class11 structural bioinformatics p2

amy (pid A16962111)

comparative structure analysis of adenylate kinase

Here we will perform PCA on all of the adenylate kinase (Adk) structures in the PDB using the bio3d function `pca()`

```
#install.packages("bio3d")
#install.packages("devtools")
#install.packages("BiocManager")

#BiocManager::install("msa")
#devtools::install_bitbucket("Grantlab/bio3d-view")
```

Use `get.seq()` to retrieve a query sequence (chain A of one Adk)

```
library(bio3d)
aa <- get.seq("1ake_A")
```

```
Warning in get.seq("1ake_A"): Removing existing file: seqs.fasta
```

```
Fetching... Please wait. Done.
```

BLAST search:

```
#b <- blast.pdb(aa)
#hits <- plot(b)
#head(hits$pdb.id)
```

```
hits <- NULL
hits$pdb.id <- c('1AKE_A','6S36_A','6RZE_A','3HPR_A','1E4V_A','5EJE_A','1E4Y_A','3X2S_A','
files <- get.pdb(hits$pdb.id, path="pdbs", split=TRUE, gzip=TRUE)
```

```
Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1AKE.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6S36.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6RZE.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3HPR.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1E4V.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/5EJE.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1E4Y.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3X2S.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6HAP.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6HAM.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/4K46.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3GMT.pdb.gz exists. Skipping download

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/4PZL.pdb.gz exists. Skipping download
```

```
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```

Use function `pdbaln()` to align and superpose ("fit") 13 identified related structures.

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

```
Reading PDB files:
pdbs/split_chain/1AKE_A.pdb
pdbs/split_chain/6S36_A.pdb
pdbs/split_chain/6RZE_A.pdb
pdbs/split_chain/3HPR_A.pdb
pdbs/split_chain/1E4V_A.pdb
pdbs/split_chain/5EJE_A.pdb
pdbs/split_chain/1E4Y_A.pdb
```

```
pdbs/split_chain/3X2S_A.pdb
pdbs/split_chain/6HAP_A.pdb
pdbs/split_chain/6HAM_A.pdb
pdbs/split_chain/4K46_A.pdb
pdbs/split_chain/3GMT_A.pdb
pdbs/split_chain/4PZL_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
..   PDB has ALT records, taking A only, rm.alt=TRUE
....   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
...

Extracting sequences

pdb/seq: 1   name: pdbs/split_chain/1AKE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 2   name: pdbs/split_chain/6S36_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 3   name: pdbs/split_chain/6RZE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 4   name: pdbs/split_chain/3HPR_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 5   name: pdbs/split_chain/1E4V_A.pdb
pdb/seq: 6   name: pdbs/split_chain/5EJE_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 7   name: pdbs/split_chain/1E4Y_A.pdb
pdb/seq: 8   name: pdbs/split_chain/3X2S_A.pdb
pdb/seq: 9   name: pdbs/split_chain/6HAP_A.pdb
pdb/seq: 10   name: pdbs/split_chain/6HAM_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 11   name: pdbs/split_chain/4K46_A.pdb
   PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 12   name: pdbs/split_chain/3GMT_A.pdb
pdb/seq: 13   name: pdbs/split_chain/4PZL_A.pdb
```

```r
ids <- basename.pdb(pdbs$id)
#plot(pdbs, labels=ids)
```

Use function `pdb.annotate()` to annotate each structure to its source species.

```
anno <- pdb.annotate(ids)
unique(anno$source)
```

```
[1] "Escherichia coli"
[2] "Escherichia coli K-12"
[3] "Escherichia coli O139:H28 str. E24377A"
[4] "Escherichia coli str. K-12 substr. MDS42"
[5] "Photobacterium profundum"
[6] "Burkholderia pseudomallei 1710b"
[7] "Francisella tularensis subsp. tularensis SCHU S4"
```

