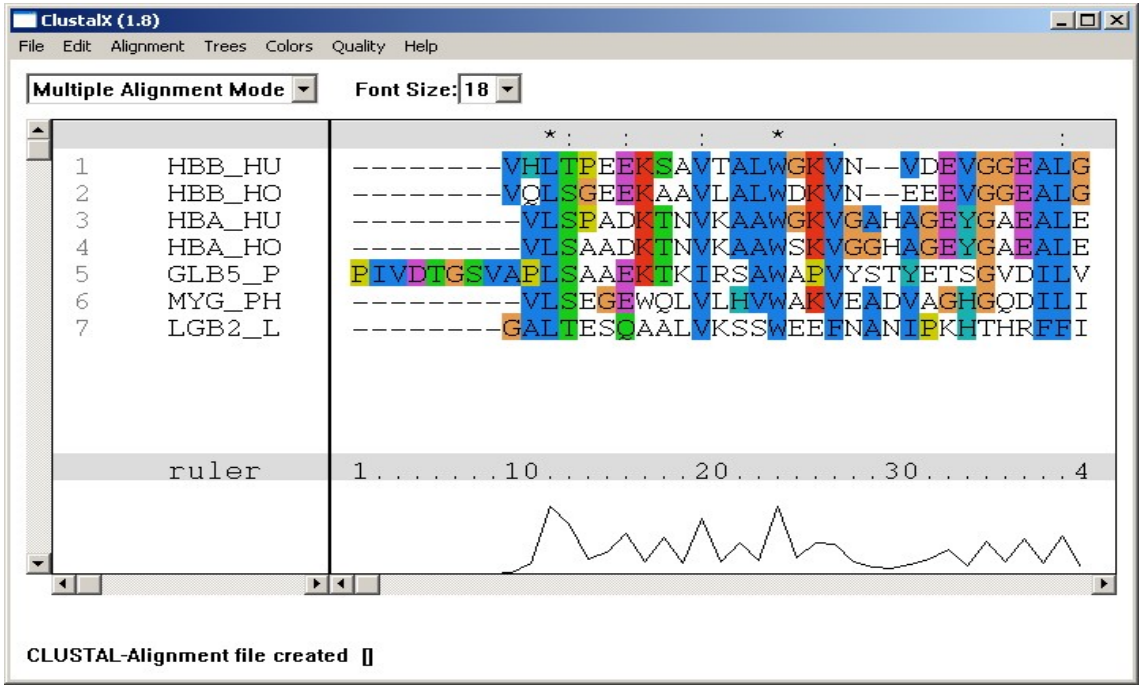
- Compute the pairwise alignments for all against all sequences.
- The similarities are stored in a matrix
- Convert the sequence similarity matrix values to distance measures , reflecting evolutionary distance between each pair of sequence.
- Construct a tree for the order in which pairs of sequence are to be aligned and combined with previous alignments.
- Progressively align the sequence together into each branch point of the guide tree, starting with the least distance pairs of sequence.

Uses of MSA

- Functional prediction
- Phylogeny
- Structural prediction
- Protein analysis
- To distinguish between orthology and parology

- Ideally, might think to build up multiple alignments through weighted sum of pairs (pairwise scores)
- But this is too computationally intensive
  - And doesn't make much biological sense
- So use heuristics and progressive alignment methods

