Novembe 08, 2023 Class 11 Alpha Fold

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AlphaFold2 stuff! AF

My results from AF live in the folder/directory `hivprodimer_23119`

```
results_dir<-"hivprdimer_23119"

pdb_files<-list.files(results_dir, pattern=".pdb", full.names=T)
```

Oh boy, gang it looks like we'er doing align and superimpose using `pdbaln()`

```
library(bio3d)
pdbs<-pdbaln(pdb_files,fit=TRUE,exefile="msa")
```

```
Reading PDB files:
hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_000
hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_000
hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000
hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000
hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000
.....

Extracting sequences

pdb/seq: 1   name: hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_001_alphafold2_multimer_v
pdb/seq: 2   name: hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_002_alphafold2_multimer_v
pdb/seq: 3   name: hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_003_alphafold2_multimer_v
pdb/seq: 4   name: hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_004_alphafold2_multimer_v
pdb/seq: 5   name: hivprdimer_23119/HivPrdimer_23119_unrelaxed_rank_005_alphafold2_multimer_v
```

The RMSD matrix

A common measure of structural dis-similarity is called RMSD (root mean square distance).

```r
rd<- rmsd(pdbs)
```

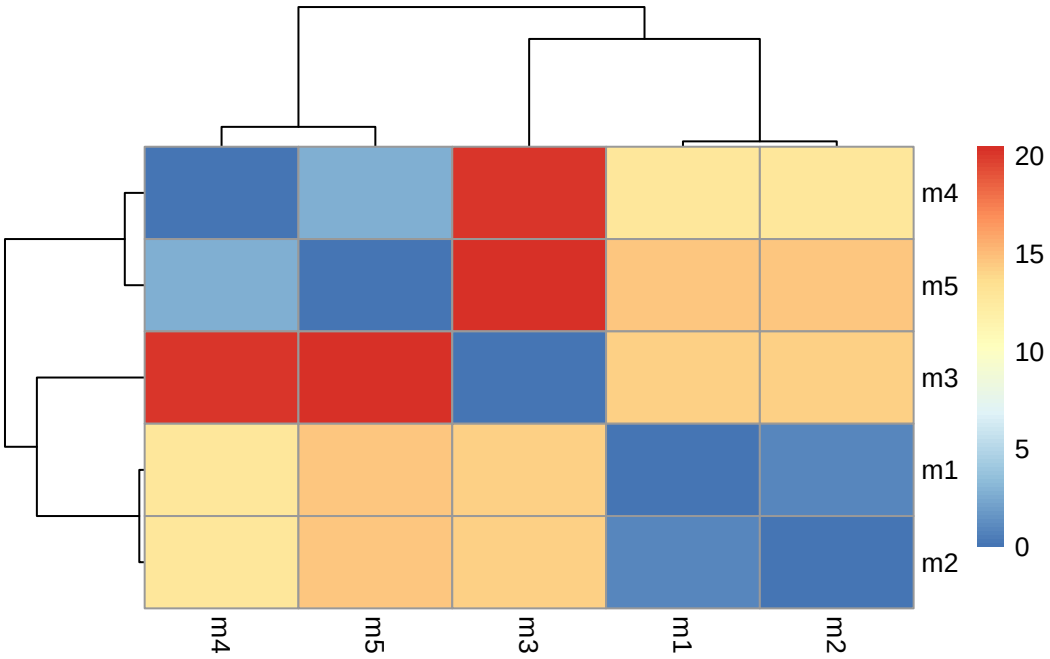
```
Warning in rmsd(pdbs): No indices provided, using the 198 non NA positions
```

```r
rd
```

```
                                                                            HivPrdimer_23119_
HivPrdimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_000
HivPrdimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_000
HivPrdimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000
HivPrdimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000
HivPrdimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000
                                                                            HivPrdimer_23119_
HivPrdimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_000
HivPrdimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_000
HivPrdimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000
HivPrdimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000
HivPrdimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000
                                                                            HivPrdimer_23119_
HivPrdimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_000
HivPrdimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_000
HivPrdimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000
HivPrdimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000
HivPrdimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000
                                                                            HivPrdimer_23119_
HivPrdimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_000
HivPrdimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_000
HivPrdimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000
HivPrdimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000
HivPrdimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000
                                                                            HivPrdimer_23119_
HivPrdimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_000
HivPrdimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_000
HivPrdimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000
HivPrdimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000
HivPrdimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000
```

```
library(pheatmap)

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



Let's view this in Mol*

```
xyz<-pdbfit(pdbs,outfile="fitted")
```

A full atom based fitting or superposition did not work very well because we have multiple chains that are in different conformations.

We want to focus our superposition on the most invariant part. (That's the "core", so to say)

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

```
core size 197 of 198  vol = 6154.839
core size 196 of 198  vol = 5399.676
core size 195 of 198  vol = 5074.795
```

