class11

Thrisha Praveen

5. The EBI AlphaFold database

Querying the AlphaFold database

Q1. Use the following sequence to search AFDB: >HIV-Pr PQITLWQRPLVTIKIG-GQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIGGFIKVR

2. Examine one of your top hits. Note that at the time of writing HIV virus structures are not included in the current AFDB. However, there are a number of very closely related sequences from other species with informative models that we can learn from.

My top hit was "Peptidase A2 domain-containing protein" from Thalassobius mangrovi. UniProt id: A0A6L8LSL6

6. Generating your own structure predictions

Followed instructions from the Lab 11 site.

7. Interpreting Results

Visualization of the models and their estimated reliability - Using Mol*

Can you identify the most variable regions by eye? Some of the most variable regions by eye occur in the alpha-helix-like structures.

Color each structure by their computed pLDDT scores Most of the structure is red (high-confidence), but the helix-like structures at the tails of the structure have a lighter-red or white color, meaning there is less confidence in those parts of the structure.

8. Custom analysis of resulting models

```
# Change this for YOUR results dir name
results_dir <- "hivprdimer_23119/"
```

```r
# 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] "HIVPrDimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_000.pdb"
[2] "HIVPrDimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_000.pdb"
[3] "HIVPrDimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_000.pdb"
[4] "HIVPrDimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.pdb"
[5] "HIVPrDimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.pdb"
```

```r
library(bio3d)

# Read all data from Models
#  and superpose/fit coords
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_
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_
```

```r
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
```

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

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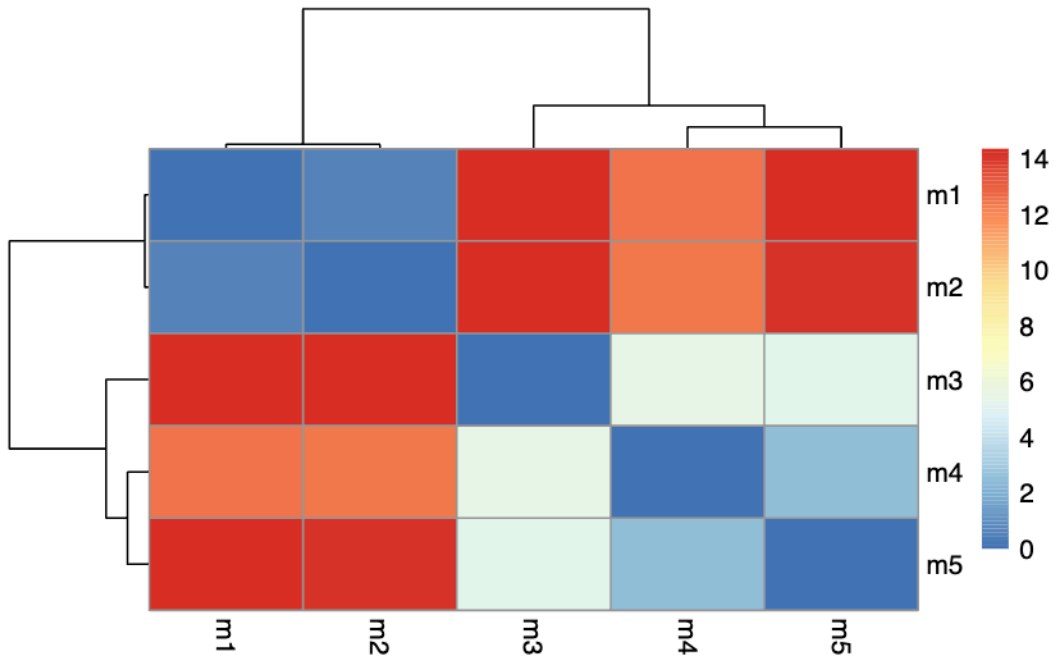
```
range(rd)
```

```
[1]  0.000 14.376
```

```
library(pheatmap)

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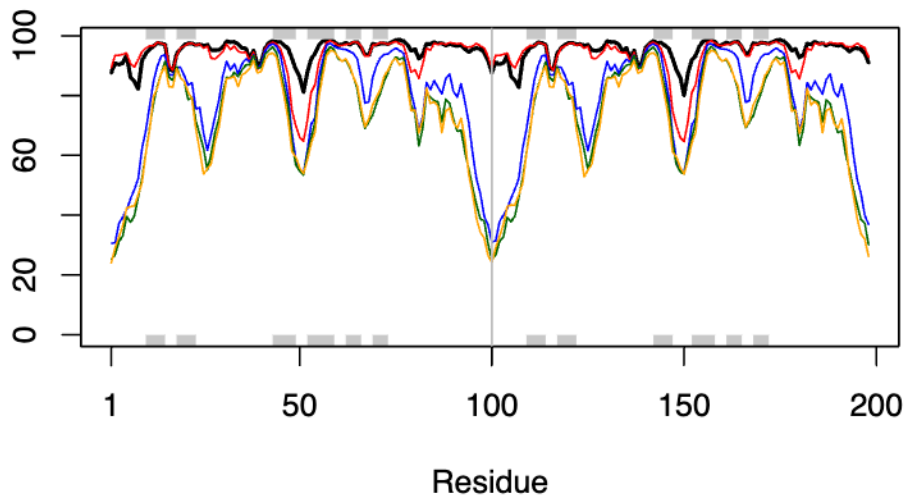