```
anno
```

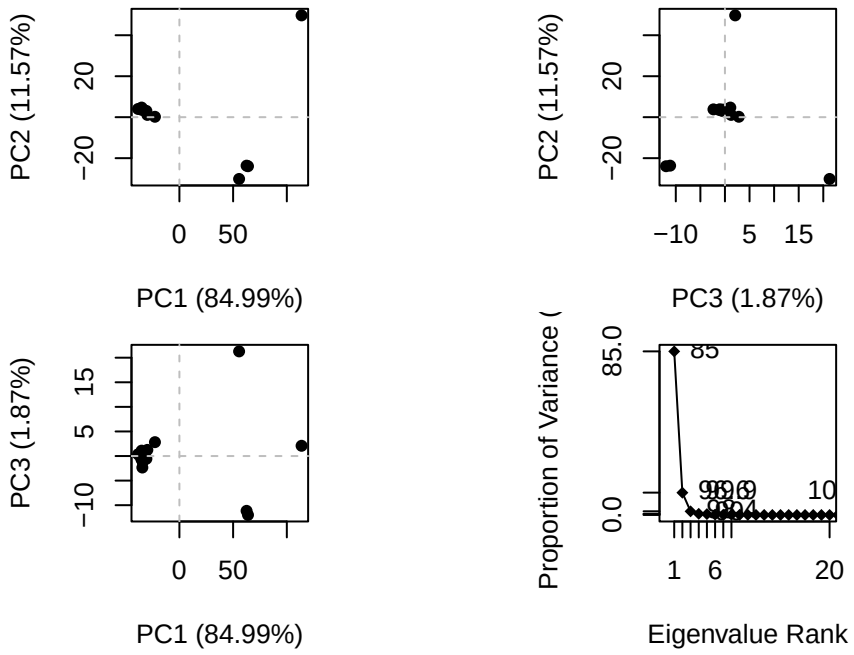
```
       structureId chainId macromoleculeType chainLength experimentalTechnique
1AKE_A        1AKE       A           Protein         214                 X-ray
6S36_A        6S36       A           Protein         214                 X-ray
6RZE_A        6RZE       A           Protein         214                 X-ray
3HPR_A        3HPR       A           Protein         214                 X-ray
1E4V_A        1E4V       A           Protein         214                 X-ray
5EJE_A        5EJE       A           Protein         214                 X-ray
1E4Y_A        1E4Y       A           Protein         214                 X-ray
3X2S_A        3X2S       A           Protein         214                 X-ray
6HAP_A        6HAP       A           Protein         214                 X-ray
6HAM_A        6HAM       A           Protein         214                 X-ray
4K46_A        4K46       A           Protein         214                 X-ray
3GMT_A        3GMT       A           Protein         230                 X-ray
4PZL_A        4PZL       A           Protein         242                 X-ray
       resolution       scopDomain                                      pfam
1AKE_A       2.00 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
6S36_A       1.60             <NA>                     Adenylate kinase (ADK)
6RZE_A       1.69             <NA>                     Adenylate kinase (ADK)
3HPR_A       2.00             <NA> Adenylate kinase, active site lid (ADK_lid)
1E4V_A       1.85 Adenylate kinase                     Adenylate kinase (ADK)
5EJE_A       1.90             <NA>                     Adenylate kinase (ADK)
1E4Y_A       1.85 Adenylate kinase                     Adenylate kinase (ADK)
3X2S_A       2.80             <NA>                     Adenylate kinase (ADK)
6HAP_A       2.70             <NA> Adenylate kinase, active site lid (ADK_lid)
6HAM_A       2.55             <NA> Adenylate kinase, active site lid (ADK_lid)
4K46_A       2.01             <NA> Adenylate kinase, active site lid (ADK_lid)
3GMT_A       2.10             <NA>                     Adenylate kinase (ADK)
```

```
4PZL_A       2.10            <NA>                      Adenylate kinase (ADK)
              ligandId
1AKE_A              AP5
6S36_A CL (3),NA,MG (2)
6RZE_A    NA (3),CL (2)
3HPR_A              AP5
1E4V_A              AP5
5EJE_A           AP5,CO
1E4Y_A              AP5
3X2S_A   JPY (2),AP5,MG
6HAP_A              AP5
6HAM_A              AP5
4K46_A      ADP,AMP,PO4
3GMT_A          SO4 (2)
4PZL_A       CA,FMT,GOL
                                                                        ligandName
1AKE_A                                                 BIS(ADENOSINE)-5'-PENTAPHOSPHATE
6S36_A                                    CHLORIDE ION (3),SODIUM ION,MAGNESIUM ION (2)
6RZE_A                                     SODIUM ION (3),CHLORIDE ION (2)
3HPR_A                                                 BIS(ADENOSINE)-5'-PENTAPHOSPHATE
1E4V_A                                                 BIS(ADENOSINE)-5'-PENTAPHOSPHATE
5EJE_A                                  BIS(ADENOSINE)-5'-PENTAPHOSPHATE,COBALT (II) ION
1E4Y_A                                                 BIS(ADENOSINE)-5'-PENTAPHOSPHATE
3X2S_A N-(pyren-1-ylmethyl)acetamide (2),BIS(ADENOSINE)-5'-PENTAPHOSPHATE,MAGNESIUM ION
6HAP_A                                                 BIS(ADENOSINE)-5'-PENTAPHOSPHATE
6HAM_A                                                 BIS(ADENOSINE)-5'-PENTAPHOSPHATE
4K46_A                   ADENOSINE-5'-DIPHOSPHATE,ADENOSINE MONOPHOSPHATE,PHOSPHATE ION
3GMT_A                                                                  SULFATE ION (2)
4PZL_A                                                 CALCIUM ION,FORMIC ACID,GLYCEROL
                                                 source
1AKE_A                                 Escherichia coli
6S36_A                                 Escherichia coli
6RZE_A                                 Escherichia coli
3HPR_A                              Escherichia coli K-12
1E4V_A                                 Escherichia coli
5EJE_A           Escherichia coli O139:H28 str. E24377A
1E4Y_A                                 Escherichia coli
3X2S_A         Escherichia coli str. K-12 substr. MDS42
6HAP_A           Escherichia coli O139:H28 str. E24377A
6HAM_A                              Escherichia coli K-12
4K46_A                         Photobacterium profundum
3GMT_A                    Burkholderia pseudomallei 1710b
4PZL_A Francisella tularensis subsp. tularensis SCHU S4
```

