Assignment 3

Hierarchical Clustering

1. Global alignment (5P)
2. Find homologous sequences (3P)
3. Hierarchical Clustering (12P)

1 Global Alignment (5P)

- Get back to your program for local alignment
- Modify the program to:
  - Calculate the global alignment
  - Work with amino acid sequences
  - Use BLOSUM62 as cost matrix
    - Retrieve from NCBI
    - Retrieve from EMBOSS
    - ...

- Cost matrix must be loaded and not hardcoded!

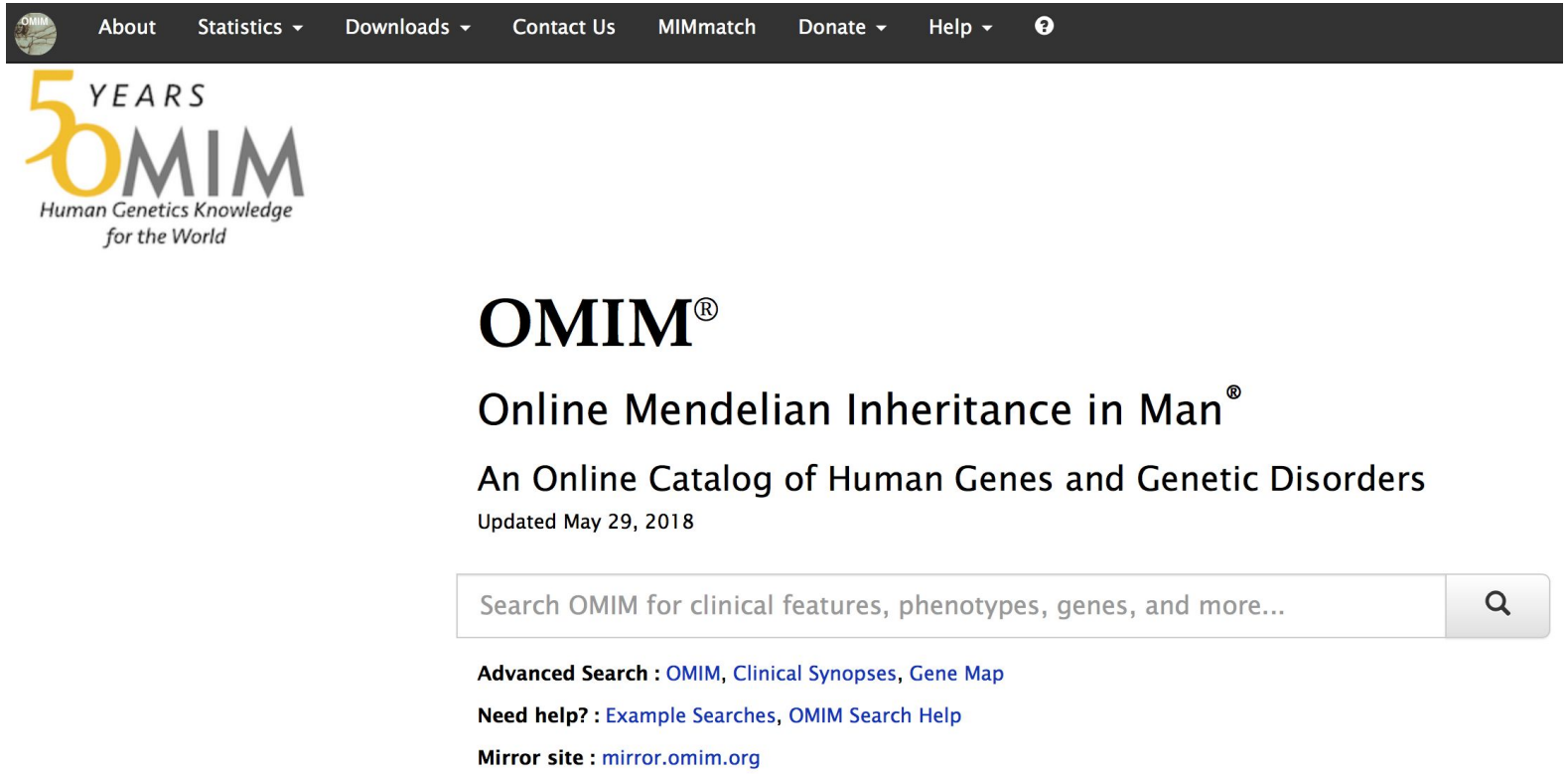
```
   A  R  N  D  C  Q  E  G  H  I  L  K  M  F  P  S  T  W  Y  V  B  Z  X  *
A  4 -1 -2 -2  0 -1 -1  0 -2 -1 -1 -1 -1 -2 -1  1  0 -3 -2  0 -2 -1  0 -4
R -1  5  0 -2 -3  1  0 -2  0 -3 -2  2 -1 -3 -2 -1 -1 -3 -2 -3 -1  0 -1 -4
N -2  0  6  1 -3  0  0  0  1 -3 -3  0 -2 -3 -2  1  0 -4 -2 -3  3  0 -1 -4
D -2 -2  1  6 -3  0  2 -1 -1 -3 -4 -1 -3 -3 -1  0 -1 -4 -3 -3  4  1 -1 -4
C  0 -3 -3 -3  9 -3 -4 -3 -3 -1 -1 -3 -1 -2 -3 -1 -1 -2 -2 -1 -3 -3 -2 -4
Q -1  1  0  0 -3  5  2 -2  0 -3 -2  1  0 -3 -1  0 -1 -2 -1 -2  0  3 -1 -4
(...)
```

