Class_11

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Background

We saw last class that the PDB has 209,886 entries (Oct/Nov 2025). UniprotKB (i.e. protein sequence database) has 199,579,901 entries.

So the PDB has only 0.11% coverage of the main sequence database.

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

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

AlphaFold

AlphaFold has 3 main outputs

- The predicted coordinates (PDB file)
- A local quality score called pLDDT (one for each amino-acid)
- A second quality score called 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 <- "Brads_HIVPR_dimer_23119/"
```

```
# File names for all PDB models
pdb_files <- list.files(path=results_dir,
                        pattern="*.pdb",
                        full.names = TRUE)

# Print our PDB file names
basename(pdb_files)
```

```
[1] "Brads_HIVPR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_4_seed_000.pdb"
[2] "Brads_HIVPR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_000.pdb"
[3] "Brads_HIVPR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_5_seed_000.pdb"
[4] "Brads_HIVPR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.pdb"
[5] "Brads_HIVPR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.pdb"
```

```
library(bio3d)
library(bio3dview)
# Read all data from Models
#  and superpose/fit coords
pdbs <- pdbaln(pdb_files, fit=TRUE, exefile="msa")
```

```
Reading PDB files:
Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_mo
Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_mo
Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_mo
Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_mo
Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_mo
.....

Extracting sequences

pdb/seq: 1   name: Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_001_alphai
pdb/seq: 2   name: Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_002_alphai
pdb/seq: 3   name: Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_003_alphai
pdb/seq: 4   name: Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_004_alphai
pdb/seq: 5   name: Brads_HIVPR_dimer_23119//Brads_HIVPR_dimer_23119_unrelaxed_rank_005_alphai
```

```
pdbs
```

```
                                1        .        .        .        .        50
[Truncated_Name:1]Brads_HIVP   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
```

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

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

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

                             151        .         .         .         .       198
[Truncated_Name:1]Brads_HIVP   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:2]Brads_HIVP   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:3]Brads_HIVP   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:4]Brads_HIVP   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:5]Brads_HIVP   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
```

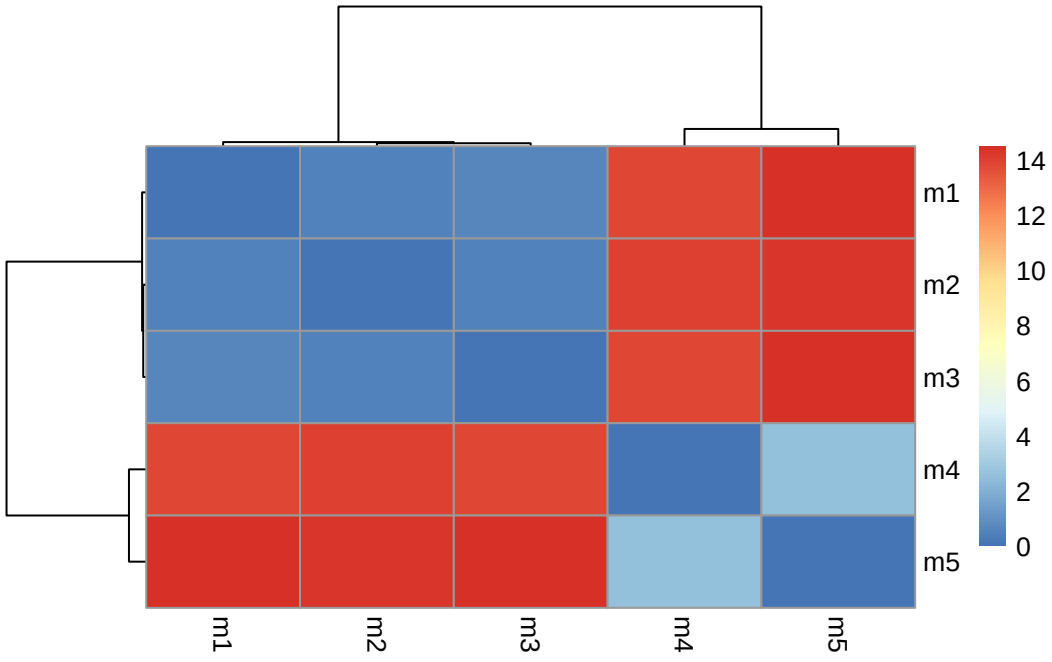
```
range(rd)
```

```
[1]  0.000 14.526
```

