Class_11

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AlphaFold Data Base (AFDB)

The EBI maintains the largest database of AlphaFold structure prediction models at: https://alphafold.ebi.ac.uk

From last class we saw that the PDB had 244,290.

The total number of protein sequences in UniProtKB is 199,579,901.

```
244290/199579901 * 100
```

```
[1] 0.1224021
```

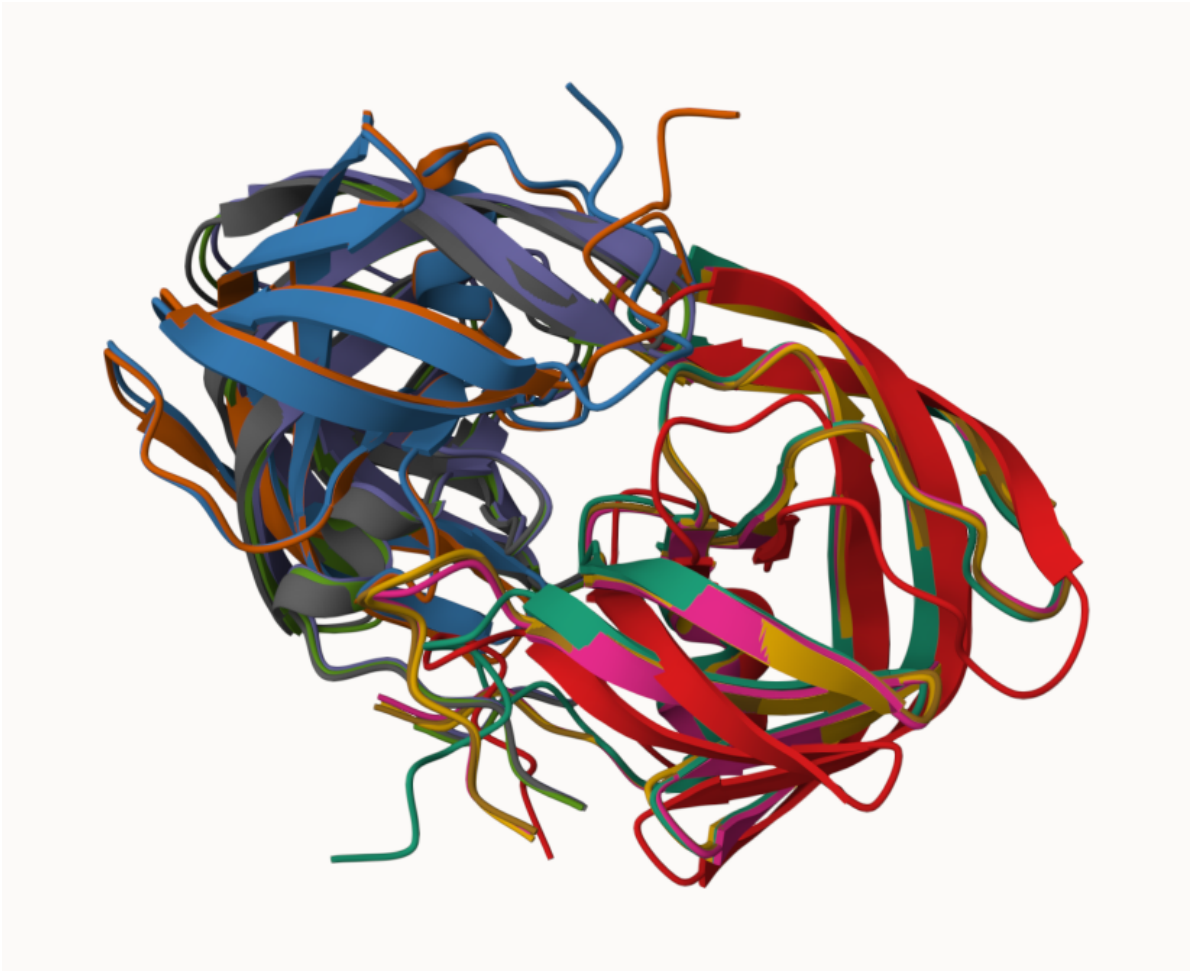
Only 0.12 percentage of all protein sequences have a structure.