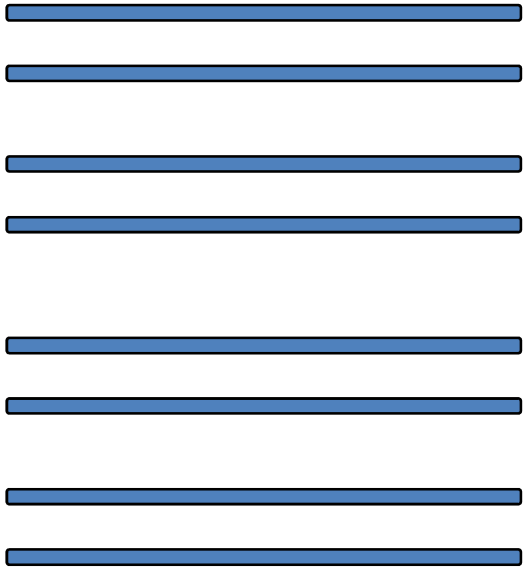
ClustalW



www.clustal.org

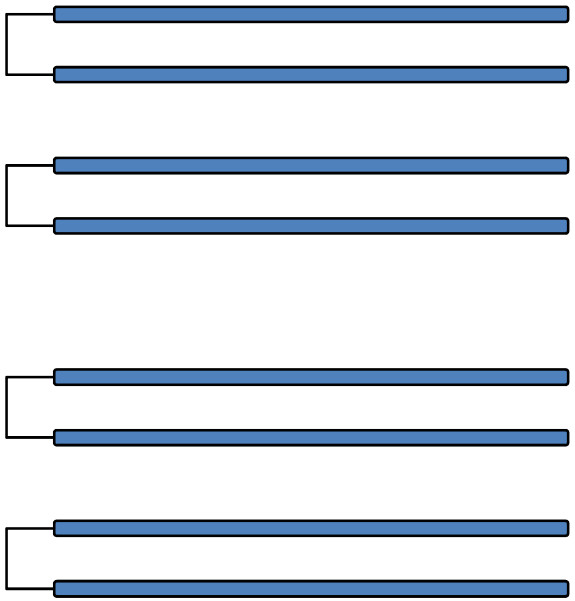
CLUSTAL

- Quick, pairwise alignment of all sequences
- Line up pairs, with the most similar first