```
1AKE_A STRUCTURE OF THE COMPLEX BETWEEN ADENYLATE KINASE FROM ESCHERICHIA COLI AND THE INHIBI
6S36_A
6RZE_A
3HPR_A
1E4V_A
5EJE_A                                                                          Cryst
1E4Y_A
3X2S_A
6HAP_A
6HAM_A
4K46_A
3GMT_A
4PZL_A                                                                      The cryst
                                                        citation rObserved   rFree
1AKE_A                  Muller, C.W., et al. J Mol Biol (1992)   0.19600      NA
6S36_A                   Rogne, P., et al. Biochemistry (2019)   0.16320 0.23560
6RZE_A                   Rogne, P., et al. Biochemistry (2019)   0.18650 0.23500
3HPR_A  Schrank, T.P., et al. Proc Natl Acad Sci U S A (2009)   0.21000 0.24320
1E4V_A                    Muller, C.W., et al. Proteins (1993)   0.19600      NA
5EJE_A  Kovermann, M., et al. Proc Natl Acad Sci U S A (2017)   0.18890 0.23580
1E4Y_A                    Muller, C.W., et al. Proteins (1993)   0.17800      NA
3X2S_A                 Fujii, A., et al. Bioconjug Chem (2015)   0.20700 0.25600
6HAP_A                Kantaev, R., et al. J Phys Chem B (2018)   0.22630 0.27760
6HAM_A                Kantaev, R., et al. J Phys Chem B (2018)   0.20511 0.24325
4K46_A                     Cho, Y.-J., et al. To be published    0.17000 0.22290
3GMT_A Buchko, G.W., et al. Biochem Biophys Res Commun (2010)   0.23800 0.29500
4PZL_A                       Tan, K., et al. To be published    0.19360 0.23680
         rWork spaceGroup
1AKE_A 0.19600  P 21 2 21
6S36_A 0.15940    C 1 2 1
6RZE_A 0.18190    C 1 2 1
3HPR_A 0.20620  P 21 21 2
1E4V_A 0.19600  P 21 2 21
5EJE_A 0.18630  P 21 2 21
1E4Y_A 0.17800   P 1 21 1
3X2S_A 0.20700 P 21 21 21
6HAP_A 0.22370    I 2 2 2
6HAM_A 0.20311       P 43
4K46_A 0.16730 P 21 21 21
3GMT_A 0.23500   P 1 21 1
4PZL_A 0.19130       P 32
```

Perform PCA

```
pc.xray <- pca(pdbs)
plot(pc.xray)
```



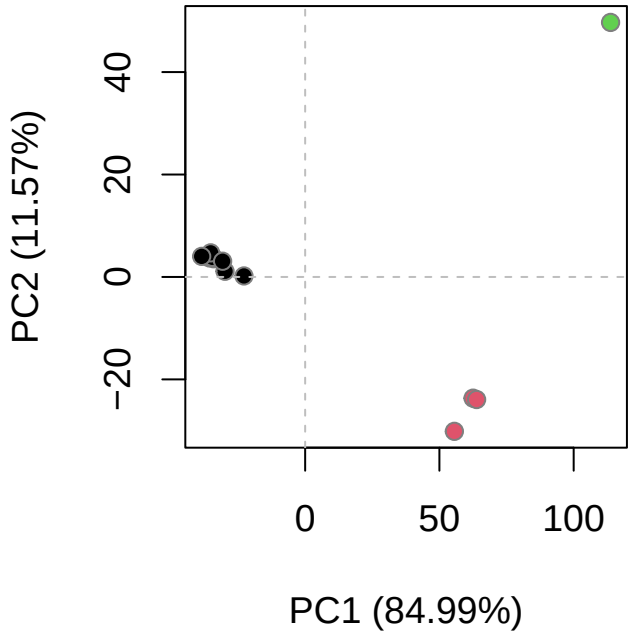
Use `rmsd()` to cluster structures based on their pairwise structural deviation

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