```
# Read a reference PDB structure
pdb <- read.pdb("1hsg")
```

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

4

```
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 = 4916.702
 core size 196 of 198  vol = 4311.481
 core size 195 of 198  vol = 4101.445
 core size 194 of 198  vol = 3907.124
 core size 193 of 198  vol = 3711.925
 core size 192 of 198  vol = 3546.511
 core size 191 of 198  vol = 3440.437
 core size 190 of 198  vol = 3317.571
 core size 189 of 198  vol = 3220.079
 core size 188 of 198  vol = 3142.057
 core size 187 of 198  vol = 3066.79
 core size 186 of 198  vol = 3015.892
 core size 185 of 198  vol = 2959.969
```

```
core size 184 of 198   vol = 2913.74
core size 183 of 198   vol = 2880.923
core size 182 of 198   vol = 2848.081
core size 181 of 198   vol = 2857.001
core size 180 of 198   vol = 2871.24
core size 179 of 198   vol = 2905.696
core size 178 of 198   vol = 2953.776
core size 177 of 198   vol = 3020.847
core size 176 of 198   vol = 3087.22
core size 175 of 198   vol = 3109.99
core size 174 of 198   vol = 3129.601
core size 173 of 198   vol = 3135.085
core size 172 of 198   vol = 3092.283
core size 171 of 198   vol = 3036.012
core size 170 of 198   vol = 2947.995
core size 169 of 198   vol = 2886.897
core size 168 of 198   vol = 2829.355
core size 167 of 198   vol = 2746.377
core size 166 of 198   vol = 2671.189
core size 165 of 198   vol = 2600.848
core size 164 of 198   vol = 2534.651
core size 163 of 198   vol = 2464.3
core size 162 of 198   vol = 2390.171
core size 161 of 198   vol = 2322.47
core size 160 of 198   vol = 2236.698
core size 159 of 198   vol = 2160.475
core size 158 of 198   vol = 2077.281
core size 157 of 198   vol = 2003.596
core size 156 of 198   vol = 1939.94
core size 155 of 198   vol = 1859.188
core size 154 of 198   vol = 1781.083
core size 153 of 198   vol = 1699.1
core size 152 of 198   vol = 1622.558
core size 151 of 198   vol = 1546.319
core size 150 of 198   vol = 1473.01
core size 149 of 198   vol = 1414.087
core size 148 of 198   vol = 1352.547
core size 147 of 198   vol = 1295.278
core size 146 of 198   vol = 1246.999
core size 145 of 198   vol = 1203.962
core size 144 of 198   vol = 1163.009
core size 143 of 198   vol = 1110.955
core size 142 of 198   vol = 1064.672
```