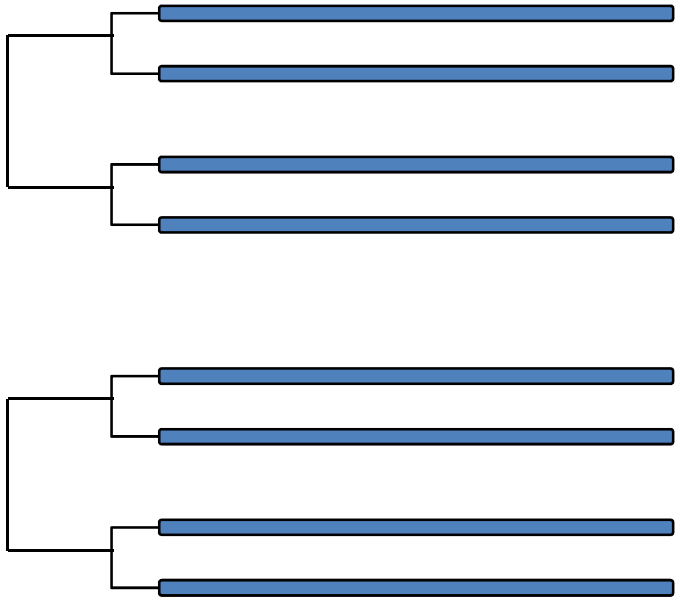
CLUSTAL

- Fix the alignment between pairs and treat as one sequence



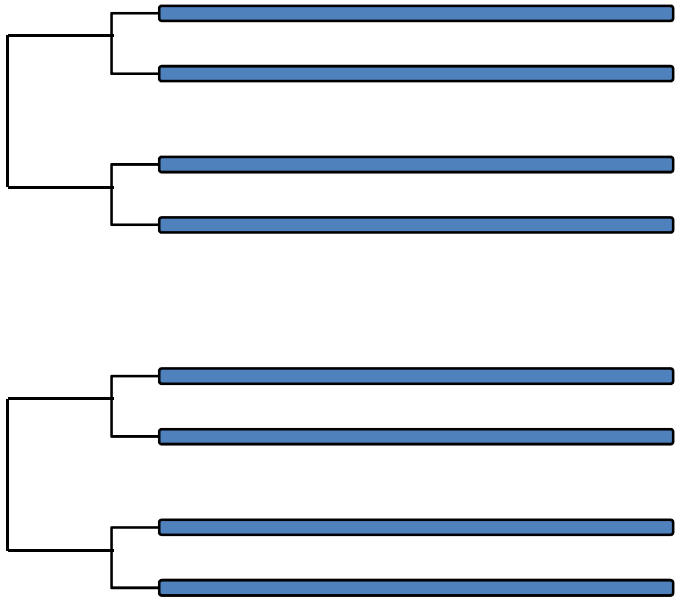
CLUSTAL

- Align your fixed pairs with each other

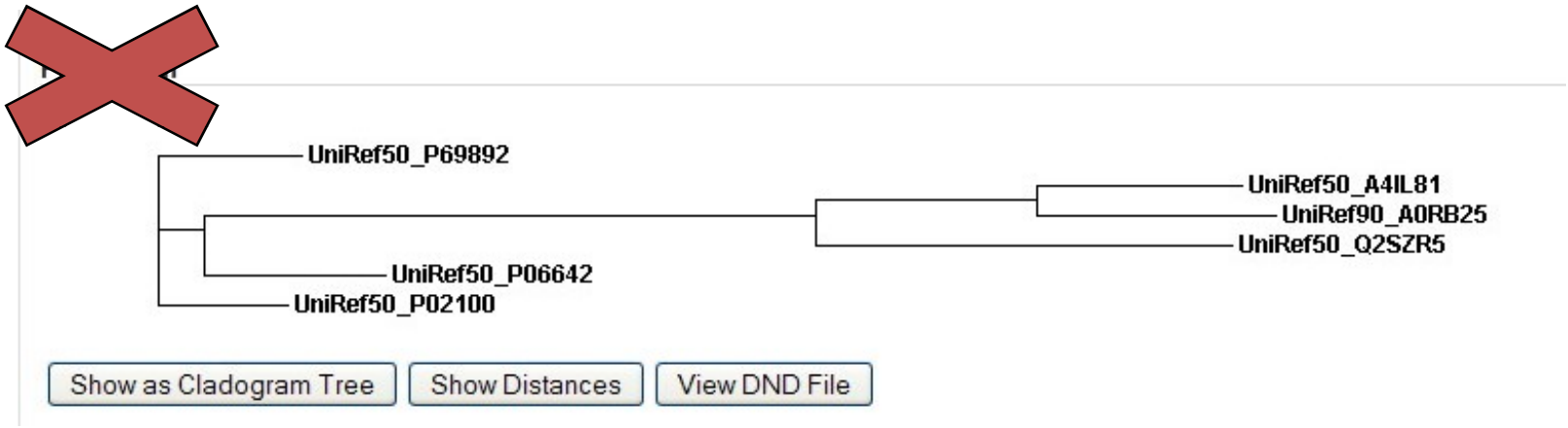


CLUSTAL

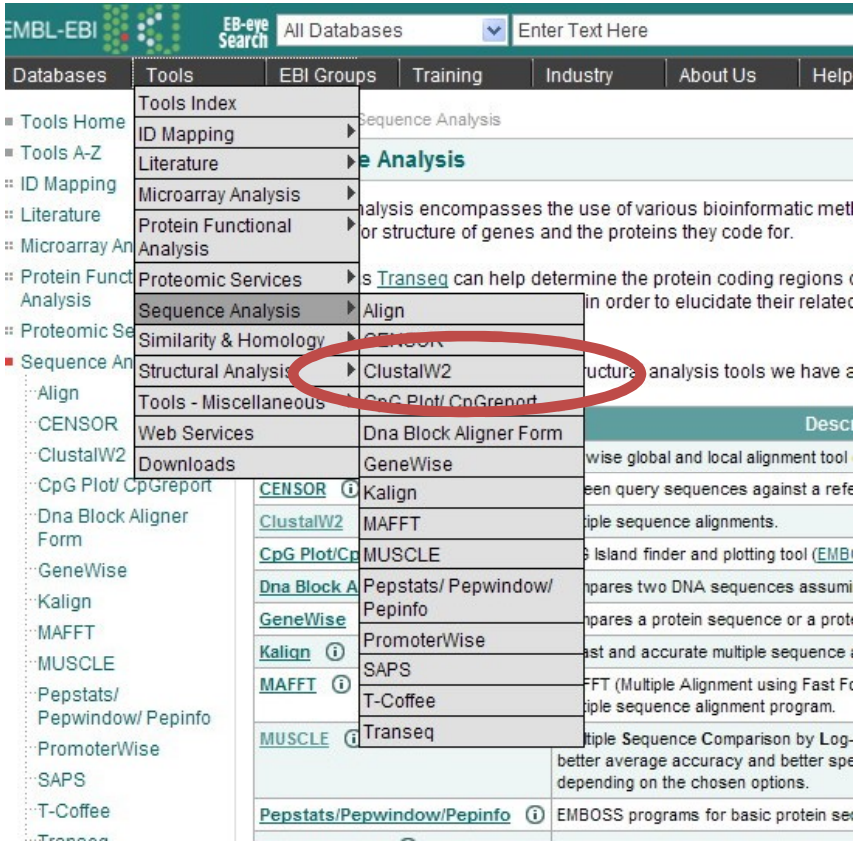
- Align your fixed pairs with each other



