Class 10: Comparative analysis of structure & Class 11: Alpha Fold

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Comparative structure analysis of Adenylate Kinase

We need some packages for today's class. These include `bio3d` and `msa`

The `msa` package is from Bioconductor. These packages focus on genomics type work and are managed by the `BiocManager` package.

Install `install.packages("BiocManager")` and then `BiocManager::install("msa")`

```
library(bio3d)

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

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

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

```
aa
```

```
             1        .         .         .         .         .         60
pdb|1AKE|A   MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
             1        .         .         .         .         .         60

            61        .         .         .         .         .        120
pdb|1AKE|A   DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDRI
            61        .         .         .         .         .        120

           121        .         .         .         .         .        180
pdb|1AKE|A   VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
```

```
           121        .         .         .         .         .         180

           181        .         .         .   214
pdb|1AKE|A   YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG
           181        .         .         .   214

Call:
  read.fasta(file = outfile)

Class:
  fasta

Alignment dimensions:
  1 sequence rows; 214 position columns (214 non-gap, 0 gap)

+ attr: id, ali, call
```

Now I can search the PDB database for related seuqences:

```
# Blast or hmmer search
#b <- blast.pdb(aa)
```

```
#hits <-  plot(b)
```

```
#attributes(b)
# List out some 'top hits'
#head(b$hit.tbl)
```

These are the related structures in the PDB database that we found via a BLAST search…

```
hits <- NULL
hits$pdb.id <- c('1AKE_A','6S36_A','6RZE_A','3HPR_A','1E4V_A','5EJE_A','1E4Y_A','3X2S_A','
```

Side-note: Lets annotate these structures (in other words find out what they are, what species they are from, stuff about the experiment they were solved in etc.)

For this we can use the `pdb.annotate()`

```
anno <- pdb.annotate(hits$pdb.id)
head(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
       resolution       scopDomain                                      pfam
1AKE_A       2.00 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
6S36_A       1.60             <NA> Adenylate kinase, active site lid (ADK_lid)
6RZE_A       1.69             <NA> Adenylate kinase, active site lid (ADK_lid)
3HPR_A       2.00             <NA> Adenylate kinase, active site lid (ADK_lid)
1E4V_A       1.85 Adenylate kinase Adenylate kinase, active site lid (ADK_lid)
5EJE_A       1.90             <NA> Adenylate kinase, active site lid (ADK_lid)
              ligandId                                      ligandName
1AKE_A             AP5                BIS(ADENOSINE)-5'-PENTAPHOSPHATE
6S36_A CL (3),NA,MG (2)    CHLORIDE ION (3),SODIUM ION,MAGNESIUM ION (2)
6RZE_A    NA (3),CL (2)                 SODIUM ION (3),CHLORIDE ION (2)
3HPR_A             AP5                BIS(ADENOSINE)-5'-PENTAPHOSPHATE
1E4V_A             AP5                BIS(ADENOSINE)-5'-PENTAPHOSPHATE
5EJE_A          CO,AP5 COBALT (II) ION,BIS(ADENOSINE)-5'-PENTAPHOSPHATE
                                  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

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
                                                citation rObserved  rFree
1AKE_A               Muller, C.W., et al. J Mol Biol (1992)    0.1960     NA
6S36_A                Rogne, P., et al. Biochemistry (2019)    0.1632 0.2356
6RZE_A                Rogne, P., et al. Biochemistry (2019)    0.1865 0.2350
3HPR_A Schrank, T.P., et al. Proc Natl Acad Sci U S A (2009)    0.2100 0.2432
1E4V_A                 Muller, C.W., et al. Proteins (1993)    0.1960     NA
5EJE_A Kovermann, M., et al. Proc Natl Acad Sci U S A (2017)    0.1889 0.2358
       rWork spaceGroup
1AKE_A 0.1960  P 21 2 21
```

```
6S36_A 0.1594    C 1 2 1
6RZE_A 0.1819    C 1 2 1
3HPR_A 0.2062  P 21 21 2
1E4V_A 0.1960  P 21 2 21
5EJE_A 0.1863  P 21 2 21
```

Now we can download all these structures for further analysis with the `get.pdb()` function.

