Class 11: Structural Bioinformatics II

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Alphafold has changed the game for protein structure prediction and allows anyone with sufficient bioinformatics skills to predict the structure of virtually any protein.

We ran AlphaFold via GoogleColab at: https://colab.research.google.com/github/sokrypton/ColabFold

In particular, we used their AlphaFold_mmseqs2 version that uses mmseqs2 rather than HMMMer for sequence search.

The main outputs include a set of **PDB structure files** along with matching **JSON format files** that tell us how good the resulting models might be.

Let's start by loading these structures up in Mol*

```
library(bio3d)
results_dir <- "hivpr1_23119_3/"

# 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] "hivpr1_23119_3_unrelaxed_rank_001_alphafold2_multimer_v3_model_5_seed_000.pdb"
[2] "hivpr1_23119_3_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_000.pdb"
[3] "hivpr1_23119_3_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000.pdb"
[4] "hivpr1_23119_3_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.pdb"
[5] "hivpr1_23119_3_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.pdb"
```

```
#install.packages("BiocManager")
#BiocManager::install("msa")
```

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

```
Reading PDB files:
hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_001_alphafold2_multimer_v3_model_5_seed_000.pdb
hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_000.pdb
hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000.pdb
hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.pdb
hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.pdb
.....

Extracting sequences

pdb/seq: 1   name: hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_001_alphafold2_multimer_v3_mo
pdb/seq: 2   name: hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_002_alphafold2_multimer_v3_mo
pdb/seq: 3   name: hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_003_alphafold2_multimer_v3_mo
pdb/seq: 4   name: hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_004_alphafold2_multimer_v3_mo
pdb/seq: 5   name: hivpr1_23119_3/hivpr1_23119_3_unrelaxed_rank_005_alphafold2_multimer_v3_mo
```

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

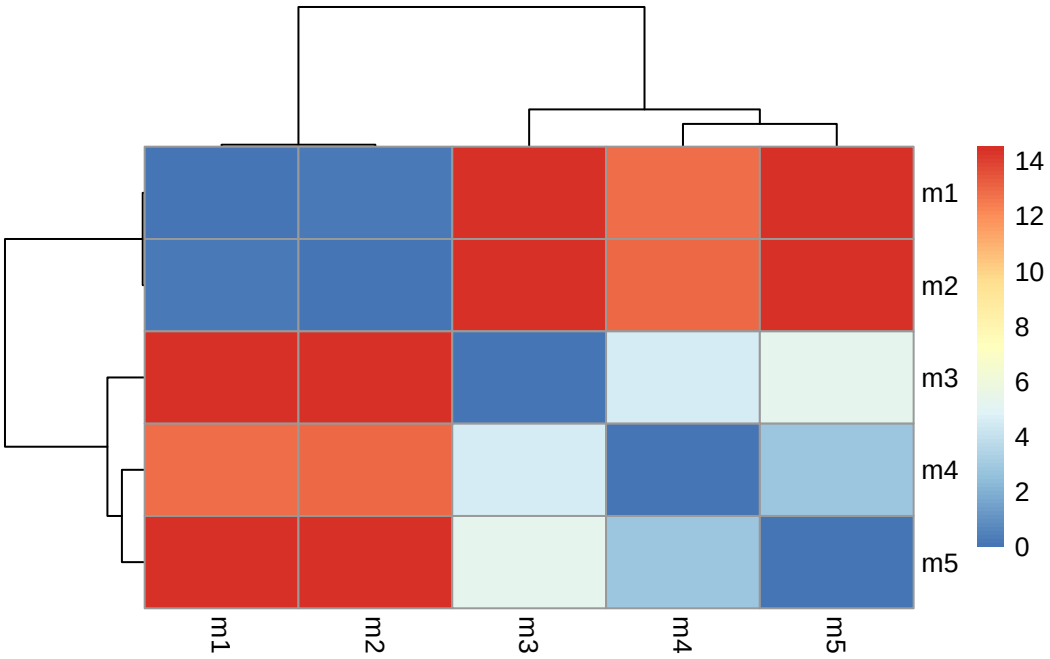
```
Warning in rmsd(pdbs, fit = T): No indices provided, using the 198 non NA positions
```

```
range(rd)
```

```
[1]  0.000 14.507
```

```
#install.packages("pheatmap")
library(pheatmap)

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

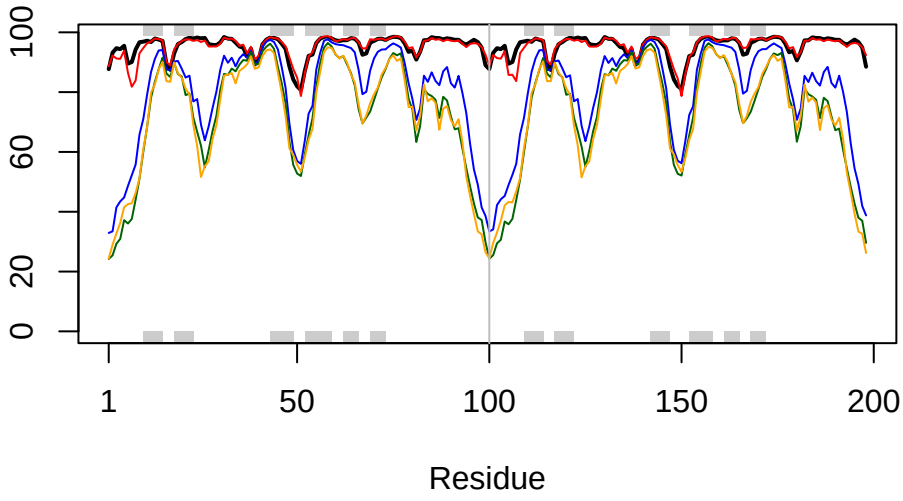



