Class 11: Structural Bioinformatics (pt2. Focus on new AlphaFold2)

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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://github.com/sokrypton/ColabFold

In particular we used their AlphaFold2_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 the PDB structures up in Mol*

```
library(bio3d)

# Change this for YOUR results dir name
results_dir <- "hivprDimer2_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] "hivpr1_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_5_seed_000.pdb"
[2] "hivpr1_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_000.pdb"
[3] "hivpr1_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000.pdb"
[4] "hivpr1_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.pdb"
[5] "hivpr1_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.pdb"
```

```
pdbs <- pdbaln(pdb_files, fit=TRUE, exefile="msa")
```

```
Reading PDB files:
hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_5_seed_000.p
hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_000.p
hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000.p
hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.p
hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.p
.....

Extracting sequences

pdb/seq: 1   name: hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_001_alphafold2_multimer_v3
pdb/seq: 2   name: hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_002_alphafold2_multimer_v3
pdb/seq: 3   name: hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_003_alphafold2_multimer_v3
pdb/seq: 4   name: hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_004_alphafold2_multimer_v3
pdb/seq: 5   name: hivprDimer2_23119//hivpr1_23119_unrelaxed_rank_005_alphafold2_multimer_v3
```

```
pdbs
```

```
                               1        .         .         .         .         50
[Truncated_Name:1]hivpr1_231   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:2]hivpr1_231   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:3]hivpr1_231   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:4]hivpr1_231   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
[Truncated_Name:5]hivpr1_231   PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
                               **************************************************
                               1        .         .         .         .         50

                              51        .         .         .         .         100
[Truncated_Name:1]hivpr1_231   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:2]hivpr1_231   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:3]hivpr1_231   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:4]hivpr1_231   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
[Truncated_Name:5]hivpr1_231   GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFP
                               **************************************************
                              51        .         .         .         .         100

                             101        .         .         .         .         150
[Truncated_Name:1]hivpr1_231   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
```

```
[Truncated_Name:2]hivpr1_231   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:3]hivpr1_231   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:4]hivpr1_231   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
[Truncated_Name:5]hivpr1_231   QITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIG
                               **************************************************
                             101         .         .         .         .        150

                             151         .         .         .         .      198
[Truncated_Name:1]hivpr1_231   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:2]hivpr1_231   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:3]hivpr1_231   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:4]hivpr1_231   GFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
[Truncated_Name:5]hivpr1_231   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
```

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

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

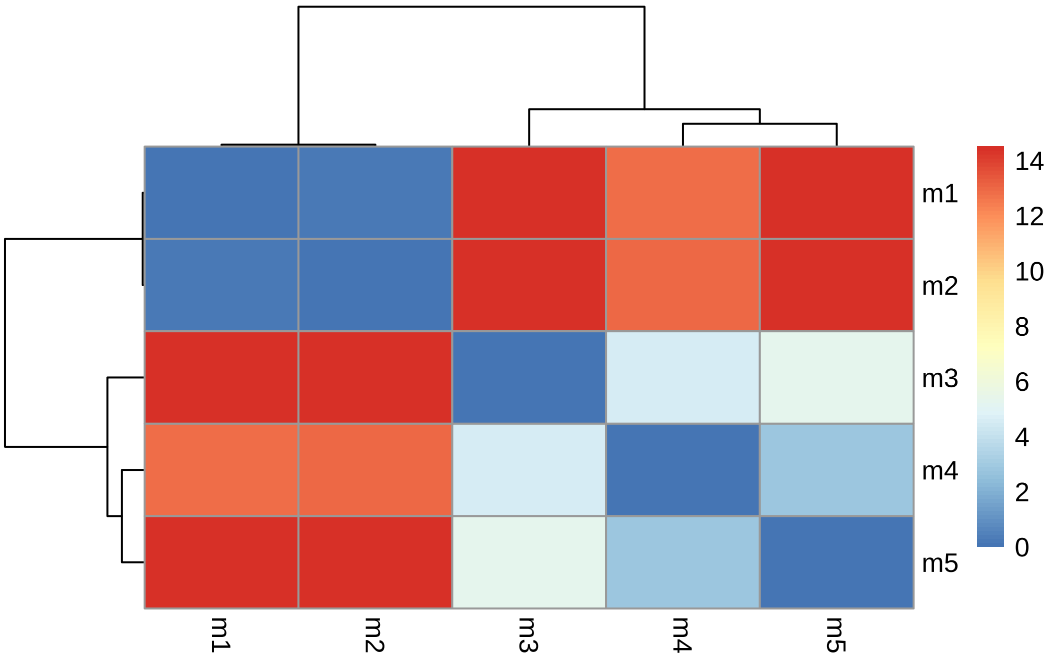
```r
range(rd)
```

```
[1]  0.000 14.507
```