```
core size 141 of 198   vol = 1028.458
core size 140 of 198   vol = 986.121
core size 139 of 198   vol = 944.003
core size 138 of 198   vol = 895.914
core size 137 of 198   vol = 853.508
core size 136 of 198   vol = 827.977
core size 135 of 198   vol = 796.874
core size 134 of 198   vol = 772.763
core size 133 of 198   vol = 743.108
core size 132 of 198   vol = 707.65
core size 131 of 198   vol = 669.172
core size 130 of 198   vol = 634.655
core size 129 of 198   vol = 594.035
core size 128 of 198   vol = 559.154
core size 127 of 198   vol = 525.971
core size 126 of 198   vol = 493.19
core size 125 of 198   vol = 466.473
core size 124 of 198   vol = 438.433
core size 123 of 198   vol = 410.725
core size 122 of 198   vol = 401.38
core size 121 of 198   vol = 391.76
core size 120 of 198   vol = 362.084
core size 119 of 198   vol = 338.183
core size 118 of 198   vol = 312.338
core size 117 of 198   vol = 282.176
core size 116 of 198   vol = 262.215
core size 115 of 198   vol = 241.577
core size 114 of 198   vol = 225.151
core size 113 of 198   vol = 204.137
core size 112 of 198   vol = 185.038
core size 111 of 198   vol = 162.728
core size 110 of 198   vol = 146.181
core size 109 of 198   vol = 133.352
core size 108 of 198   vol = 123.207
core size 107 of 198   vol = 109.228
core size 106 of 198   vol = 98.824
core size 105 of 198   vol = 89.735
core size 104 of 198   vol = 81.206
core size 103 of 198   vol = 74.188
core size 102 of 198   vol = 67.042
core size 101 of 198   vol = 62.043
core size 100 of 198   vol = 58.432
core size 99 of 198   vol = 55.149
```

```
core size 98 of 198   vol = 51.114
core size 97 of 198   vol = 45.798
core size 96 of 198   vol = 41.161
core size 95 of 198   vol = 35.619
core size 94 of 198   vol = 29.784
core size 93 of 198   vol = 23.233
core size 92 of 198   vol = 16.669
core size 91 of 198   vol = 9.459
core size 90 of 198   vol = 4.595
core size 89 of 198   vol = 3.161
core size 88 of 198   vol = 2.678
core size 87 of 198   vol = 2.293
core size 86 of 198   vol = 1.935
core size 85 of 198   vol = 1.619
core size 84 of 198   vol = 1.367
core size 83 of 198   vol = 1.09
core size 82 of 198   vol = 0.906
core size 81 of 198   vol = 0.764
core size 80 of 198   vol = 0.649
core size 79 of 198   vol = 0.596
core size 78 of 198   vol = 0.53
core size 77 of 198   vol = 0.486
FINISHED: Min vol ( 0.5 ) reached
```

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

```
# 78 positions (cumulative volume <= 0.5 Angstrom^3)
  start end length
1    10  25     16
2    28  48     21
3    53  93     41
```
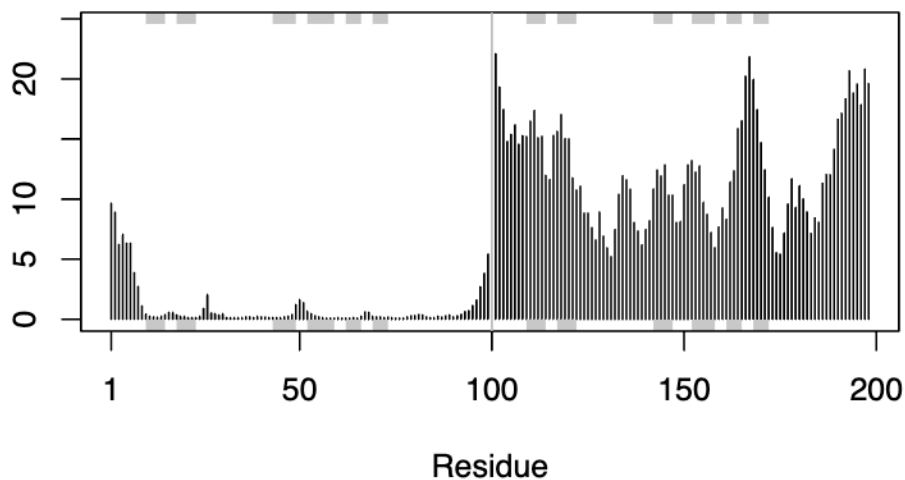
```r
xyz <- pdbfit(pdbs, core.inds, outpath="corefit_structures")
```

