Class 11: Structural Bioinformatics pt 2

Montserrat (PID:A16536527)

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Background

we saw last day that the PDB has 209.886 entries (Oct/Nov 20235). UniProtKB (i.e. protein sequence database) has 199,579,901 entries.

```
209886/199579901 * 100
```

```
[1] 0.1051639
```

so the PDB has only 0.1% coverage of the main sequence database.

Enter AlphaFold data base (AFDB) < https://alphafold.ebi.ac.uk > taht attempts to provide computed models for all sequences in UniProt.

accoridng to website, AlphaFold DB provides open access to over 200 million protein structure predictions to accelerate scientific research.

##AlphaFold

AlphaFold has 3 main outpouts - predicted coordinates (PDB files) -local quality score called pLDDD (one for each amino-acid) - a second quality score PAE Predicted Aligned Error (for each pair of amino-acid)

We can run AlphaFold ourselves if we are not happy with AFDB (i.e. no coverage or poor model)

Interpreting/ analyzing AF results in R

```
results_dir <- "HIVPR_dimer_23119/"
```

```
pdb_files <- list.files(path=results_dir,
                        pattern="*.pdb",
                        full.names = TRUE)
# Print our PDB file names
basename(pdb_files)
```

```
[1] "HIVPR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_4_seed_000.pdb"
[2] "HIVPR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_000.pdb"
[3] "HIVPR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_5_seed_000.pdb"
[4] "HIVPR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.pdb"
[5] "HIVPR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.pdb"
```

```
library(bio3d)

# Read all data from Models
#  and superpose/fit coords
pdbs <- pdbaln(pdb_files, fit=TRUE, exefile="msa")
```

```
Reading PDB files:
HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_4_seed_0
HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_0
HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_5_seed_0
HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_0
HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_0
.....

Extracting sequences

pdb/seq: 1   name: HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_001_alphafold2_multime
pdb/seq: 2   name: HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_002_alphafold2_multime
pdb/seq: 3   name: HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_003_alphafold2_multime
pdb/seq: 4   name: HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_004_alphafold2_multime
pdb/seq: 5   name: HIVPR_dimer_23119//HIVPR_dimer_23119_unrelaxed_rank_005_alphafold2_multime
```

```
pdbs
```

```
                                1        .        .        .        .         50
[Truncated_Name:1]HIVPR_dime    PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:2]HIVPR_dime    PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:3]HIVPR_dime    PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:4]HIVPR_dime    PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:5]HIVPR_dime    PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
                                **************************************************
                                1        .        .        .        .         50

                               51        .        .        .        .        100
[Truncated_Name:1]HIVPR_dime    GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:2]HIVPR_dime    GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:3]HIVPR_dime    GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:4]HIVPR_dime    GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:5]HIVPR_dime    GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
                                **************************************************
                               51        .        .        .        .        100

                              101        .        .        .        .        150
[Truncated_Name:1]HIVPR_dime    QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:2]HIVPR_dime    QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:3]HIVPR_dime    QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:4]HIVPR_dime    QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:5]HIVPR_dime    QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
                                **************************************************
                              101        .        .        .        .        150

                              151        .        .        .        .      198
[Truncated_Name:1]HIVPR_dime    GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:2]HIVPR_dime    GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:3]HIVPR_dime    GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:4]HIVPR_dime    GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:5]HIVPR_dime    GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
                                *********************************************
                              151        .        .        .        .      198

Call:
  pdbaln(files = pdb_files, fit = TRUE, exefile = "msa")

Class:
```

```
  pdbs, fasta

Alignment dimensions:
  5 sequence rows; 198 position columns (198 non-gap, 0 gap)

+ attr: xyz, resno, b, chain, id, ali, resid, sse, call
```

RMSD is a standard measure of structural distance between coordinate sets. We can use the rmsd() function to calculate the RMSD between all pairs models.

```
rd <- rmsd(pdbs, fit=T)
```

```
Warning in rmsd(pdbs, fit = T): No indices provided, using the 198 non NA positions
```

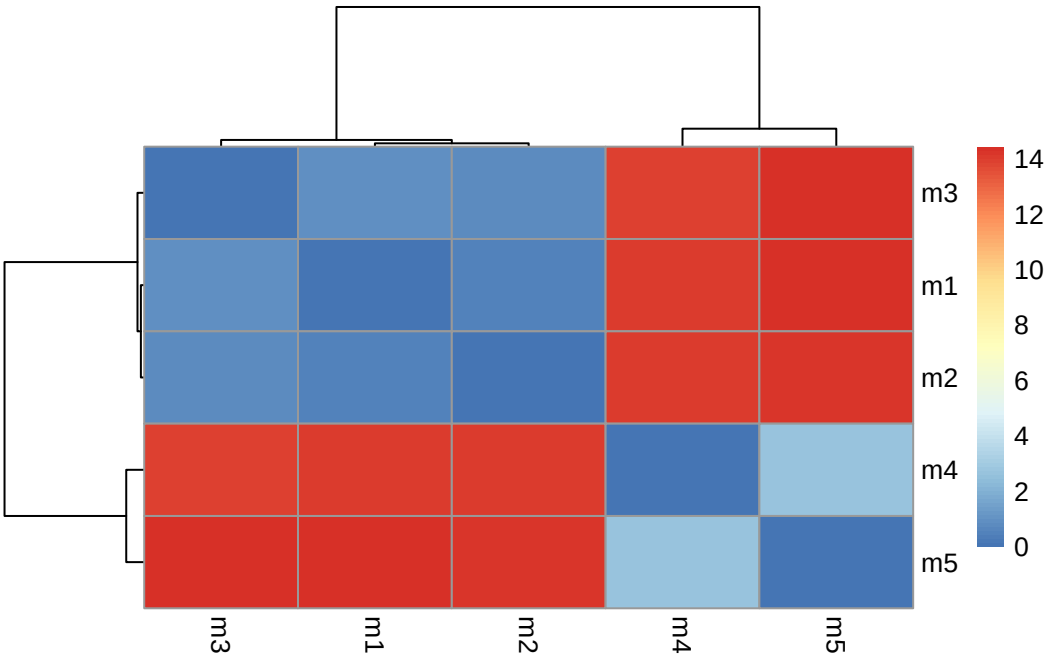
```
range(rd)
```

```
[1]  0.000 14.428
```

Draw a heatmap of these RMSD matrix values

```
library(pheatmap)

colnames(rd) <- paste0("m",1:5)
rownames(rd) <- paste0("m",1:5)
pheatmap(rd)
```



Alignment File

```
aln_file <- list.files(path=results_dir,
                       pattern=".a3m$",
                        full.names = TRUE)
aln_file
```

```
[1] "HIVPR_dimer_23119//HIVPR_dimer_23119.a3m"
```