Heatmap:

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

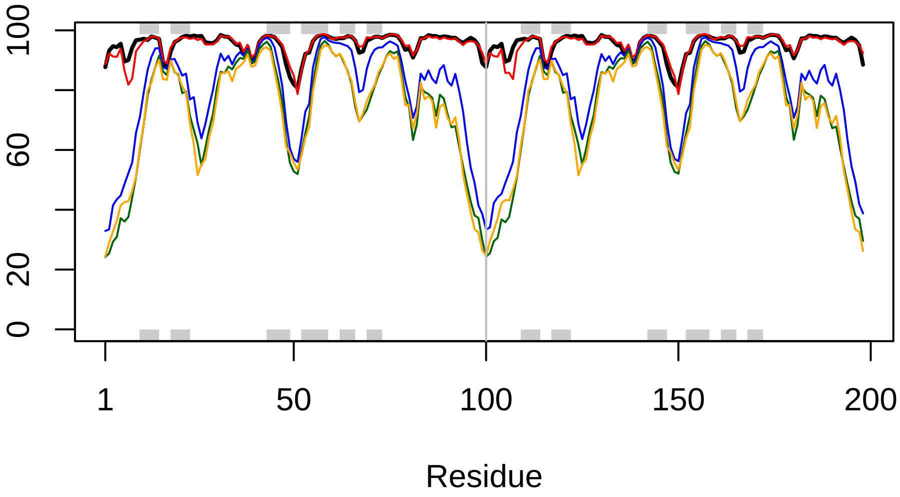
```
colnames(rd) <- paste0("m",1:5)
rownames(rd) <- paste0("m",1:5)
pheatmap(rd)
```



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

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

```
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 = 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
```

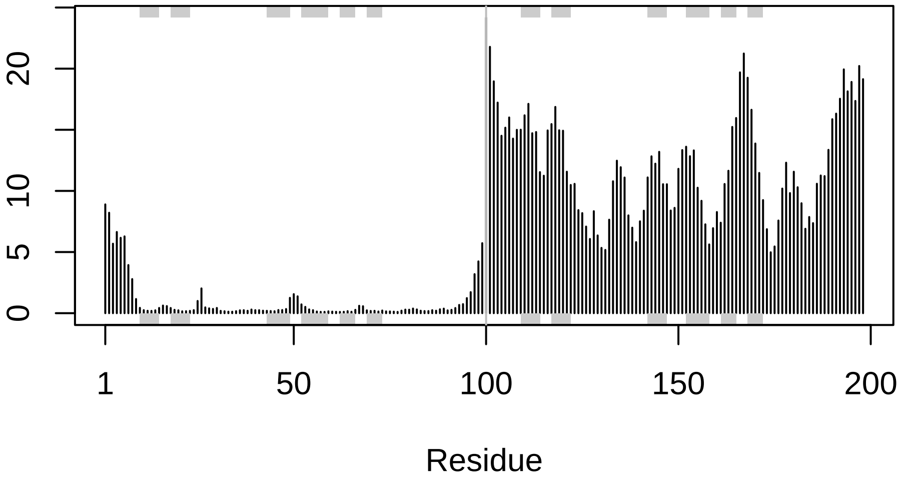
```
core.inds <- print(core, vol=0.5)
```

```
# 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")
```



Predicted Alignment Error for domains

```
library(jsonlite)

# Listing of all PAE JSON files
pae_files <- list.files(path=results_dir,
                        pattern=".*model.*\\.json",
                        full.names = TRUE)

pae1 <- read_json(pae_files[1],simplifyVector = TRUE)
pae5 <- read_json(pae_files[5],simplifyVector = TRUE)

attributes(pae1)
```

```
$names
[1] "plddt"   "max_pae" "pae"     "ptm"     "iptm"
```

```
# Per-residue pLDDT scores
#  same as B-factor of PDB..
head(pae1$plddt)
```

```
[1] 87.69 93.19 94.69 94.38 95.50 89.56
```