```
# Download releated PDB files
#gzips file size smaller, path creates folder of current directory
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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```

Now we have all of these related structures we can Align and Superpose...

```
# Align releated PDBs
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
```

```
pdbs
```

```
                                 1        .         .         .         40
[Truncated_Name:1]1AKE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:2]6S36_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:3]6RZE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:4]3HPR_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:5]1E4V_A.pdb     ----------MRIILLGAPVAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:6]5EJE_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:7]1E4Y_A.pdb     ----------MRIILLGALVAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:8]3X2S_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:9]6HAP_A.pdb     ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:10]6HAM_A.pdb    ----------MRIILLGAPGAGKGTQAQFIMEKYGIPQIS
[Truncated_Name:11]4K46_A.pdb    ----------MRIILLGAPGAGKGTQAQFIMAKFGIPQIS
[Truncated_Name:12]3GMT_A.pdb    ----------MRLILLGAPGAGKGTQANFIKEKFGIPQIS
[Truncated_Name:13]4PZL_A.pdb    TENLYFQSNAMRIILLGAPGAGKGTQAKIIEQKYNIAHIS
                                           **^*****  *******  *  *^ *  **
                                 1        .         .         .         40

                                41        .         .         .         80
[Truncated_Name:1]1AKE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:2]6S36_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:3]6RZE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:4]3HPR_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:5]1E4V_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:6]5EJE_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDACKLVTDELVIALVKE
[Truncated_Name:7]1E4Y_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVKE
[Truncated_Name:8]3X2S_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDCGKLVTDELVIALVKE
[Truncated_Name:9]6HAP_A.pdb      TGDMLRAAVKSGSELGKQAKDIMDAGKLVTDELVIALVRE
[Truncated_Name:10]6HAM_A.pdb     TGDMLRAAIKSGSELGKQAKDIMDAGKLVTDEIIIALVKE
[Truncated_Name:11]4K46_A.pdb     TGDMLRAAIKAGTELGKQAKSVIDAGQLVSDDIILGLVKE
[Truncated_Name:12]3GMT_A.pdb     TGDMLRAAVKAGTPLGVEAKTYMDEGKLVPDSLIIGLVKE
```