AFDB is attempting to fill in this gap in knowledge.

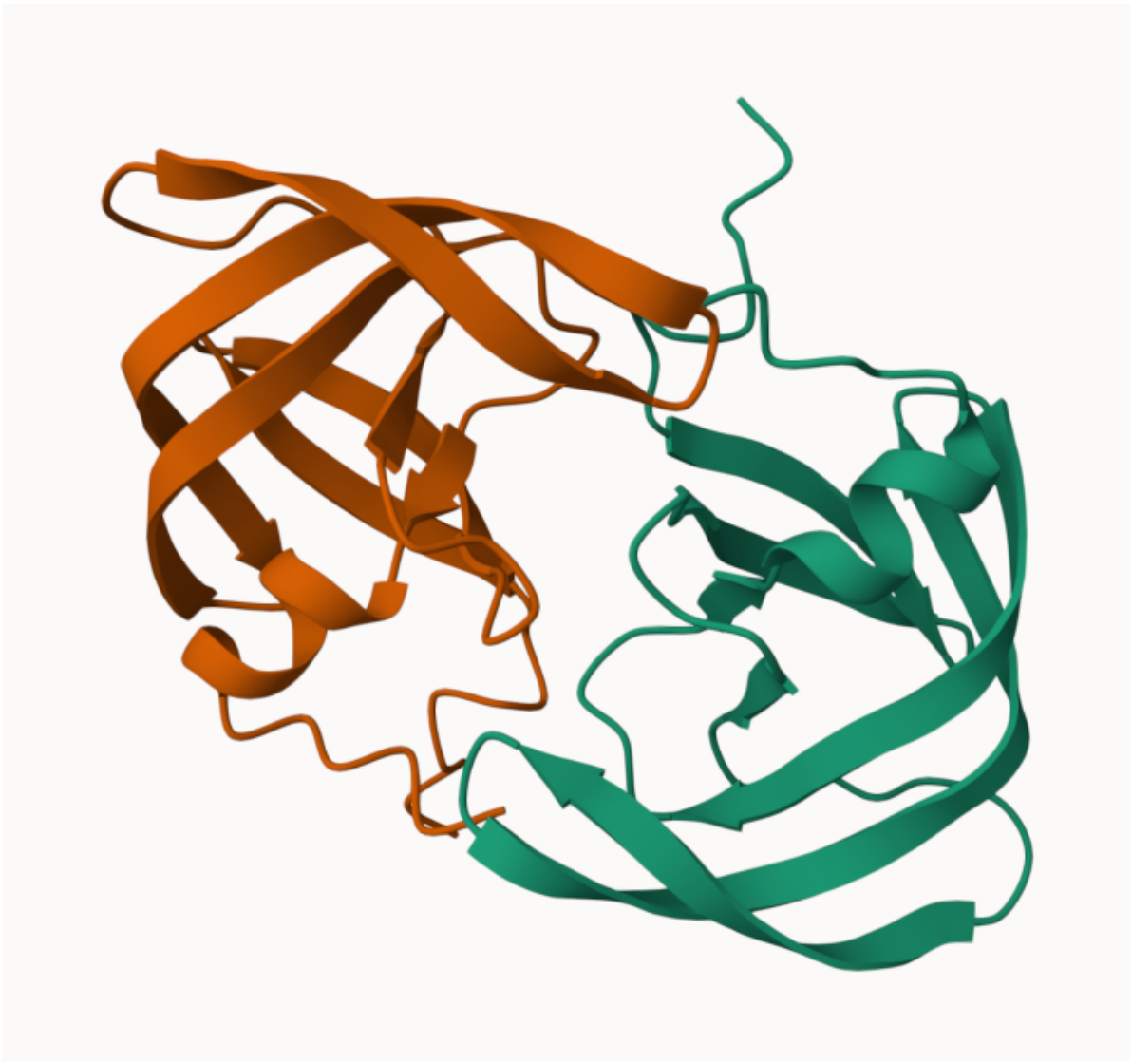
There are two types of quality scores in AlphaFold; one for residues (i.e each amino acid) called PLDDT score. The second PAE score measure the confidence in the relative position of two residues (i.e a score for every pair of residues).