2.1 Find Sequence (1P)

- Phenylketonuria (PKU) is a frequent hereditary disease
  - Can be well treated if found early
  - Life long and strict low-phenylalanine diet
  - Otherwise severe effects on brain development

1. Find the disease causing protein in OMIM database
2. Retrieve Sequence of (human) protein from UniProt

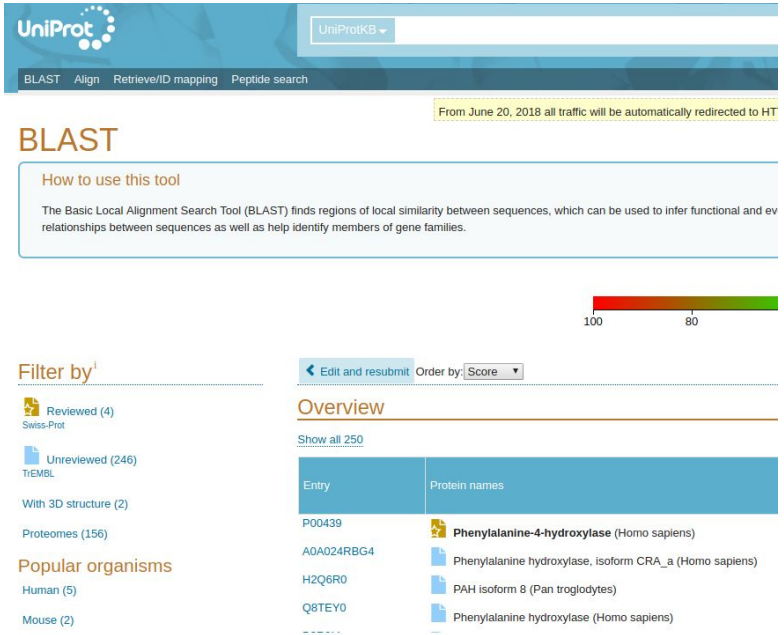
OMIM database



2.2 Find homologous sequences (2P)

Retrieve homologous protein sequences using NCBI's BLASTP -> blast the UniProt sequence

1.1. Write out finding for BLAST
   1. Homo sapiens
   2. Mus musculus
   3. Bos taurus
   4. Rattus norvegicus
   5. Gallus gallus
   6. Xenopus tropicalis
   7. Drosophila melanogaster
   8. Danio rerio



Example, you can use different blasters

What we want

Provide information on:

- Name of the disease causing protein
- Its UniProt-ID
- Its amount of amino acids

- State the used accession numbers for all eight sequences from blasting the Uniprot sequence
- Store sequences in a single FASTA file (e.g. sequences.fasta):

```
>Homo Sapiens
MSTAVLEN
.....
.....

>Mus musculus
MAAVVLEN
.....

>Bos taurus
MSALVLES
.....
```

sequences.fasta

3.1 Hierarchical Clustering (7P)

- Implement the algorithm for hierarchical clustering
- Program reads a single FASTA file + scoring matrix
- Compute similarity matrix on all pairs of sequences from the file
- Print all pairwise scores in tabularized manner

	Homo	Mus	Bos	...
Homo		2216	2225	...
...			....	...