```
Warning in rmsd(pdbs): No indices provided, using the 204 non NA positions
```

```
hc.rd <- hclust(dist(rd))
grps.rd <- cutree(hc.rd, k=3)

plot(pc.xray, 1:2, col="grey50", bg=grps.rd, pch=21, cex=1)
```



custom analysis of ColabFold models

Here we will perform a custom analysis on the results of running ColabFold on the following protein sequence query:

> >HIV-Pr-Dimer PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLP-GRWKPKMIGGIGGFIKVRQYD QILIEICGHKAIGTVLVGPTPVNIIGRN-LLTQIGCTLNF:PQITLWQRPLVTIKIGGQLK EALLDTGADDTVLEEMSLP-GRWKPKMIGGIGGFIKVRQYDQILIEICGHKAIGTVLVGPT PVNIIGRN-LLTQIGCTLNF

```
results_dir <- "HIVPrDimer_23119"
pdb_files <- list.files(path=results_dir,
                        pattern="*.pdb",
                        full.names = TRUE)
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"
```

```
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
```

```
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
```

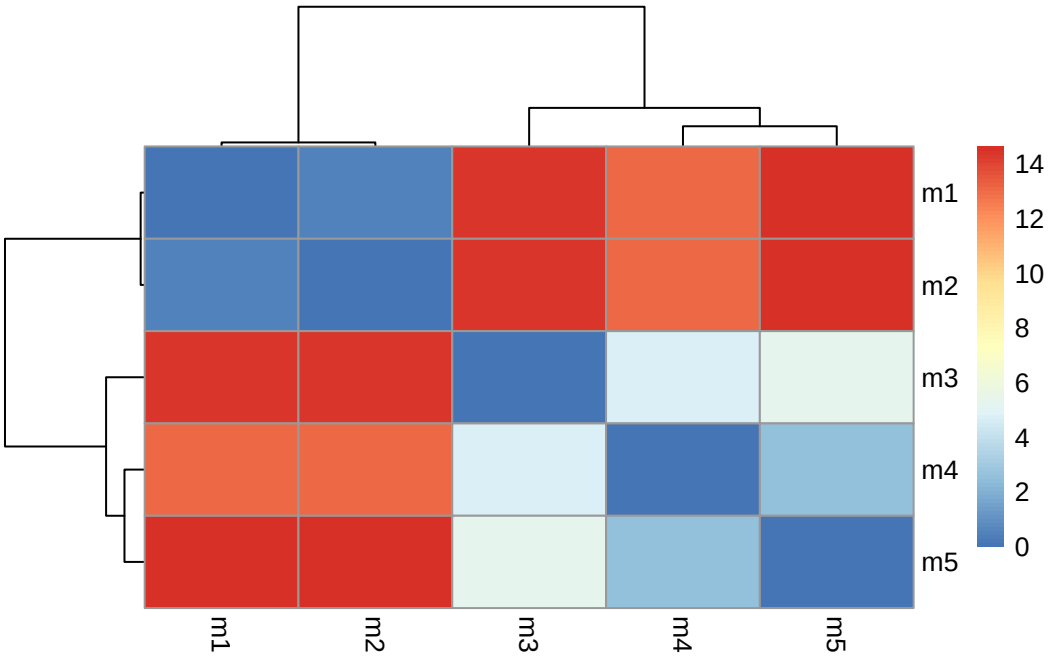
```
range(rd)
```