Generating your own structure predictions

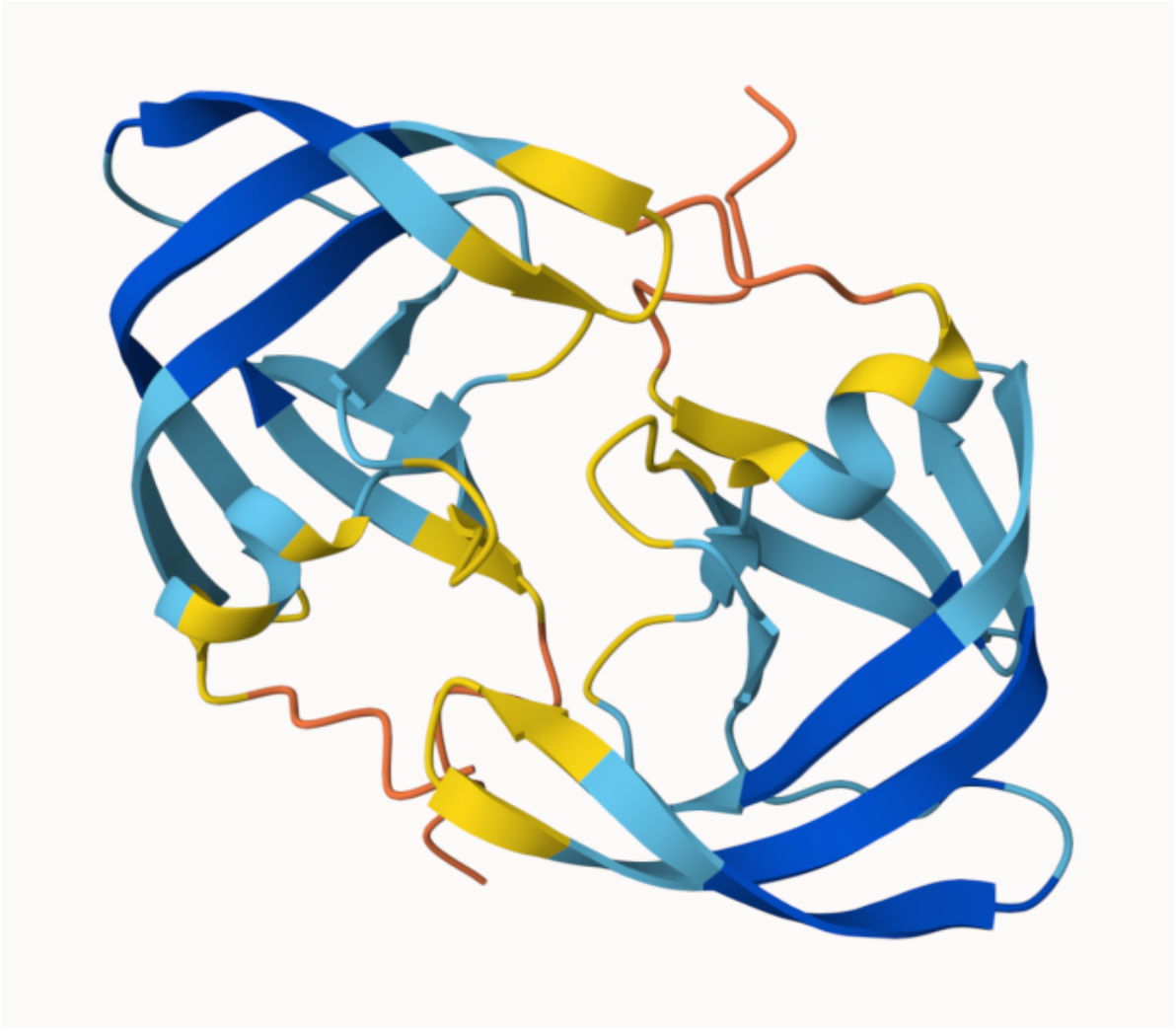
Figure of 5 generated HIV-PR models



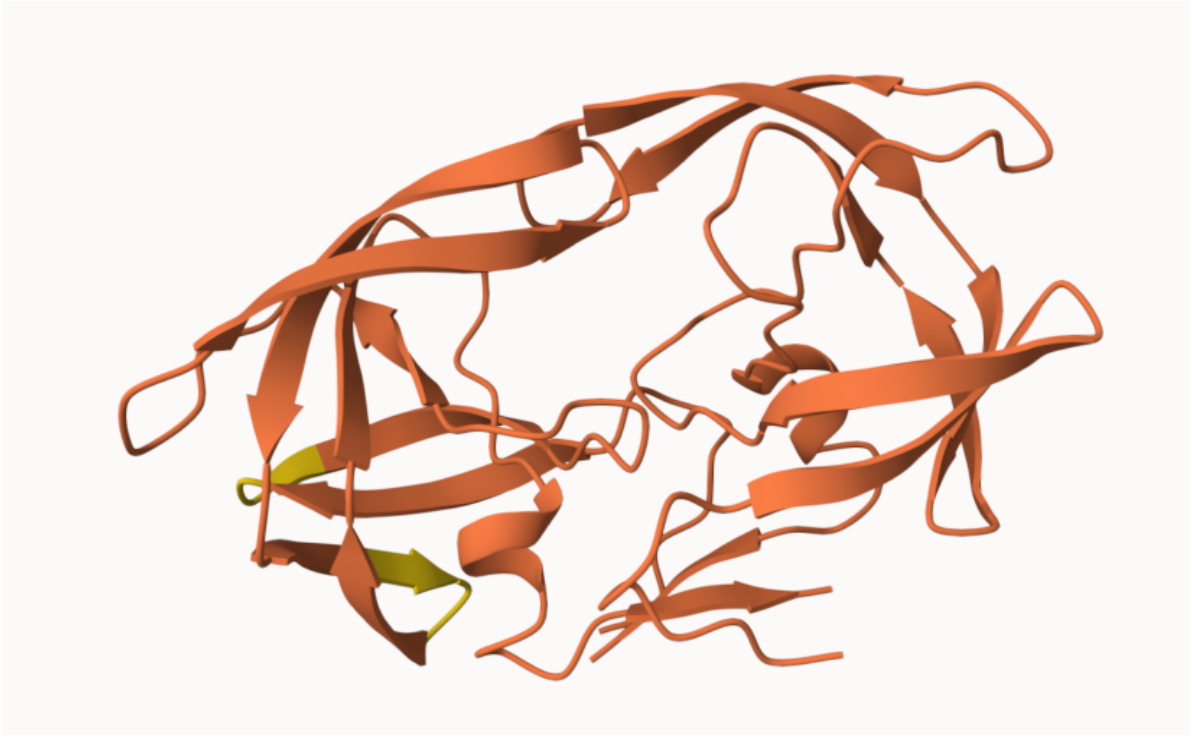
And the top ranked model colored by chain



And the top ranked model colored by confidence



This is the actual model



Custom analysis of resulting models in R

Read key result files into R. The first thing I need to know is what my results directory/foldre is called (i.e. it's name is different for every AlphaFold job)

```
results.dir <- "HIV_PR_dimer_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] "HIV_PR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_4_seed_000.pdb"
[2] "HIV_PR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed_000.pdb"
[3] "HIV_PR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_5_seed_000.pdb"
[4] "HIV_PR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_000.pdb"
[5] "HIV_PR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_000.pdb"
```

```
library(bio3d)

m1 <- read.pdb(pdb_files[1])
pdbs <- pdbaln(pdb_files, fit=TRUE, exefile="msa")
```

```
Reading PDB files:
HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_4_seed
HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_1_seed
HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_5_seed
HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed
HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed
.....

Extracting sequences

pdb/seq: 1   name: HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_001_alphafold2_multi
pdb/seq: 2   name: HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_002_alphafold2_multi
pdb/seq: 3   name: HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_003_alphafold2_multi
pdb/seq: 4   name: HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_004_alphafold2_multi
pdb/seq: 5   name: HIV_PR_dimer_23119//HIV_PR_dimer_23119_unrelaxed_rank_005_alphafold2_multi
```