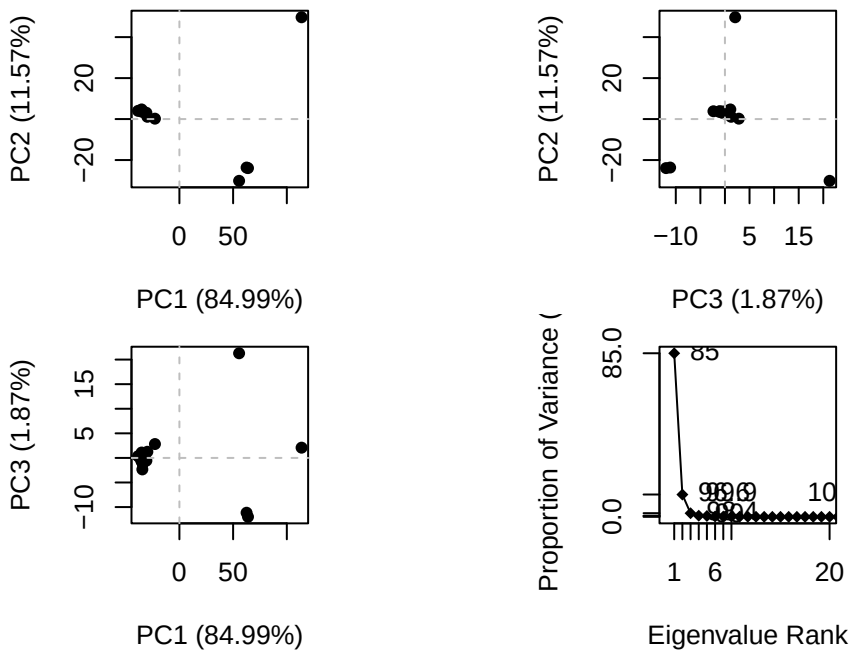
```
[Truncated_Name:13]4PZL_A.pdb   TGDMIRETIKSGSALGQELKKVLDAGELVSDEFIIKIVKD
                                ****^*  ^* *^ **   *  ^*   ** *  ^^ ^*^^
                               41        .         .         .         80

                               81        .         .         .         120
[Truncated_Name:1]1AKE_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:2]6S36_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:3]6RZE_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:4]3HPR_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:5]1E4V_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:6]5EJE_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:7]1E4Y_A.pdb    RIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:8]3X2S_A.pdb    RIAQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:9]6HAP_A.pdb    RICQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:10]6HAM_A.pdb   RICQEDSRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFD
[Truncated_Name:11]4K46_A.pdb   RIAQDDCAKGFLLDGFPRTIPQADGLKEVGVVVDYVIEFD
[Truncated_Name:12]3GMT_A.pdb   RLKEADCANGYLFDGFPRTIAQADAMKEAGVAIDYVLEID
[Truncated_Name:13]4PZL_A.pdb   RISKNDCNNGFLLDGVPRTIPQAQELDKLGVNIDYIVEVD
                                *^   *   *^* ** **** **  ^   *^ ^**^^* *
                               81        .         .         .         120

                              121        .         .         .         160
[Truncated_Name:1]1AKE_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:2]6S36_A.pdb    VPDELIVDKIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:3]6RZE_A.pdb    VPDELIVDAIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:4]3HPR_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDGTG
[Truncated_Name:5]1E4V_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:6]5EJE_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:7]1E4Y_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:8]3X2S_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:9]6HAP_A.pdb    VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:10]6HAM_A.pdb   VPDELIVDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTG
[Truncated_Name:11]4K46_A.pdb   VADSVIVERMAGRRAHLASGRTYHNVYNPPKVEGKDDVTG
[Truncated_Name:12]3GMT_A.pdb   VPFSEIIERMSGRRTHPASGRTYHVKFNPPKVEGKDDVTG
[Truncated_Name:13]4PZL_A.pdb   VADNLLIERITGRRIHPASGRTYHTKFNPPKVADKDDVTG
                                *    ^^^ ^ *** *  *** **  ^*****  *** **
                              121        .         .         .         160

                              161        .         .         .         200
[Truncated_Name:1]1AKE_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:2]6S36_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:3]6RZE_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:4]3HPR_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
```

```
[Truncated_Name:5]1E4V_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:6]5EJE_A.pdb    EELTTRKDDQEECVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:7]1E4Y_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:8]3X2S_A.pdb    EELTTRKDDQEETVRKRLCEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:9]6HAP_A.pdb    EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:10]6HAM_A.pdb   EELTTRKDDQEETVRKRLVEYHQMTAPLIGYYSKEAEAGN
[Truncated_Name:11]4K46_A.pdb   EDLVIREDDKEETVLARLGVYHNQTAPLIAYYGKEAEAGN
[Truncated_Name:12]3GMT_A.pdb   EPLVQRDDDKEETVKKRLDVYEAQTKPLITYYGDWARRGA
[Truncated_Name:13]4PZL_A.pdb   EPLITRTDDNEDTVKQRLSVYHAQTAKLIDFYRNFSSTNT
                                * *  * ** *^ *  **  *   *  ** ^*
                               161        .         .         .         200

                               201        .         .      227
[Truncated_Name:1]1AKE_A.pdb      T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:2]6S36_A.pdb      T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:3]6RZE_A.pdb      T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:4]3HPR_A.pdb      T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:5]1E4V_A.pdb      T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:6]5EJE_A.pdb      T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:7]1E4Y_A.pdb      T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:8]3X2S_A.pdb      T--KYAKVDGTKPVAEVRADLEKILG-
[Truncated_Name:9]6HAP_A.pdb      T--KYAKVDGTKPVCEVRADLEKILG-
[Truncated_Name:10]6HAM_A.pdb     T--KYAKVDGTKPVCEVRADLEKILG-
[Truncated_Name:11]4K46_A.pdb     T--QYLKFDGTKAVAEVSAELEKALA-
[Truncated_Name:12]3GMT_A.pdb     E-------NGLKAPA-----YRKISG-
[Truncated_Name:13]4PZL_A.pdb     KIPKYIKINGDQAVEKVSQDIFDQLNK
                                           *
                               201        .         .      227
```

```
Call:
  pdbaln(files = files, fit = TRUE, exefile = "msa")

Class:
  pdbs, fasta

Alignment dimensions:
  13 sequence rows; 227 position columns (204 non-gap, 23 gap)

+ attr: xyz, resno, b, chain, id, ali, resid, sse, call
```