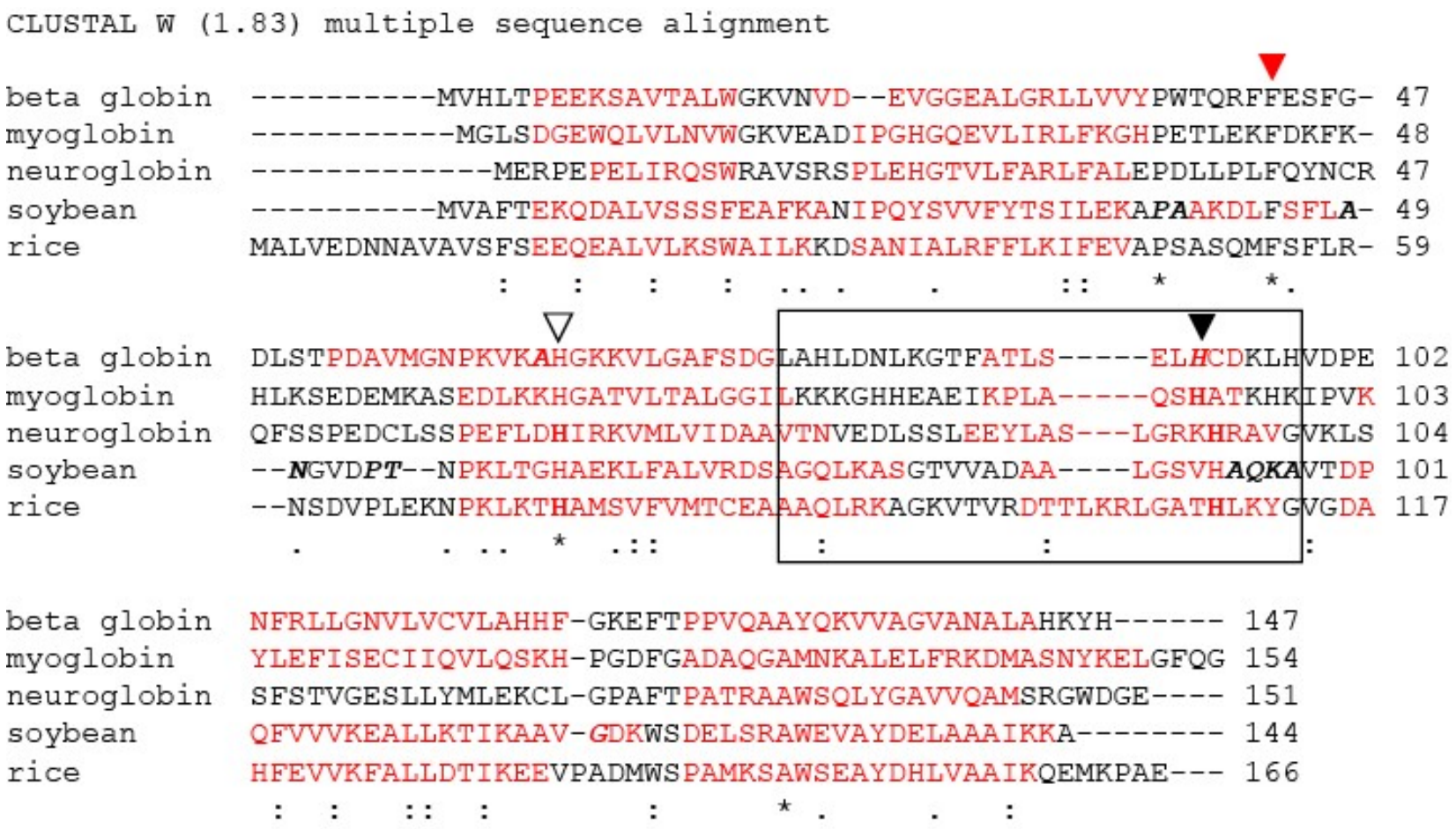
- Note, this is not a phylogram!
- Only a guide tree for the alignment