```
core size 194 of 198  vol = 4802.518
core size 193 of 198  vol = 4520.256
core size 192 of 198  vol = 4305.362
core size 191 of 198  vol = 4089.792
core size 190 of 198  vol = 3886.145
core size 189 of 198  vol = 3758.321
core size 188 of 198  vol = 3620.18
core size 187 of 198  vol = 3496.698
core size 186 of 198  vol = 3389.985
core size 185 of 198  vol = 3320.114
core size 184 of 198  vol = 3258.683
core size 183 of 198  vol = 3208.591
core size 182 of 198  vol = 3156.736
core size 181 of 198  vol = 3141.668
core size 180 of 198  vol = 3136.574
core size 179 of 198  vol = 3155.52
core size 178 of 198  vol = 3185.362
core size 177 of 198  vol = 3204.487
core size 176 of 198  vol = 3211.978
core size 175 of 198  vol = 3234.993
core size 174 of 198  vol = 3244.062
core size 173 of 198  vol = 3237.845
core size 172 of 198  vol = 3218.77
core size 171 of 198  vol = 3180.743
core size 170 of 198  vol = 3130.369
core size 169 of 198  vol = 3067.881
core size 168 of 198  vol = 2989.546
core size 167 of 198  vol = 2928.272
core size 166 of 198  vol = 2851.193
core size 165 of 198  vol = 2780.877
core size 164 of 198  vol = 2708.433
core size 163 of 198  vol = 2636.516
core size 162 of 198  vol = 2563.25
core size 161 of 198  vol = 2478.024
core size 160 of 198  vol = 2404.793
core size 159 of 198  vol = 2330.997
core size 158 of 198  vol = 2250.477
core size 157 of 198  vol = 2159.432
core size 156 of 198  vol = 2070.759
core size 155 of 198  vol = 1983.579
core size 154 of 198  vol = 1917.913
core size 153 of 198  vol = 1842.556
core size 152 of 198  vol = 1775.398
```

```
core size 151 of 198  vol = 1695.133
core size 150 of 198  vol = 1632.173
core size 149 of 198  vol = 1570.391
core size 148 of 198  vol = 1497.238
core size 147 of 198  vol = 1434.802
core size 146 of 198  vol = 1367.706
core size 145 of 198  vol = 1302.596
core size 144 of 198  vol = 1251.985
core size 143 of 198  vol = 1207.976
core size 142 of 198  vol = 1167.112
core size 141 of 198  vol = 1118.27
core size 140 of 198  vol = 1081.664
core size 139 of 198  vol = 1029.75
core size 138 of 198  vol = 981.766
core size 137 of 198  vol = 944.446
core size 136 of 198  vol = 899.224
core size 135 of 198  vol = 859.402
core size 134 of 198  vol = 814.694
core size 133 of 198  vol = 771.862
core size 132 of 198  vol = 733.807
core size 131 of 198  vol = 702.053
core size 130 of 198  vol = 658.757
core size 129 of 198  vol = 622.574
core size 128 of 198  vol = 578.29
core size 127 of 198  vol = 543.07
core size 126 of 198  vol = 510.934
core size 125 of 198  vol = 481.595
core size 124 of 198  vol = 464.672
core size 123 of 198  vol = 451.721
core size 122 of 198  vol = 430.417
core size 121 of 198  vol = 409.141
core size 120 of 198  vol = 378.942
core size 119 of 198  vol = 348.325
core size 118 of 198  vol = 324.738
core size 117 of 198  vol = 312.394
core size 116 of 198  vol = 300.89
core size 115 of 198  vol = 279.976
core size 114 of 198  vol = 263.434
core size 113 of 198  vol = 250.263
core size 112 of 198  vol = 229.592
core size 111 of 198  vol = 209.929
core size 110 of 198  vol = 196.379
core size 109 of 198  vol = 180.628
```

```
core size 108 of 198  vol = 167.088
core size 107 of 198  vol = 155.875
core size 106 of 198  vol = 142.595
core size 105 of 198  vol = 128.924
core size 104 of 198  vol = 114.054
core size 103 of 198  vol = 100.936
core size 102 of 198  vol = 90.431
core size 101 of 198  vol = 81.972
core size 100 of 198  vol = 74.017
core size 99 of 198  vol = 66.855
core size 98 of 198  vol = 59.525
core size 97 of 198  vol = 52.263
core size 96 of 198  vol = 43.699
core size 95 of 198  vol = 35.813
core size 94 of 198  vol = 28.888
core size 93 of 198  vol = 20.692
core size 92 of 198  vol = 14.975
core size 91 of 198  vol = 9.146
core size 90 of 198  vol = 5.232
core size 89 of 198  vol = 3.53
core size 88 of 198  vol = 2.657
core size 87 of 198  vol = 1.998
core size 86 of 198  vol = 1.333
core size 85 of 198  vol = 1.141
core size 84 of 198  vol = 1.012
core size 83 of 198  vol = 0.891
core size 82 of 198  vol = 0.749
core size 81 of 198  vol = 0.618
core size 80 of 198  vol = 0.538
core size 79 of 198  vol = 0.479
FINISHED: Min vol ( 0.5 ) reached
```

```
core.inds<-core
```

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

To evaluate how good our multi-chain or multi-domain models are, we need to look at the PAE scores (predicted alignment error)

There are output as JSON format files. Let's find all their file names:

```
pae_files<-list.files(results_dir,pattern="000.json",full.names=T)
pae_files
```

```
[1] "hivprdimer_23119/HivPrdimer_23119_scores_rank_001_alphafold2_multimer_v3_model_1_seed_0
[2] "hivprdimer_23119/HivPrdimer_23119_scores_rank_002_alphafold2_multimer_v3_model_5_seed_0
[3] "hivprdimer_23119/HivPrdimer_23119_scores_rank_003_alphafold2_multimer_v3_model_4_seed_0
[4] "hivprdimer_23119/HivPrdimer_23119_scores_rank_004_alphafold2_multimer_v3_model_2_seed_0
[5] "hivprdimer_23119/HivPrdimer_23119_scores_rank_005_alphafold2_multimer_v3_model_3_seed_0
```

```
library(jsonlite)

pae1<- read_json(pae_files[1],simplifyVector=TRUE)
attributes(pae1)
```

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

```
pae1$max_pae
```

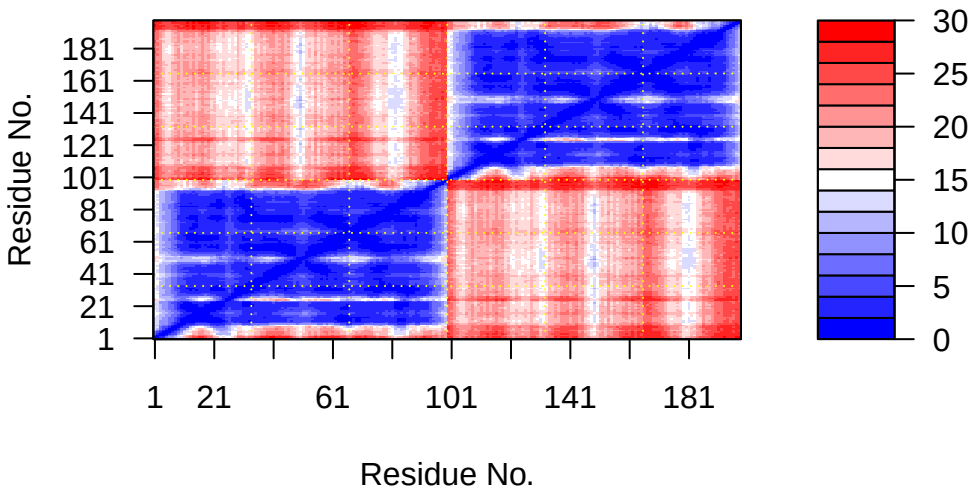
```
[1] 15.54688
```

```
pae5<- read_json(pae_files[5],simplifyVector=TRUE)
pae5$max_pae
```

```
[1] 29.29688
```

The 5th has 2x the error that the 1st one has.

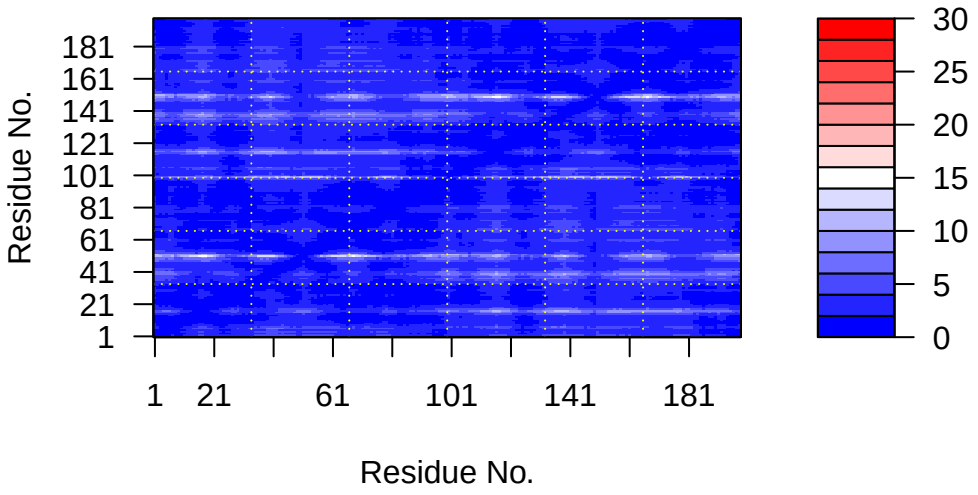
```
plot.dmat(pae5$pae,
          xlab="Residue No.",
          ylab="Residue No.",
          zlim=c(0,30))
```



This plot above shows low error in the first chain and high error in the second chain.

We could put this in an `apply()` function to read all 5 pae for each of the alignments.

```
plot.dmat(pae1$pae,
          xlab="Residue No.",
          ylab="Residue No.",
          zlim=c(0,30))
```



Note that this has far less red, which indicates less error. I also added zlim to limit the z to be plotting the same axis size (or intensity/error size)

We can run AF on google compute infrastructure which is very very helpful. We can read these results into R, and process to help make sense of the results in R, which would help us make sense of the PLDDT and PAE scores.