```r
rf <- rmsf(xyz)

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

Predicted Alignment Error for domains

```r
library(jsonlite)

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

```r
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"
```

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

```
[1] 87.69 90.81 90.38 90.88 93.44 86.06
```
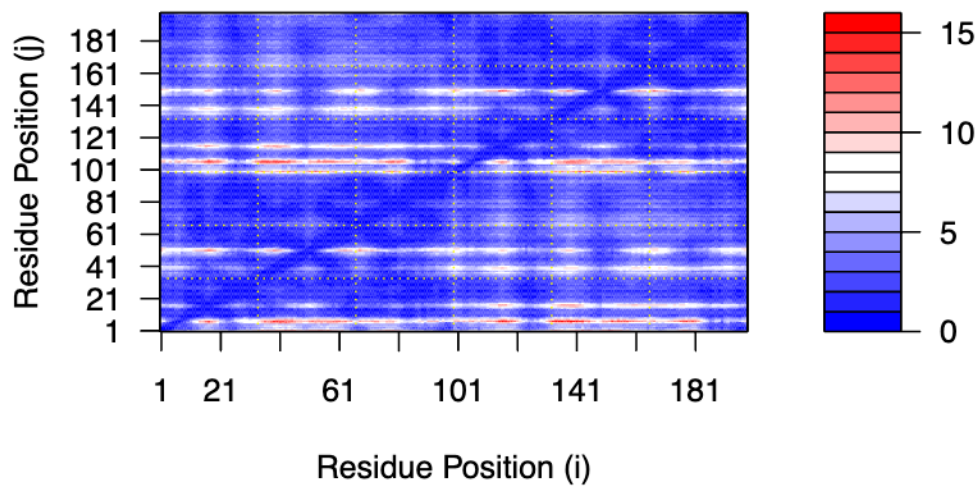
```
pae1$max_pae
```
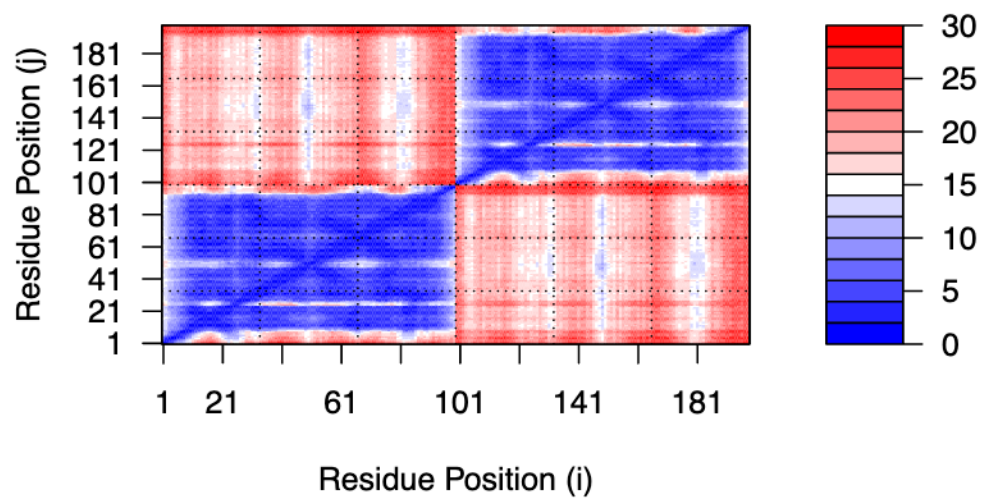
```
[1] 15.47656
```