Drawing a heatmat

```
library(pheatmap)

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

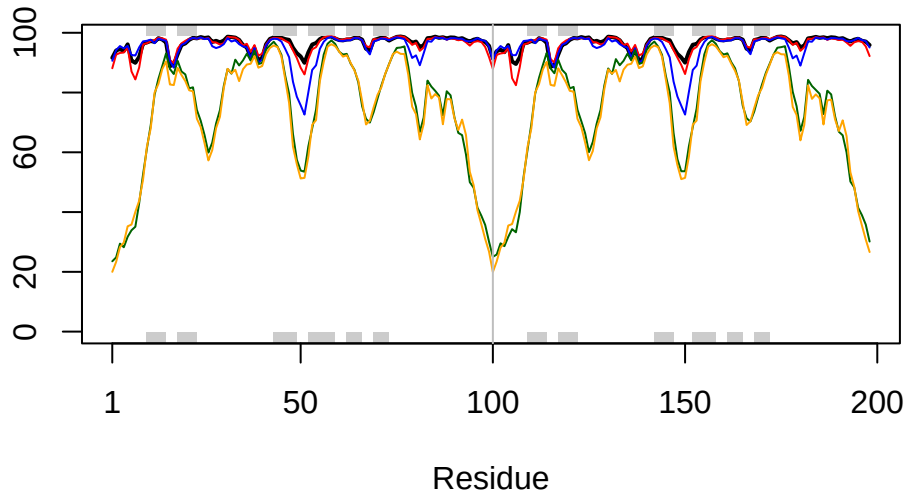


Now lets plot the pLDDT values across all models.

```
pdb <- read.pdb("1hsg")
```

```
  Note: Accessing on-line PDB file
```

```
plotb3(pdbs$b[1,], typ="l", lwd=2, sse=pdb)
points(pdbs$b[2,], typ="l", col="red")
points(pdbs$b[3,], typ="l", col="blue")
points(pdbs$b[4,], typ="l", col="darkgreen")
points(pdbs$b[5,], typ="l", col="orange")
abline(v=100, col="gray")
```




```
core <- core.find(pdbs)
```

```
 core size 197 of 198  vol = 5437.294
 core size 196 of 198  vol = 4705.336
 core size 195 of 198  vol = 1827.704
 core size 194 of 198  vol = 1121.539
 core size 193 of 198  vol = 1047.76
 core size 192 of 198  vol = 999.32
 core size 191 of 198  vol = 953.718
 core size 190 of 198  vol = 910.755
```

```
core size 189 of 198  vol = 870.203
core size 188 of 198  vol = 836.304
core size 187 of 198  vol = 805.237
core size 186 of 198  vol = 775.99
core size 185 of 198  vol = 752.564
core size 184 of 198  vol = 712.023
core size 183 of 198  vol = 685.568
core size 182 of 198  vol = 663.911
core size 181 of 198  vol = 645.881
core size 180 of 198  vol = 627.97
core size 179 of 198  vol = 611.812
core size 178 of 198  vol = 595.931
core size 177 of 198  vol = 581.132
core size 176 of 198  vol = 566.736
core size 175 of 198  vol = 548.587
core size 174 of 198  vol = 534.114
core size 173 of 198  vol = 505.214
core size 172 of 198  vol = 491.225
core size 171 of 198  vol = 473.905
core size 170 of 198  vol = 460.426
core size 169 of 198  vol = 444.81
core size 168 of 198  vol = 431.661
core size 167 of 198  vol = 421.542
core size 166 of 198  vol = 405.601
core size 165 of 198  vol = 392.666
core size 164 of 198  vol = 381.077
core size 163 of 198  vol = 367.559
core size 162 of 198  vol = 358.379
core size 161 of 198  vol = 346.865
core size 160 of 198  vol = 334.809
core size 159 of 198  vol = 324.09
core size 158 of 198  vol = 312.153
core size 157 of 198  vol = 301.296
core size 156 of 198  vol = 290.431
core size 155 of 198  vol = 281.319
core size 154 of 198  vol = 272.529
core size 153 of 198  vol = 263.215
core size 152 of 198  vol = 253.54
core size 151 of 198  vol = 240.86
core size 150 of 198  vol = 227.447
core size 149 of 198  vol = 215.581
core size 148 of 198  vol = 202.041
core size 147 of 198  vol = 195.426
```