Principal Component Analysis

```
#perform PCA
pc.xray <- pca(pdbs)
plot(pc.xray)
```




```
# Visualize first principal component
pc1 <- mktrj(pc.xray, pc=1, file="pc_1.pdb")
```

Alpha Fold

The top hit is Peptidase A2 domain-containing protein from Thalassobius mangrovi

Custom analysis of resulting models

```
library(bio3d)
results_dir <- "hivpr_dimer_23119/"
```

```
library(bio3d)
# File names for all PDB models
pdb_files <- list.files(path=results_dir,
                        pattern="*.pdb",
                        full.names = TRUE)
pdb_files
```

```
[1] "hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_s
[2] "hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_s
[3] "hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_s
[4] "hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_s
[5] "hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_s
```

```
# Read all data from Models
#  and superpose/fit coords
#pdbs <- pdbaln(pdb_files, fit=TRUE)
```

Previous code results in an error message.

```
# Optionally install the MSA package for use with pdbaln()
#install.packages("BiocManager")
#BiocManager::install("msa")

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

```
Reading PDB files:
hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_001_alphafold2_multimer_v3_model_1_seed_0
hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_002_alphafold2_multimer_v3_model_5_seed_0
hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_003_alphafold2_multimer_v3_model_4_seed_0
hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_004_alphafold2_multimer_v3_model_2_seed_0
hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_005_alphafold2_multimer_v3_model_3_seed_0
.....

Extracting sequences
```

```
pdb/seq: 1   name: hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_001_alphafold2_multime
pdb/seq: 2   name: hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_002_alphafold2_multime
pdb/seq: 3   name: hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_003_alphafold2_multime
pdb/seq: 4   name: hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_004_alphafold2_multime
pdb/seq: 5   name: hivpr_dimer_23119//hivpr_dimer_23119_unrelaxed_rank_005_alphafold2_multime
```

```
pdbs
```

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

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

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

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