3.1 Hierarchical Clustering (7P)

- Build a guide tree using hierarchical clustering
- Find maximum in the similarity matrix
- Program call
  - java -jar GdBioinf_[Assignment_nr]_Gruppe_[Gruppen_nr].jar sequences.fasta blosum.txt
- Output the tree
  - BE AWARE OF SEQUENCE NUMBERING, see below
- Assume sequence 1 and 4 are merged to '14', then 5 and 7 to 57, then the virtual sequence 14 is merged with 3 etc, the output of your program should look like this: (1,4), (5,7), (14,3) etc.

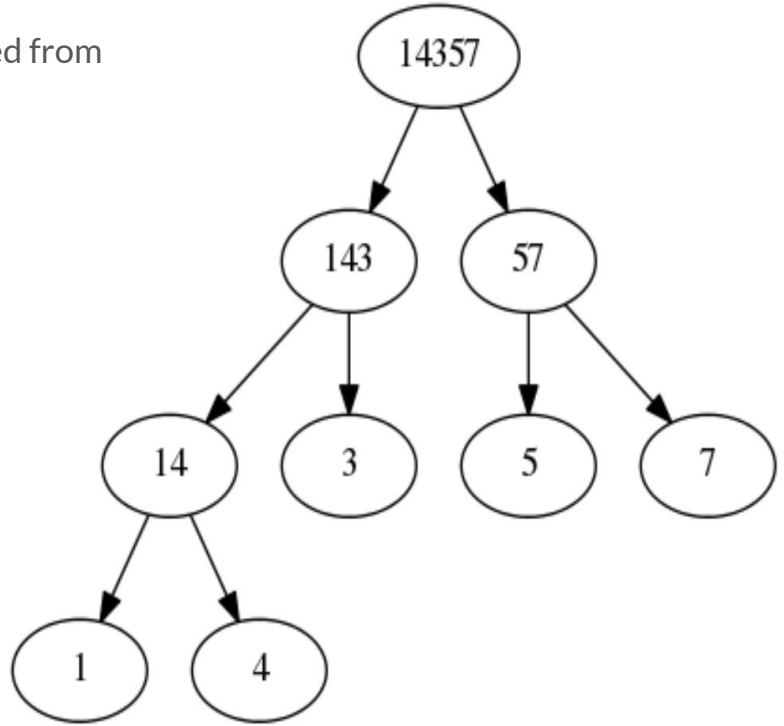
1. Homo sapiens
2. Mus musculus
3. Bos taurus
4. Rattus norvegicus
5. Gallus gallus
6. Xenopus tropicalis
7. Drosophila melanogaster
8. Danio rerio

3.2 Visualization (5P)

- Draw the tree such that novel clusters are added from bottom-to-top and from left-to-right
- As in the picture below
- E.g., using graphviz http://www.graphviz.org/

```
digraph G {
    14 -> 1;
    14 -> 4;
    143 -> 14;
    143 -> 3;
    14357 -> 57;
    14357 -> 143;
    57 -> 5;
    5 -> 7;
}

dot -Tpng filename.txt  > filename.png
```



What we want

Submit

- Global alignment algorithm
- Algorithm for clustering & distance matrix calculation
- Similarity matrix of all eight sequences with similarity score
- State the used accession numbers for all eight sequences from blasting the Uniprot sequence

sequences.fasta

- Store sequences in a single FASTA file (e.g. sequences.fasta)
- Cluster-structure (see slide before)

Deadline

- Deadline for submission 13.06.2018 at 12:00 p.m.
- SUBMIT HERE
  - https://box.hu-berlin.de/u/d/f94821b8a39b41259e9e/
- Code as .jar/.py.R
- Remember correct source code nomenclature
  - GdBioinf_[Assignment_nr]_Gruppe_[Gruppen_nr].jar