Class 11: Protein Structure Prediction with AlphaFold

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Here we post process and inspect our modeling results from AlphaFold2 (AF2).

My results from AF2 live in the folder/directory `hivprdimer_23119`

```r
results_dir <- "hivprdimer_23119/"

#listing only pdb files in the dir, and giving full names as a vector
pdb_files <- list.files(results_dir, pattern = ".pdb", full.names = TRUE)
```

We first need to align and superpose these PDB models and we can use the `pdbaln()` function for this

```r
library(bio3d)
# Align releated PDBs
pdbs <- pdbaln(pdb_files, fit = TRUE, exefile = "msa")
```

```
Reading PDB files:
hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_00
hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_00
hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_00
hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_00
hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_00
.....

Extracting sequences

pdb/seq: 1   name: hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_001_alphafold2_multimer
pdb/seq: 2   name: hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_002_alphafold2_multimer
pdb/seq: 3   name: hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_003_alphafold2_multimer
pdb/seq: 4   name: hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_004_alphafold2_multimer
```

```
pdb/seq: 5   name: hivprdimer_23119//hivprdimer_23119_unrelaxed_rank_005_alphafold2_multimer
```

> pdbs

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

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

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

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

The RMSD Matrix

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

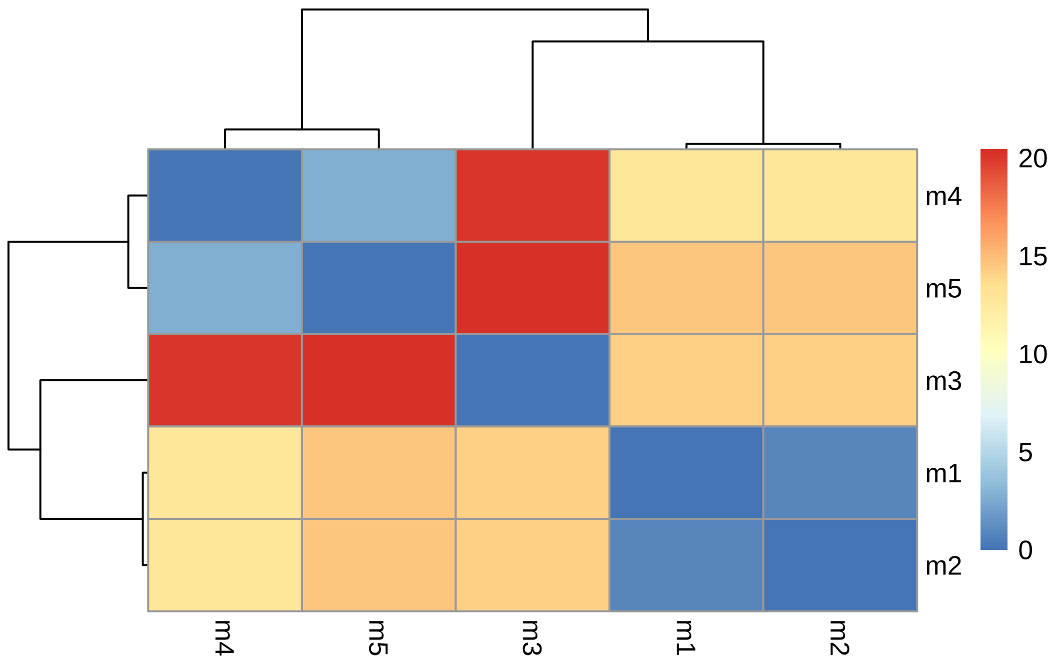
```r
rd <- rmsd(pdbs)
```

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

```r
#Visualizing using pheatmap
library(pheatmap)

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

pheatmap(rd)
```



Let's view these in Mol*. Here we want the fitted coordinates to load into Molstar.

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

It's still shite! A full atom based fitting or superposition did not work very well because we have multiple chains that are in different conformations, causing 'smearing' in our visualizing.