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

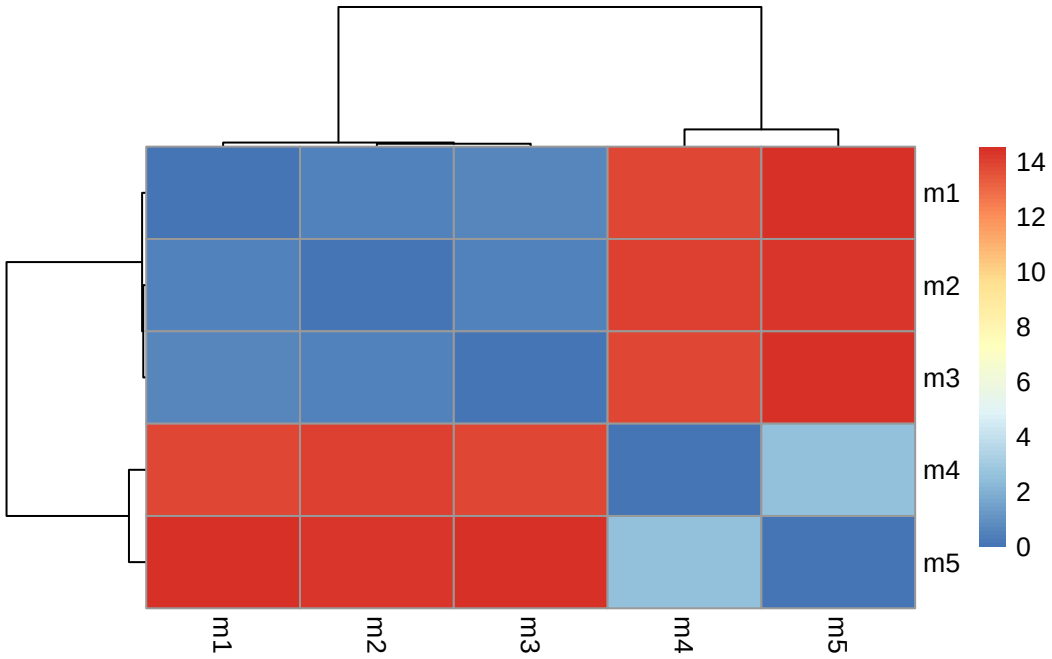
```
Warning in rmsd(pdbs, fit = T): No indices provided, using the 198 non NA positions
```

```
range(rd)
```

```
[1]  0.000 14.526
```

```
library(pheatmap)

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

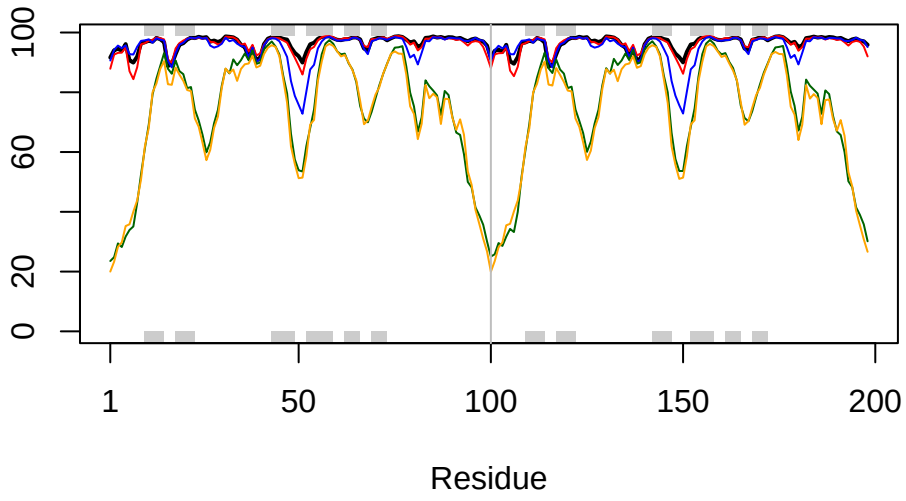


Now lets plot the pLDDT values across all models. Recall that this information is in the B-factor column of each model and that this is stored in our aligned pdbs object as pdbs$b with a row per structure/model.