```
# Read a reference PDB structure
pdb <- read.pdb("1hsg")
```

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

```
#Plotting a graph of the structure with the B-factor values. This tells you how close our

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")
```



We can improve the superposition of our models by finding the most consistent "rigid core"

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

```
core size 197 of 198  vol = 5017.575
core size 196 of 198  vol = 4299.435
core size 195 of 198  vol = 4030.748
core size 194 of 198  vol = 3797.206
core size 193 of 198  vol = 3567.079
core size 192 of 198  vol = 3378.418
core size 191 of 198  vol = 3249.288
core size 190 of 198  vol = 3149.195
core size 189 of 198  vol = 3070.236
core size 188 of 198  vol = 2993.935
core size 187 of 198  vol = 2917.544
core size 186 of 198  vol = 2865.238
core size 185 of 198  vol = 2834.939
core size 184 of 198  vol = 2825.486
core size 183 of 198  vol = 2833.877
core size 182 of 198  vol = 2894.587
core size 181 of 198  vol = 2975.737
core size 180 of 198  vol = 3026.384
```

```
core size 179 of 198  vol = 3070.781
core size 178 of 198  vol = 3121.088
core size 177 of 198  vol = 3127.533
core size 176 of 198  vol = 3102.18
core size 175 of 198  vol = 3060.317
core size 174 of 198  vol = 2993.711
core size 173 of 198  vol = 2902.618
core size 172 of 198  vol = 2841.698
core size 171 of 198  vol = 2771.266
core size 170 of 198  vol = 2708.043
core size 169 of 198  vol = 2615.992
core size 168 of 198  vol = 2540.542
core size 167 of 198  vol = 2471.706
core size 166 of 198  vol = 2396.453
core size 165 of 198  vol = 2324.645
core size 164 of 198  vol = 2258.422
core size 163 of 198  vol = 2189.703
core size 162 of 198  vol = 2118.426
core size 161 of 198  vol = 2048.438
core size 160 of 198  vol = 1964.121
core size 159 of 198  vol = 1877.923
core size 158 of 198  vol = 1801.933
core size 157 of 198  vol = 1719.451
core size 156 of 198  vol = 1640.389
core size 155 of 198  vol = 1561.767
core size 154 of 198  vol = 1490.107
core size 153 of 198  vol = 1416.212
core size 152 of 198  vol = 1345.494
core size 151 of 198  vol = 1287.606
core size 150 of 198  vol = 1225.523
core size 149 of 198  vol = 1168.6
core size 148 of 198  vol = 1123.809
core size 147 of 198  vol = 1069.607
core size 146 of 198  vol = 1028.33
core size 145 of 198  vol = 986.295
core size 144 of 198  vol = 947.191
core size 143 of 198  vol = 910.624
core size 142 of 198  vol = 868.922
core size 141 of 198  vol = 829.982
core size 140 of 198  vol = 788.548
core size 139 of 198  vol = 749.234
core size 138 of 198  vol = 713.554
core size 137 of 198  vol = 679.035
```