```
pae5$max_pae
```

```
[1] 29.32812
```
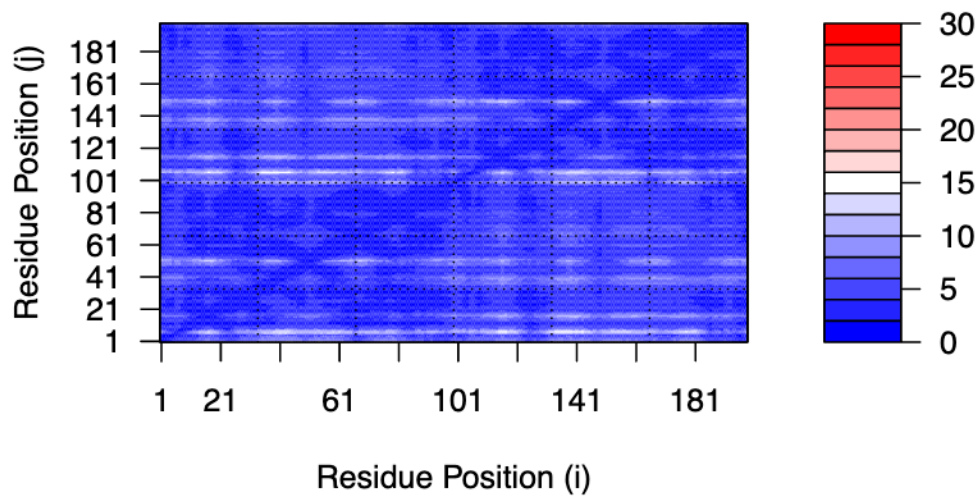
```
plot.dmat(pae1$pae,
          xlab="Residue Position (i)",
          ylab="Residue Position (j)")
```



```
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))
```

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Residue conservation from alignment file

```
aln_file <- list.files(path=results_dir,
                       pattern=".a3m$",
                       full.names = TRUE)
aln_file
```

```
[1] "hivprdimer_23119//HIVPrDimer_23119.a3m"
```

```
aln <- read.fasta(aln_file[1], to.upper = TRUE)
```
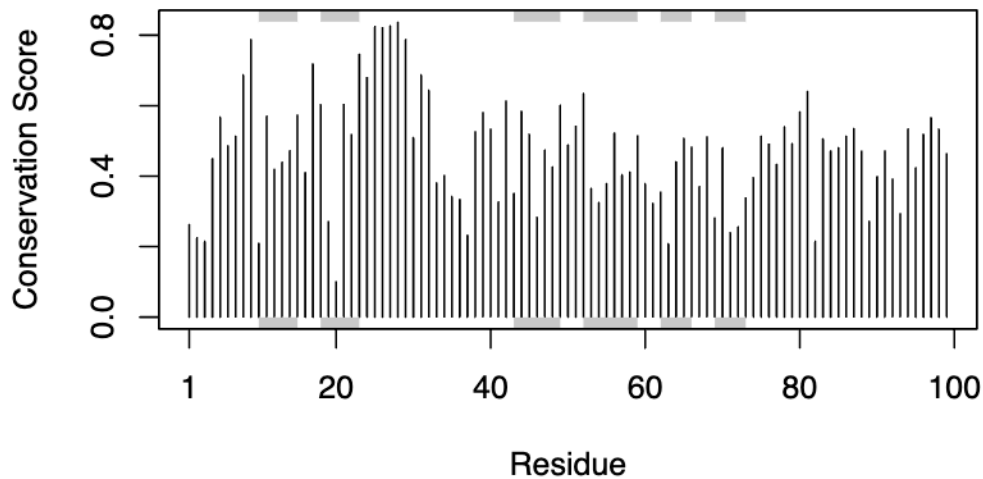
```
[1] " ** Duplicated sequence id's: 101 **"
[2] " ** Duplicated sequence id's: 101 **"
```

```
dim(aln$ali)
```

```
[1] 5378  132
```

```
sim <- conserv(aln)
```

```
plotb3(sim[1:99], sse=trim.pdb(pdb, chain="A"),
       ylab="Conservation Score")
```



```
con <- consensus(aln, cutoff = 0.9)
con$seq
```

```
  [1] "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-"
 [19] "-" "-" "-" "-" "-" "-" "D" "T" "G" "A" "-" "-" "-" "-" "-" "-" "-" "-"
 [37] "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-"
 [55] "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-"
 [73] "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-"
 [91] "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-"
[109] "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-" "-"
[127] "-" "-" "-" "-" "-" "-"
```

```
m1.pdb <- read.pdb(pdb_files[1])
occ <- vec2resno(c(sim[1:99], sim[1:99]), m1.pdb$atom$resno)
write.pdb(m1.pdb, o=occ, file="m1_conserv.pdb")
```