```
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 = 5367.841
 core size 196 of 198  vol = 4671.097
 core size 195 of 198  vol = 1819.594
 core size 194 of 198  vol = 1118.521
 core size 193 of 198  vol = 1047.988
 core size 192 of 198  vol = 997.67
 core size 191 of 198  vol = 952.094
 core size 190 of 198  vol = 908.824
 core size 189 of 198  vol = 868.253
 core size 188 of 198  vol = 835.231
 core size 187 of 198  vol = 804.274
 core size 186 of 198  vol = 774.795
 core size 185 of 198  vol = 751.276
 core size 184 of 198  vol = 728.023
 core size 183 of 198  vol = 701.342
 core size 182 of 198  vol = 681.31
 core size 181 of 198  vol = 661.848
 core size 180 of 198  vol = 644.402
 core size 179 of 198  vol = 610.606
 core size 178 of 198  vol = 593.697
```

```
core size 177 of 198  vol = 578.193
core size 176 of 198  vol = 563.826
core size 175 of 198  vol = 545.052
core size 174 of 198  vol = 531.659
core size 173 of 198  vol = 502.216
core size 172 of 198  vol = 488.28
core size 171 of 198  vol = 474.763
core size 170 of 198  vol = 458.856
core size 169 of 198  vol = 441.214
core size 168 of 198  vol = 427.948
core size 167 of 198  vol = 418.318
core size 166 of 198  vol = 405.661
core size 165 of 198  vol = 394.816
core size 164 of 198  vol = 381.475
core size 163 of 198  vol = 370.923
core size 162 of 198  vol = 356.421
core size 161 of 198  vol = 344.258
core size 160 of 198  vol = 332.311
core size 159 of 198  vol = 320.972
core size 158 of 198  vol = 308.714
core size 157 of 198  vol = 297.817
core size 156 of 198  vol = 286.444
core size 155 of 198  vol = 277.395
core size 154 of 198  vol = 268.366
core size 153 of 198  vol = 258.834
core size 152 of 198  vol = 248.871
core size 151 of 198  vol = 236.132
core size 150 of 198  vol = 222.878
core size 149 of 198  vol = 211.181
core size 148 of 198  vol = 197.496
core size 147 of 198  vol = 190.8
core size 146 of 198  vol = 183.949
core size 145 of 198  vol = 176.845
core size 144 of 198  vol = 168.498
core size 143 of 198  vol = 161.109
core size 142 of 198  vol = 151.241
core size 141 of 198  vol = 144.797
core size 140 of 198  vol = 138.772
core size 139 of 198  vol = 133.15
core size 138 of 198  vol = 125.457
core size 137 of 198  vol = 118.062
core size 136 of 198  vol = 110.467
core size 135 of 198  vol = 105.382
```