```
[1]  0.000 14.631
```

Create a heatmap of RMSD matrix values

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

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



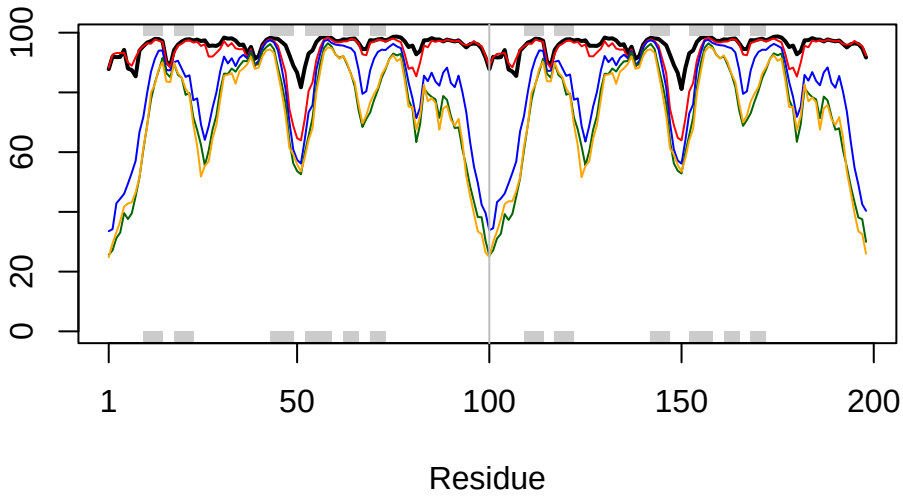
Based on this plot, models 1 and 2 are the most similar, and models 1 and 5 are the most dissimilar.

Next, plot pLDDT values across all models (saved in `pdbs$b`)

```
# 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")
```



We can improve superposition by finding the most consistent "rigid core" common across all the models using `core.find()`

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

```
core size 197 of 198  vol = 4578.336
core size 196 of 198  vol = 3931.103
core size 195 of 198  vol = 3709.727
core size 194 of 198  vol = 3496.014
core size 193 of 198  vol = 3302.428
core size 192 of 198  vol = 3146.468
core size 191 of 198  vol = 3048.959
core size 190 of 198  vol = 2970.348
core size 189 of 198  vol = 2893.007
core size 188 of 198  vol = 2831.818
core size 187 of 198  vol = 2774.499
core size 186 of 198  vol = 2728.035
core size 185 of 198  vol = 2704.937
core size 184 of 198  vol = 2701.97
core size 183 of 198  vol = 2715.897
core size 182 of 198  vol = 2809.84
core size 181 of 198  vol = 2888.937
```

```
core size 180 of 198  vol = 2967.269
core size 179 of 198  vol = 3036.243
core size 178 of 198  vol = 3066.274
core size 177 of 198  vol = 3096.82
core size 176 of 198  vol = 3056.401
core size 175 of 198  vol = 3014.755
core size 174 of 198  vol = 2974.999
core size 173 of 198  vol = 2898.037
core size 172 of 198  vol = 2810.159
core size 171 of 198  vol = 2747.518
core size 170 of 198  vol = 2684.42
core size 169 of 198  vol = 2620.339
core size 168 of 198  vol = 2550.863
core size 167 of 198  vol = 2492.567
core size 166 of 198  vol = 2422.963
core size 165 of 198  vol = 2358.901
core size 164 of 198  vol = 2298.277
core size 163 of 198  vol = 2235.903
core size 162 of 198  vol = 2171.006
core size 161 of 198  vol = 2093.544
core size 160 of 198  vol = 2029.129
core size 159 of 198  vol = 1950.943
core size 158 of 198  vol = 1881.001
core size 157 of 198  vol = 1801.491
core size 156 of 198  vol = 1728.877
core size 155 of 198  vol = 1660.022
core size 154 of 198  vol = 1586.134
core size 153 of 198  vol = 1532.702
core size 152 of 198  vol = 1460.171
core size 151 of 198  vol = 1399.236
core size 150 of 198  vol = 1333.893
core size 149 of 198  vol = 1271.731
core size 148 of 198  vol = 1219.48
core size 147 of 198  vol = 1175.987
core size 146 of 198  vol = 1138.462
core size 145 of 198  vol = 1102.108
core size 144 of 198  vol = 1049.627
core size 143 of 198  vol = 1014.047
core size 142 of 198  vol = 970.56
core size 141 of 198  vol = 929.163
core size 140 of 198  vol = 889.089
core size 139 of 198  vol = 846.653
core size 138 of 198  vol = 805.785
```