I want to focus our superposition on the most invariant part (the rigid "core") so that we get less 'smearing' when visualizing. To do so, we will use the function `core.find()`, which finds the most common invariant part of the given sequences.

```r
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
```

```r
core.inds <- core #defining inds argument of pdbfit(), which is an xyz component that pdbf

xyz <- pdbfit(pdbs, inds = core.inds, outpath = "core_fitted")
#load "core_fitted" into Mol*... it's better!
```

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

They are output as JSON format files. Let’s find all their file names:

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

```
[1] "hivprdimer_23119//config.json"
[2] "hivprdimer_23119//hivprdimer_23119_predicted_aligned_error_v1.json"
[3] "hivprdimer_23119//hivprdimer_23119_scores_rank_001_alphafold2_multimer_v3_model_1_seed_(
[4] "hivprdimer_23119//hivprdimer_23119_scores_rank_002_alphafold2_multimer_v3_model_5_seed_
[5] "hivprdimer_23119//hivprdimer_23119_scores_rank_003_alphafold2_multimer_v3_model_4_seed_
[6] "hivprdimer_23119//hivprdimer_23119_scores_rank_004_alphafold2_multimer_v3_model_2_seed_
[7] "hivprdimer_23119//hivprdimer_23119_scores_rank_005_alphafold2_multimer_v3_model_3_seed_
```

```r
pae_files <- list.files(results_dir, pattern = "0.json", full.names = TRUE) #excluding the
pae_files
```

```
[1] "hivprdimer_23119//hivprdimer_23119_scores_rank_001_alphafold2_multimer_v3_model_1_seed_
[2] "hivprdimer_23119//hivprdimer_23119_scores_rank_002_alphafold2_multimer_v3_model_5_seed_
[3] "hivprdimer_23119//hivprdimer_23119_scores_rank_003_alphafold2_multimer_v3_model_4_seed_
[4] "hivprdimer_23119//hivprdimer_23119_scores_rank_004_alphafold2_multimer_v3_model_2_seed_
[5] "hivprdimer_23119//hivprdimer_23119_scores_rank_005_alphafold2_multimer_v3_model_3_seed_
```

Using `jsonlite` to open the JSON files:

```r
library(jsonlite)

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

Looking at PAE for top and bottom ‘ranked’ files:

```r
pae1$max_pae
```

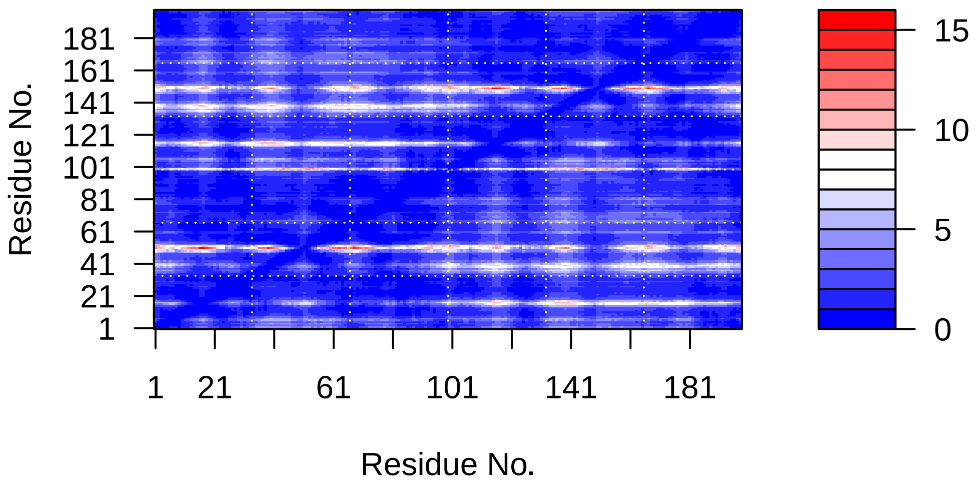
```
[1] 15.54688
```

```r
pae5$max_pae
```

```
[1] 29.29688
```

Plotting pae1: lowest PAE of all

```r
plot.dmat(pae1$pae,
          xlab = "Residue No.",
          ylab = "Residue No.")
```



Main Points

We can run AF on Google Compute infrastructure We can read these results into R and process to help make sense of these models and their PAE and pLDDT scores.