```
core size 136 of 198  vol = 639.012
core size 135 of 198  vol = 599.236
core size 134 of 198  vol = 556.226
core size 133 of 198  vol = 521.307
core size 132 of 198  vol = 484.526
core size 131 of 198  vol = 453.614
core size 130 of 198  vol = 422.947
core size 129 of 198  vol = 404.641
core size 128 of 198  vol = 397.064
core size 127 of 198  vol = 371.629
core size 126 of 198  vol = 355.609
core size 125 of 198  vol = 334.859
core size 124 of 198  vol = 313.691
core size 123 of 198  vol = 291.489
core size 122 of 198  vol = 268.734
core size 121 of 198  vol = 245.865
core size 120 of 198  vol = 236.559
core size 119 of 198  vol = 218.641
core size 118 of 198  vol = 201.313
core size 117 of 198  vol = 183.861
core size 116 of 198  vol = 167.249
core size 115 of 198  vol = 151.276
core size 114 of 198  vol = 137.843
core size 113 of 198  vol = 124.983
core size 112 of 198  vol = 112.07
core size 111 of 198  vol = 101.394
core size 110 of 198  vol = 91.994
core size 109 of 198  vol = 82.201
core size 108 of 198  vol = 74.644
core size 107 of 198  vol = 70.256
core size 106 of 198  vol = 64.859
core size 105 of 198  vol = 58.745
core size 104 of 198  vol = 54.966
core size 103 of 198  vol = 49.885
core size 102 of 198  vol = 45.389
core size 101 of 198  vol = 41.648
core size 100 of 198  vol = 38.714
core size 99 of 198  vol = 36.289
core size 98 of 198  vol = 33.698
core size 97 of 198  vol = 28.156
core size 96 of 198  vol = 23.583
core size 95 of 198  vol = 19.899
core size 94 of 198  vol = 16.637
```

```
 core size 93 of 198  vol = 12.448
 core size 92 of 198  vol = 9.42
 core size 91 of 198  vol = 8.296
 core size 90 of 198  vol = 5.783
 core size 89 of 198  vol = 4.006
 core size 88 of 198  vol = 2.903
 core size 87 of 198  vol = 2.24
 core size 86 of 198  vol = 1.765
 core size 85 of 198  vol = 1.408
 core size 84 of 198  vol = 1.164
 core size 83 of 198  vol = 0.969
 core size 82 of 198  vol = 0.833
 core size 81 of 198  vol = 0.675
 core size 80 of 198  vol = 0.579
 core size 79 of 198  vol = 0.529
 core size 78 of 198  vol = 0.456
 FINISHED: Min vol ( 0.5 ) reached
```

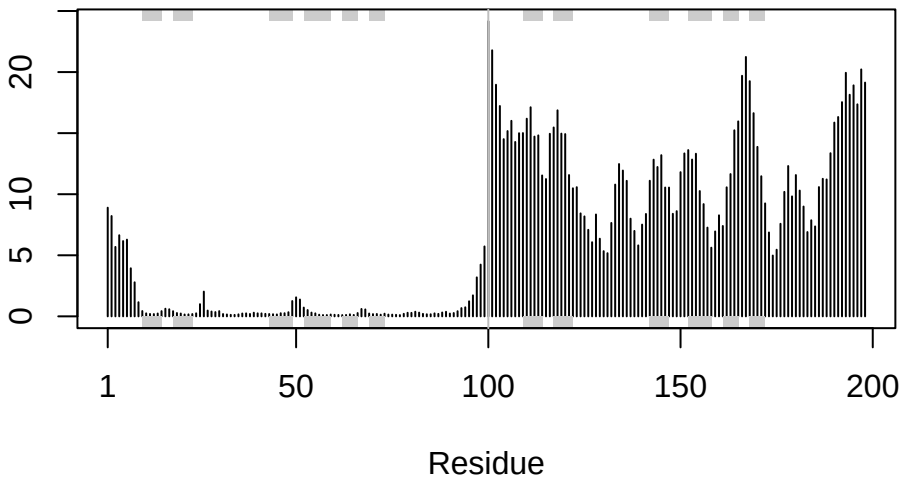
```
core.inds <- print(core, vol=0.5)
```

```
# 79 positions (cumulative volume <= 0.5 Angstrom^3)
  start end length
1    10  24     15
2    27  48     22
3    53  94     42
```

```
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