```
core size 137 of 198  vol = 775.019
core size 136 of 198  vol = 743.075
core size 135 of 198  vol = 715.68
core size 134 of 198  vol = 689.773
core size 133 of 198  vol = 660.314
core size 132 of 198  vol = 630.951
core size 131 of 198  vol = 597.191
core size 130 of 198  vol = 566.973
core size 129 of 198  vol = 532.874
core size 128 of 198  vol = 496.192
core size 127 of 198  vol = 463.167
core size 126 of 198  vol = 431.877
core size 125 of 198  vol = 408.848
core size 124 of 198  vol = 376.594
core size 123 of 198  vol = 362.36
core size 122 of 198  vol = 353.633
core size 121 of 198  vol = 331.501
core size 120 of 198  vol = 312.518
core size 119 of 198  vol = 286.715
core size 118 of 198  vol = 262.336
core size 117 of 198  vol = 245.109
core size 116 of 198  vol = 228.342
core size 115 of 198  vol = 210.366
core size 114 of 198  vol = 197.519
core size 113 of 198  vol = 179.392
core size 112 of 198  vol = 161.891
core size 111 of 198  vol = 148.359
core size 110 of 198  vol = 134.477
core size 109 of 198  vol = 121.261
core size 108 of 198  vol = 109.516
core size 107 of 198  vol = 103.031
core size 106 of 198  vol = 96.443
core size 105 of 198  vol = 88.455
core size 104 of 198  vol = 81.816
core size 103 of 198  vol = 74.88
core size 102 of 198  vol = 68.386
core size 101 of 198  vol = 65.937
core size 100 of 198  vol = 62.345
core size 99 of 198  vol = 58.836
core size 98 of 198  vol = 52.868
core size 97 of 198  vol = 47.796
core size 96 of 198  vol = 41.292
core size 95 of 198  vol = 33.831
```

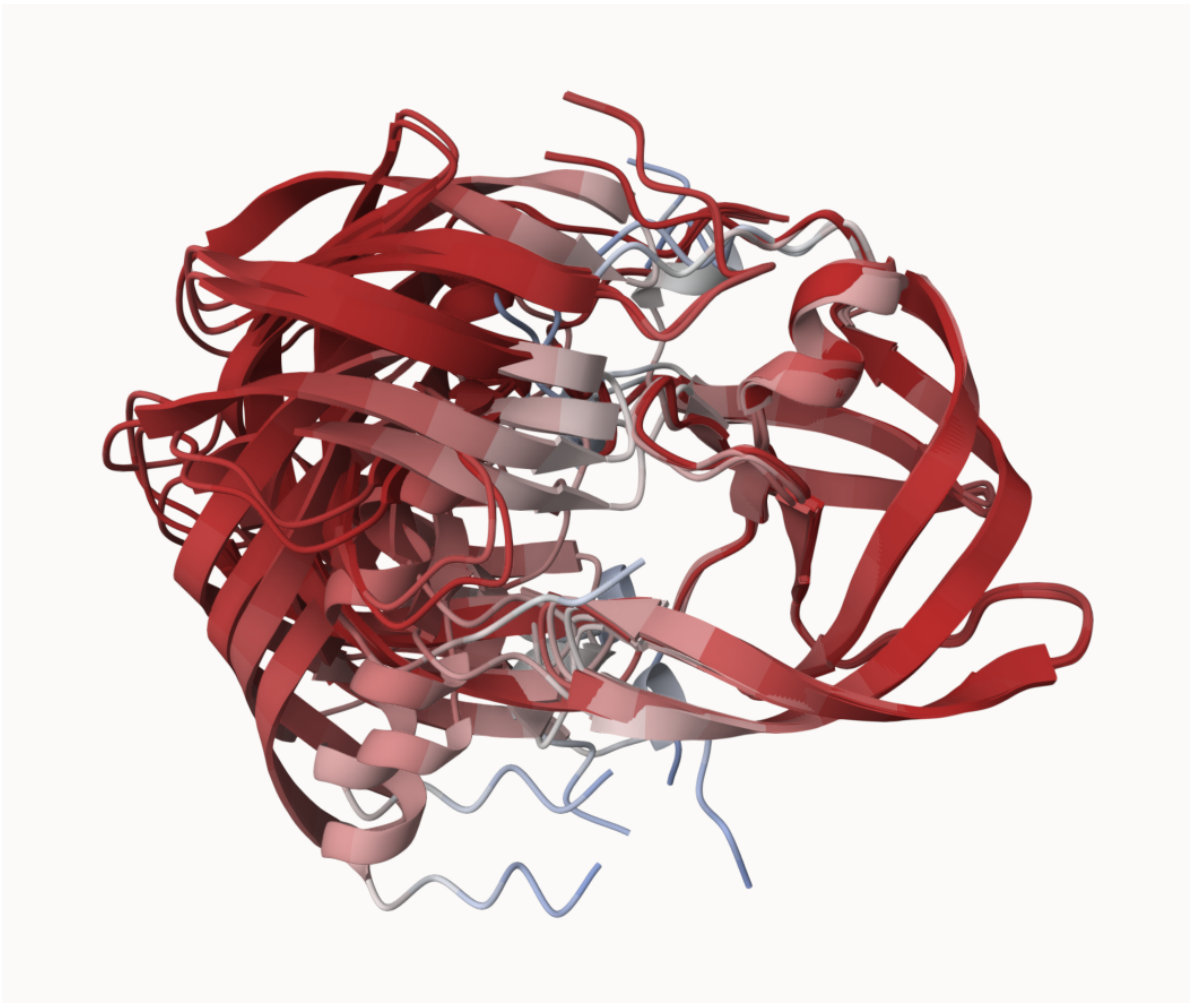
```
 core size 94 of 198  vol = 24.912
 core size 93 of 198  vol = 18.912
 core size 92 of 198  vol = 12.7
 core size 91 of 198  vol = 7.35
 core size 90 of 198  vol = 4.922
 core size 89 of 198  vol = 3.421
 core size 88 of 198  vol = 2.553
 core size 87 of 198  vol = 1.917
 core size 86 of 198  vol = 1.513
 core size 85 of 198  vol = 1.201
 core size 84 of 198  vol = 1.046
 core size 83 of 198  vol = 0.922
 core size 82 of 198  vol = 0.755
 core size 81 of 198  vol = 0.668
 core size 80 of 198  vol = 0.596
 core size 79 of 198  vol = 0.549
 core size 78 of 198  vol = 0.493
 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  25     16
2    28  48     21
3    53  94     42
```

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

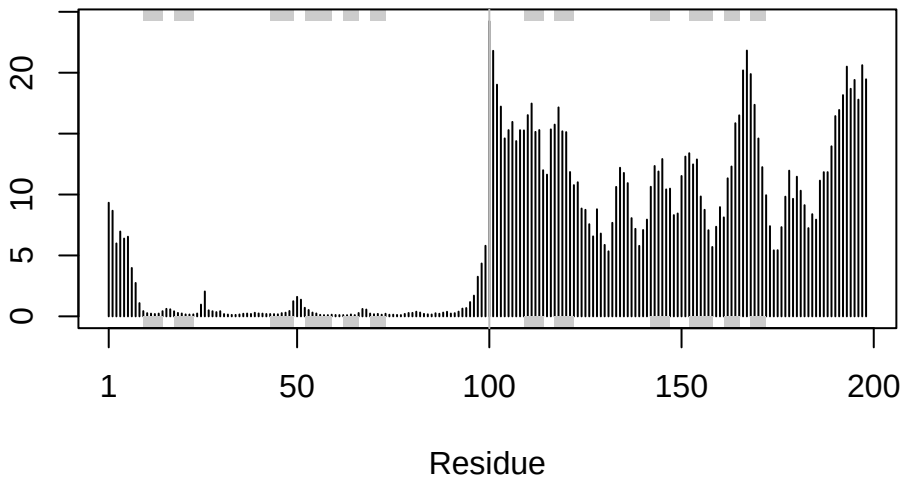
Open the models with new superposition coordinates in Mol* and color by pLDDT scores:



Examine RMSF, a measure of conformational variance, between positions of the structure.