```
core size 134 of 198  vol = 99.255
core size 133 of 198  vol = 95.295
core size 132 of 198  vol = 91.902
core size 131 of 198  vol = 88.223
core size 130 of 198  vol = 83.595
core size 129 of 198  vol = 79.882
core size 128 of 198  vol = 76.019
core size 127 of 198  vol = 72.229
core size 126 of 198  vol = 68.734
core size 125 of 198  vol = 65.306
core size 124 of 198  vol = 62.542
core size 123 of 198  vol = 58.725
core size 122 of 198  vol = 54.665
core size 121 of 198  vol = 49.975
core size 120 of 198  vol = 47.169
core size 119 of 198  vol = 43.12
core size 118 of 198  vol = 40.037
core size 117 of 198  vol = 36.841
core size 116 of 198  vol = 34.069
core size 115 of 198  vol = 32.146
core size 114 of 198  vol = 29.041
core size 113 of 198  vol = 26.377
core size 112 of 198  vol = 23.828
core size 111 of 198  vol = 21.978
core size 110 of 198  vol = 20.223
core size 109 of 198  vol = 18.766
core size 108 of 198  vol = 17.225
core size 107 of 198  vol = 15.672
core size 106 of 198  vol = 13.934
core size 105 of 198  vol = 12.677
core size 104 of 198  vol = 11.582
core size 103 of 198  vol = 10.284
core size 102 of 198  vol = 9.614
core size 101 of 198  vol = 7.989
core size 100 of 198  vol = 6.988
core size 99 of 198  vol = 6.002
core size 98 of 198  vol = 5.254
core size 97 of 198  vol = 4.6
core size 96 of 198  vol = 4.017
core size 95 of 198  vol = 3.124
core size 94 of 198  vol = 2.833
core size 93 of 198  vol = 2.596
core size 92 of 198  vol = 2.286
```

```
 core size 91 of 198  vol = 1.772
 core size 90 of 198  vol = 1.417
 core size 89 of 198  vol = 1.095
 core size 88 of 198  vol = 0.899
 core size 87 of 198  vol = 0.789
 core size 86 of 198  vol = 0.596
 core size 85 of 198  vol = 0.461
 FINISHED: Min vol ( 0.5 ) reached
```

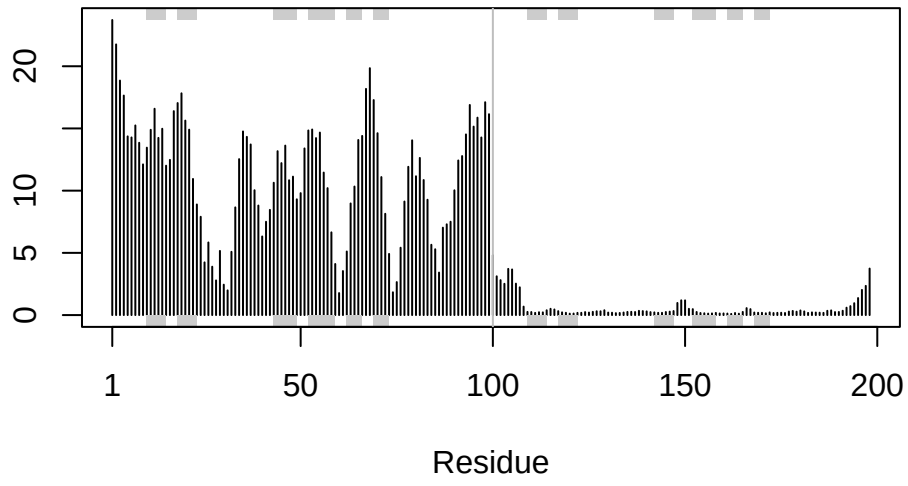
```
core.inds <- print(core, vol=0.5)
```