ClustalW at the EBI



ClustalW



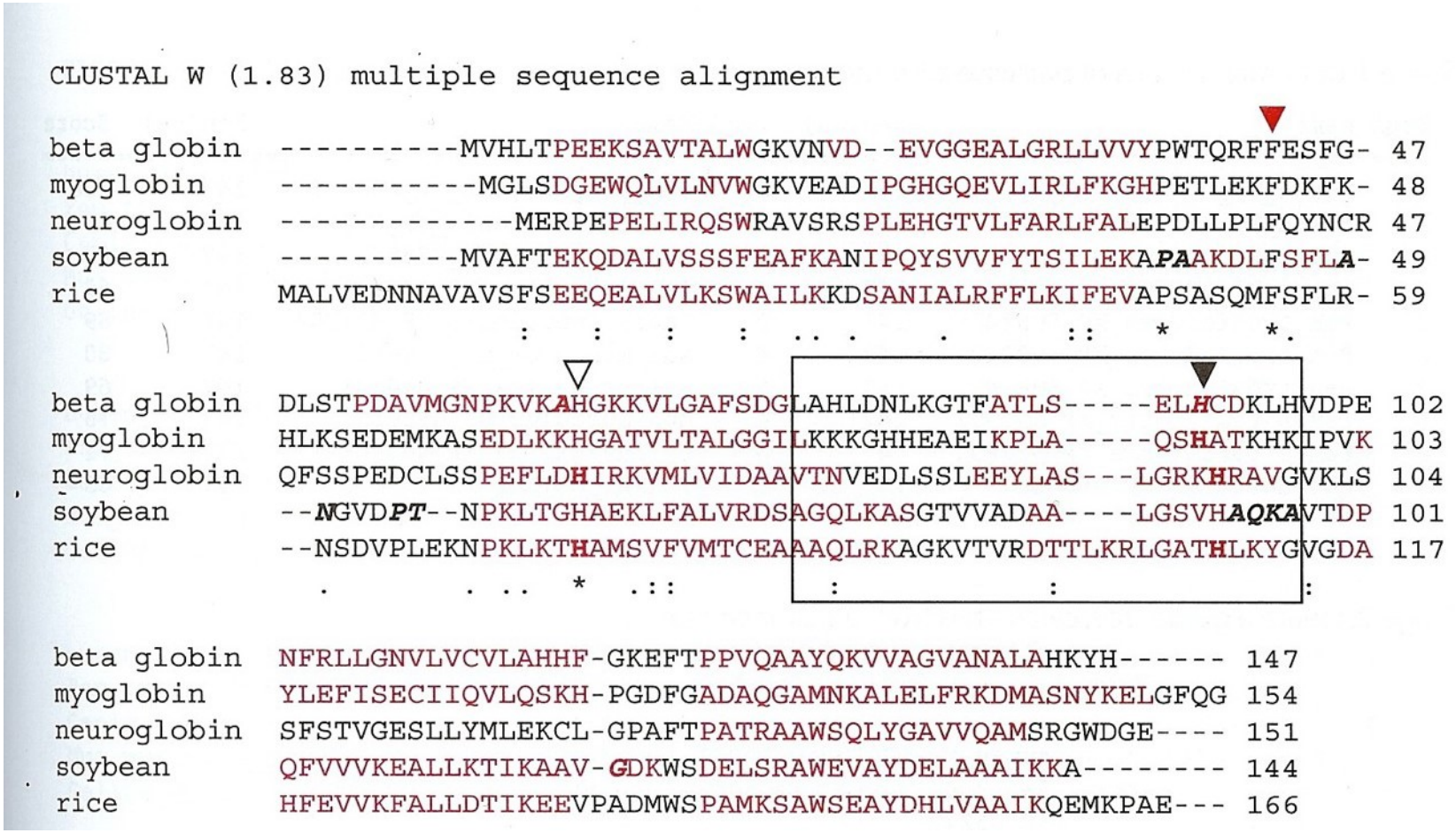
Note how the region of a conserved histidine (▼) varies depending on which of five prominent algorithms is used