```
rf <- rmsf(xyz)

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



The first chain (left of residue 100) is more similar across models than chain 2.

predicted alignment error (PAE) for domains

```
library(jsonlite)

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"
```

```
head(pae1$plddt)
```

```
[1] 87.81 92.00 91.81 91.88 94.25 88.00
```

Lower PAE scores indicate a better model. Model 1 is better than model 5.

```
pae1$max_pae
```

```
[1] 14.09375
```

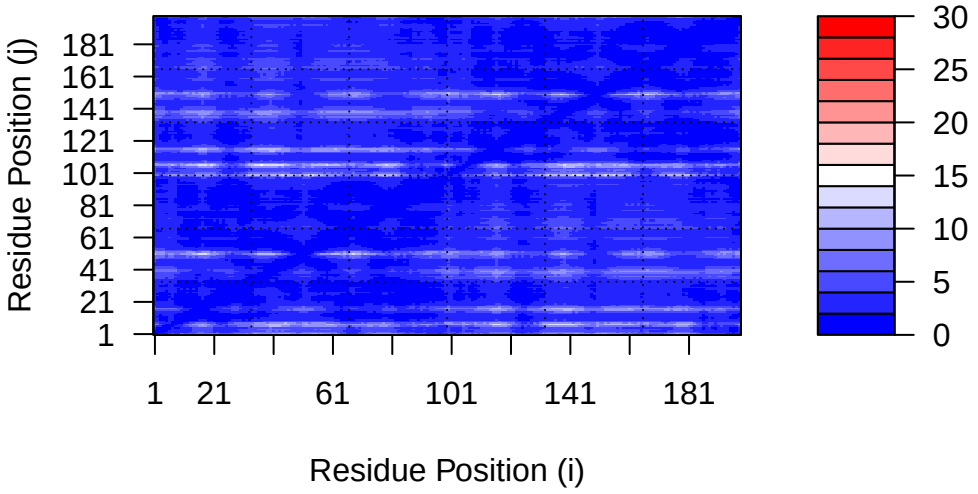
```
pae5$max_pae
```

```
[1] 29.29688
```