```
[Truncated_Name:5]hivpr_dime   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
```

Calculate the RMSD between all models.

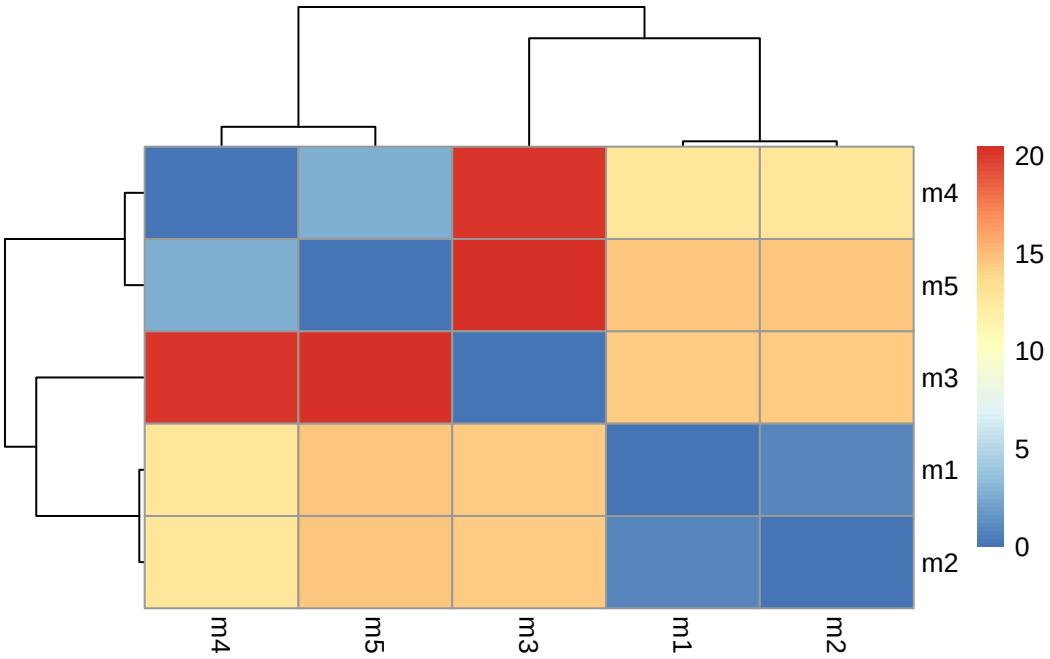
```
rd <- rmsd(pdbs)
```

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

```
range(rd)
```

```
[1]  0.000 20.432
```

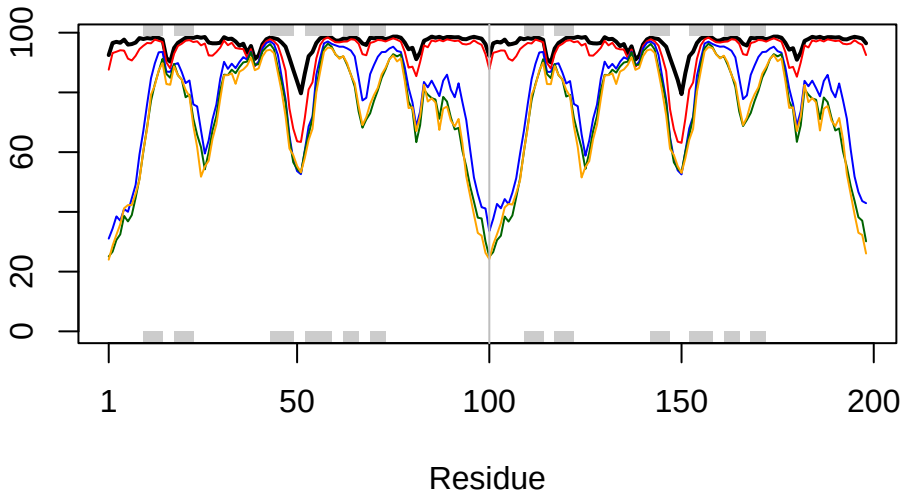
```
library(pheatmap)

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
```

```
plotb3(pdbs$b, typ="l", lwd=2, sse=pdb)
points(pdbs$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")
```



Improve the superposition/fitting of our models by finding the most consistent "rigid core" common across all the models. For this we will use the core.find() function:

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

```
core size 197 of 198  vol = 6119.978
core size 196 of 198  vol = 5369.631
core size 195 of 198  vol = 5007.166
core size 194 of 198  vol = 4736.496
core size 193 of 198  vol = 4457.094
core size 192 of 198  vol = 4232.564
core size 191 of 198  vol = 4012.815
core size 190 of 198  vol = 3810.213
core size 189 of 198  vol = 3678.285
core size 188 of 198  vol = 3549.395
core size 187 of 198  vol = 3431.938
core size 186 of 198  vol = 3316.333
core size 185 of 198  vol = 3243.309
core size 184 of 198  vol = 3149.827
core size 183 of 198  vol = 3078.402
core size 182 of 198  vol = 3019.868
core size 181 of 198  vol = 2958.106
```