```
core size 146 of 198  vol = 188.721
core size 145 of 198  vol = 181.778
core size 144 of 198  vol = 173.615
core size 143 of 198  vol = 165.946
core size 142 of 198  vol = 156.117
core size 141 of 198  vol = 149.814
core size 140 of 198  vol = 143.616
core size 139 of 198  vol = 135.81
core size 138 of 198  vol = 127.851
core size 137 of 198  vol = 122.596
core size 136 of 198  vol = 117.203
core size 135 of 198  vol = 109.848
core size 134 of 198  vol = 104.812
core size 133 of 198  vol = 98.776
core size 132 of 198  vol = 94.799
core size 131 of 198  vol = 90.494
core size 130 of 198  vol = 87.403
core size 129 of 198  vol = 83.558
core size 128 of 198  vol = 79.08
core size 127 of 198  vol = 75.056
core size 126 of 198  vol = 71.238
core size 125 of 198  vol = 67.735
core size 124 of 198  vol = 64.289
core size 123 of 198  vol = 61.381
core size 122 of 198  vol = 57.515
core size 121 of 198  vol = 53.254
core size 120 of 198  vol = 48.654
core size 119 of 198  vol = 45.832
core size 118 of 198  vol = 41.819
core size 117 of 198  vol = 38.71
core size 116 of 198  vol = 36.294
core size 115 of 198  vol = 33.386
core size 114 of 198  vol = 30.472
core size 113 of 198  vol = 27.786
core size 112 of 198  vol = 25.403
core size 111 of 198  vol = 22.827
core size 110 of 198  vol = 21.106
core size 109 of 198  vol = 19.327
core size 108 of 198  vol = 17.796
core size 107 of 198  vol = 16.235
core size 106 of 198  vol = 14.508
core size 105 of 198  vol = 12.969
core size 104 of 198  vol = 11.834
```

```
 core size 103 of 198  vol = 11.185
 core size 102 of 198  vol = 10.298
 core size 101 of 198  vol = 8.898
 core size 100 of 198  vol = 7.813
 core size 99 of 198  vol = 6.074
 core size 98 of 198  vol = 5.286
 core size 97 of 198  vol = 4.43
 core size 96 of 198  vol = 3.873
 core size 95 of 198  vol = 3.321
 core size 94 of 198  vol = 2.855
 core size 93 of 198  vol = 2.293
 core size 92 of 198  vol = 1.937
 core size 91 of 198  vol = 1.631
 core size 90 of 198  vol = 1.331
 core size 89 of 198  vol = 0.957
 core size 88 of 198  vol = 0.803
 core size 87 of 198  vol = 0.647
 core size 86 of 198  vol = 0.532
 core size 85 of 198  vol = 0.444
 FINISHED: Min vol ( 0.5 ) reached
```

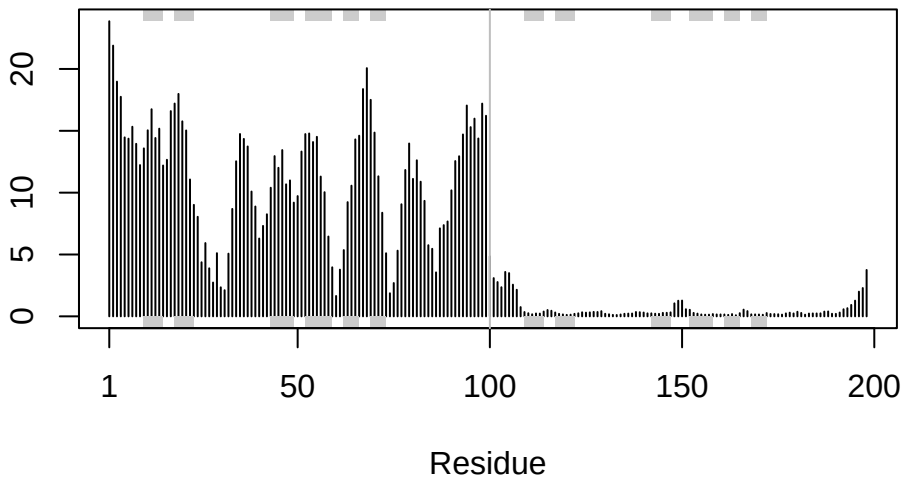
```
core.inds <- print(core, vol=0.5)
```

```
# 86 positions (cumulative volume <= 0.5 Angstrom^3)
  start end length
1     7   7      1
2     9  49     41
3    52  95     44
```

```
xyz <- pdbfit(pdbs, core.inds, outpath="corefit_structures")

rf <- rmsf(xyz)

plotb3(rf, sse=pdb)
abline(v=100, col="gray", ylab="RMSF")
```


0
5
10
20
1
50
100
150
200
Residue