Plot the N by N (where N is the number of residues) PAE scores

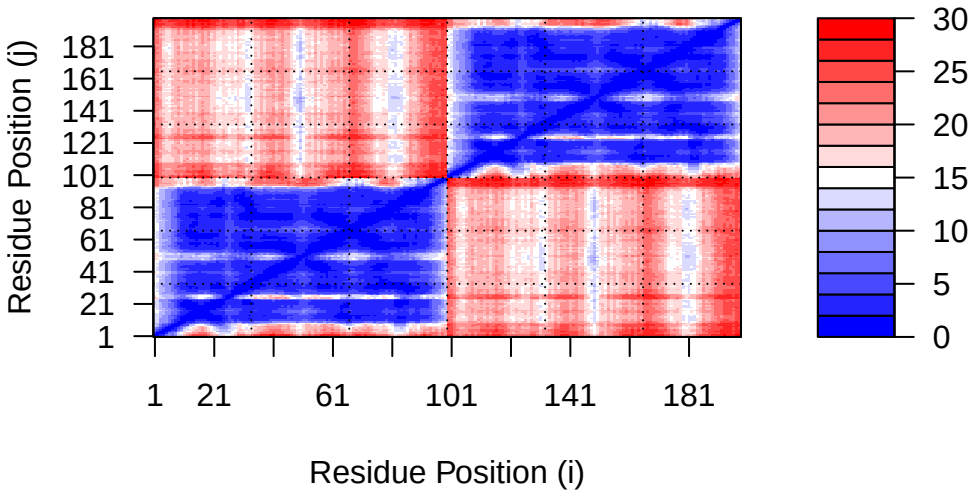
Model1

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



Model5

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



We can see that the PAE scores for model 5 are high for residue positions i 101-200 vs j 1-100 and vice versa, meaning that model 5 does a poor job of predicting the alignment of the two chains with respect to each other.

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 **"
```

How many sequences are in this alignment?

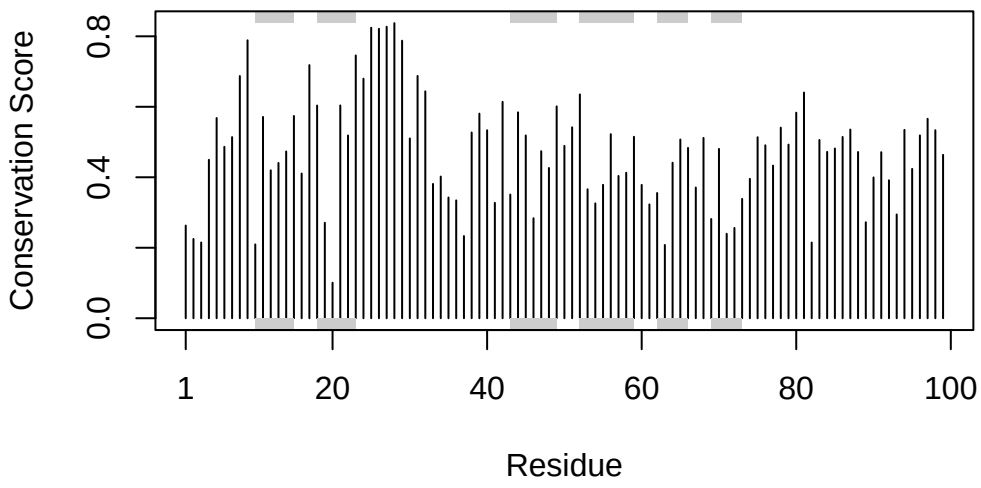
5378 sequences

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

```
[1] 5378  132
```

Use function `conserv()` to score residue conservation

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



The highest conservation scores are for residues 25-28

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

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

To highlight these conserved residues (like have functional importance):

```
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")
```

View in Mol* and color by occupancy. The dark purple region shows the active site.