```
# 86 positions (cumulative volume <= 0.5 Angstrom^3)
  start end length
1     9  50     42
2    52  95     44
```

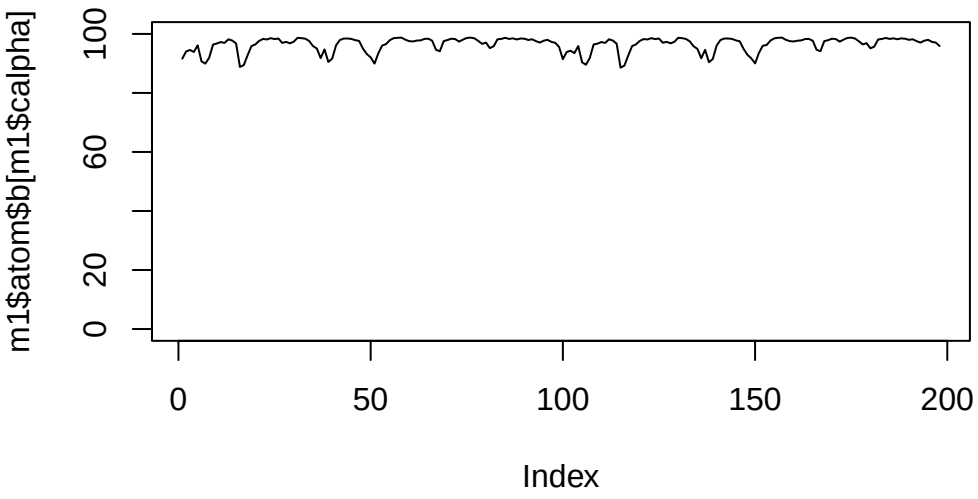
```
xyz <- pdbfit(pdbs, core.inds, outpath="corefit_structures")
```

```
rf <- rmsf(xyz)

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



```
plot(m1$atom$b[m1$calpha], type = "l", ylim=c(0,100))
```



Residue conservation from alignment file

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

```
[1] "HIV_PR_dimer_23119//HIV_PR_dimer_23119.a3m"
```

```
aln <- read.fasta(aln_file[1], to.upper = TRUE)
```

```
[1] " ** Duplicated sequence id's: 101 **"
[2] " ** Duplicated sequence id's: 101 **"
```

How many sequences are in this alignment?

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

```
[1] 5397  132
```

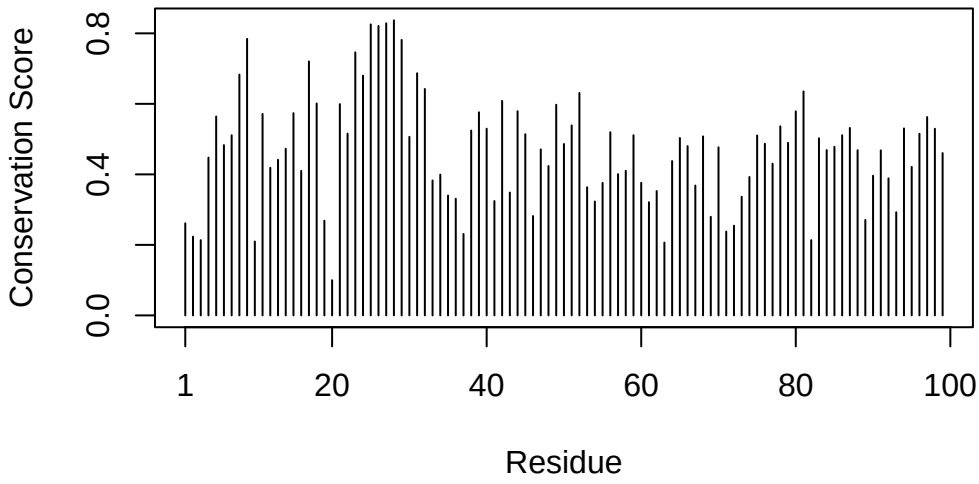
We can score residue conservation in the alignment with the `conserv()` function.

```
sim <- conserv(aln)

plotb3(sim[1:99], sse=trim.pdb(m1, chain="A"),
       ylab="Conservation Score")
```

```
Warning in pdb2sse(sse): No helix and sheet defined in input 'sse' PDB object:
try using dssp()
```

```
Warning in plotb3(sim[1:99], sse = trim.pdb(m1, chain = "A"), ylab =
"Conservation Score"): Length of input 'sse' does not equal the length of input
'x'; Ignoring 'sse'
```



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

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

For a final visualization of these functionally important sites we can map this conservation score to the Occupancy column of a PDB file for viewing in molecular viewer programs such as Mol*, PyMol, VMD, chimera etc.

```
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")
```