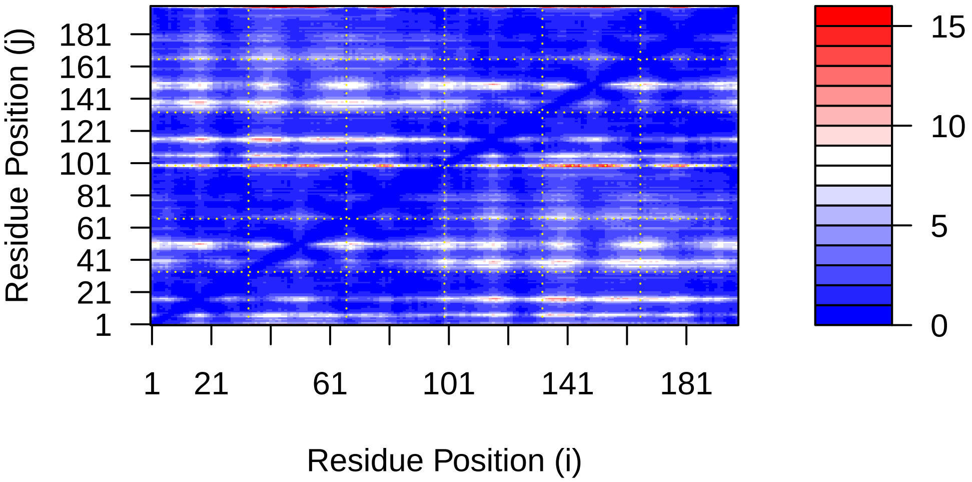
```
pae1$max_pae
```

```
[1] 15.89844
```

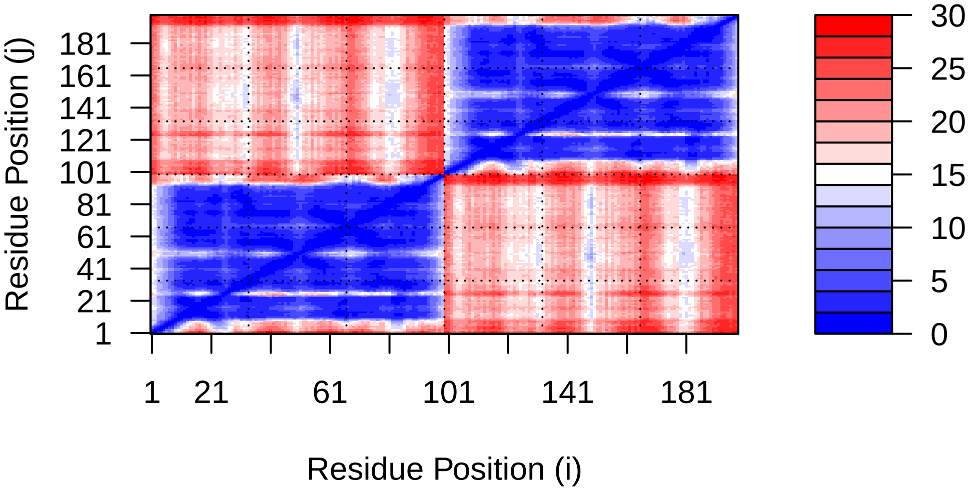
```
pae5$max_pae
```

```
[1] 29.25
```

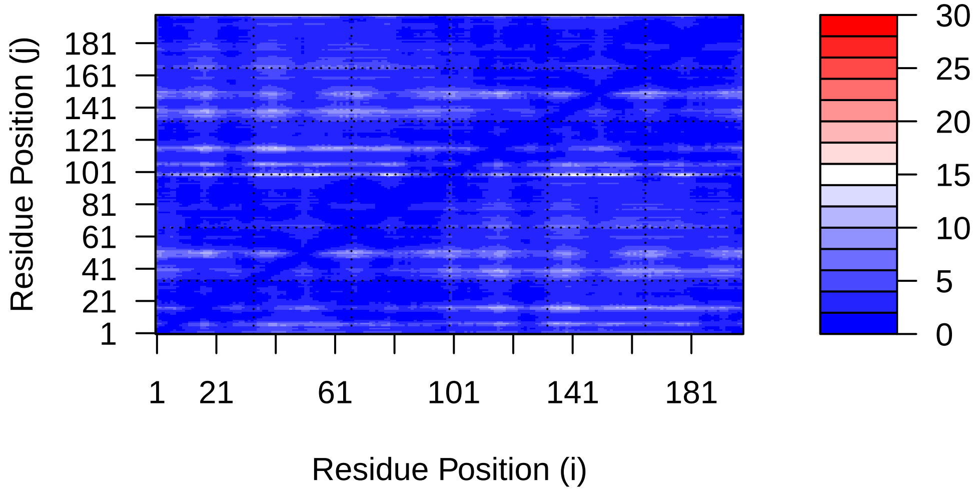
```
plot.dmat(pae1$pae,
          xlab="Residue Position (i)",
          ylab="Residue Position (j)")
```



```
plot.dmat(pae5$pae,
          xlab="Residue Position (i)",
          ylab="Residue Position (j)",
          grid.col = "black",
          zlim=c(0,30))
```



```
plot.dmat(pae1$pae,
          xlab="Residue Position (i)",
          ylab="Residue Position (j)",
          grid.col = "black",
          zlim=c(0,30))
```


Residue Position (j)
181
161
141
121
101
81
61
41
21
1
1
21
61
101
141
181
Residue Position (i)
30
25
20
15
10
5
0