Homology vs. Similarity

- Presence of similar features because of common decent
- Cannot be observed since the ancestors are not anymore
- Is inferred as a conclusion based on ‘similarity’
- Homology is like pregnancy: Either one is or one isn’t! (Gribskov – 1999)

- Quantifies a ‘likeness’
- Uses statistics to determine ‘significance’ of a similarity
- Statistically significant similar sequences are considered ‘homologous’

ClustalW example



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CLUSTAL W (1.83) multiple sequence alignment

beta globin   ----------MVHLTPEEKSAVTALWGKVNVD--EVGGEALGRLLVVYPWTQRFFESFG- 47
myoglobin     -----------MGLSDGEWQLVLNVWGKVEADIPGHGQEVLIRLFKGHPETLEKFDKFK- 48
neuroglobin   ------------MERPEPELIRQSWRAVSRSPLEHGTVLFARLFALEPDLLPLFQYNCR 47
soybean       ----------MVAFTEKQDALVSSSFEAFKANIPQYSVVFYTSILEKAPAAKDLFSFLA- 49
rice          MALVEDNNAVAVSFSEEQEALVLKSWAILKKDSANIALRFFLKIFEVAPSASQMFSFLR- 59
                         :   :   :  .. .    .      ::   *     *.

beta globin   DLSTPDAVMGNPKVKAHGKKVLGAFSDGLAHLDNLKGTFATLS-----ELHCDKLHVDPE 102
myoglobin     HLKSEDEMKASEDLKKHGATVLTALGGILKKKGHHEAEIKPLA-----QSHATKHKIPVK 103
neuroglobin   QFSSPEDCLSSPEFLDHIRKVMLVIDAAVTNVEDLSSLEEYLAS---LGRKHRAVGVKLS 104
soybean       --NGVDPT--NPKLTGHAEKLFALVRDSAGQLKASGTVVADAA----LGSVHAQKAVTDP 101
rice          --NSDVPLEKNPKLKTHAMSVFVMTCEAAAQLRKAGKVTVRDTTLKRLGATHLKYGVGDA 117
                 .       . ..  *  .::          :           :           :

beta globin   NFRLLGNVLVCVLAHHF-GKEFTPPVQAAYQKVVAGVANALAHKYH------ 147
myoglobin     YLEFISECIIQVLQSKH-PGDFGADAQGAMNKALELFRKDMASNYKELGFQG 154
neuroglobin   SFSTVGESLLYMLEKCL-GPAFTPATRAAWSQLYGAVVQAMSRGWDGE---- 151
soybean       QFVVVKEALLKTIKAAV-GDKWSDELSRAWEVAYDELAAAIKKA-------- 144
rice          HFEVVKFALLDTIKEEVPADMWSPAMKSAWSEAYDHLVAAIKQEMKPAE--- 166
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Pevsner, Jonathan. Bioinformatics and Functional Genomics. 2nd. Baltimore Maryland: Wiley-Blackwell, 2009. 179-207. Print.

Summary of ClustalW method

- For years, ClustalW was the best method available.
- It's still a solid performer, provided that sequences are closely related and do not have significant structural differences
- Distinguishing characteristics:
  - Progressive alignment based on a guide tree
  - Gap parameters informed by hydrophobicity of amino acids and by previously inserted gaps
  - Amino acid substitution matrices derived from observed sequence divergence (different matrices for different groups).

THANK YOU