```
core size 180 of 198  vol = 2927.306
core size 179 of 198  vol = 2899.182
core size 178 of 198  vol = 2898.894
core size 177 of 198  vol = 2915.917
core size 176 of 198  vol = 2933.733
core size 175 of 198  vol = 2948.254
core size 174 of 198  vol = 2979.453
core size 173 of 198  vol = 2999.025
core size 172 of 198  vol = 2979.648
core size 171 of 198  vol = 2964.773
core size 170 of 198  vol = 2942.972
core size 169 of 198  vol = 2908.3
core size 168 of 198  vol = 2864.574
core size 167 of 198  vol = 2821.943
core size 166 of 198  vol = 2778.522
core size 165 of 198  vol = 2710.333
core size 164 of 198  vol = 2641.042
core size 163 of 198  vol = 2579.594
core size 162 of 198  vol = 2513.106
core size 161 of 198  vol = 2429.205
core size 160 of 198  vol = 2345.942
core size 159 of 198  vol = 2272.876
core size 158 of 198  vol = 2204.156
core size 157 of 198  vol = 2140.014
core size 156 of 198  vol = 2050.59
core size 155 of 198  vol = 1983.639
core size 154 of 198  vol = 1907.44
core size 153 of 198  vol = 1845.477
core size 152 of 198  vol = 1769.722
core size 151 of 198  vol = 1709.078
core size 150 of 198  vol = 1636.924
core size 149 of 198  vol = 1579.485
core size 148 of 198  vol = 1509.587
core size 147 of 198  vol = 1456.495
core size 146 of 198  vol = 1398.53
core size 145 of 198  vol = 1341.387
core size 144 of 198  vol = 1293.081
core size 143 of 198  vol = 1248.378
core size 142 of 198  vol = 1193.388
core size 141 of 198  vol = 1140.285
core size 140 of 198  vol = 1098.208
core size 139 of 198  vol = 1061.118
core size 138 of 198  vol = 1015.106
```

```
core size 137 of 198  vol = 978.862
core size 136 of 198  vol = 933.985
core size 135 of 198  vol = 889.711
core size 134 of 198  vol = 848.21
core size 133 of 198  vol = 804.689
core size 132 of 198  vol = 768.031
core size 131 of 198  vol = 724.517
core size 130 of 198  vol = 684.306
core size 129 of 198  vol = 644.893
core size 128 of 198  vol = 609.842
core size 127 of 198  vol = 568.284
core size 126 of 198  vol = 536.469
core size 125 of 198  vol = 506.102
core size 124 of 198  vol = 486.685
core size 123 of 198  vol = 462.316
core size 122 of 198  vol = 431.163
core size 121 of 198  vol = 404.541
core size 120 of 198  vol = 373.619
core size 119 of 198  vol = 348.087
core size 118 of 198  vol = 325.641
core size 117 of 198  vol = 302.829
core size 116 of 198  vol = 284.101
core size 115 of 198  vol = 260.484
core size 114 of 198  vol = 245.38
core size 113 of 198  vol = 230.906
core size 112 of 198  vol = 212.841
core size 111 of 198  vol = 198.554
core size 110 of 198  vol = 182.254
core size 109 of 198  vol = 172.636
core size 108 of 198  vol = 161.91
core size 107 of 198  vol = 152.145
core size 106 of 198  vol = 141.393
core size 105 of 198  vol = 131.934
core size 104 of 198  vol = 123.075
core size 103 of 198  vol = 112.898
core size 102 of 198  vol = 101.096
core size 101 of 198  vol = 90.574
core size 100 of 198  vol = 79.79
core size 99 of 198  vol = 70.252
core size 98 of 198  vol = 63.673
core size 97 of 198  vol = 58.103
core size 96 of 198  vol = 49.453
core size 95 of 198  vol = 40.86
```

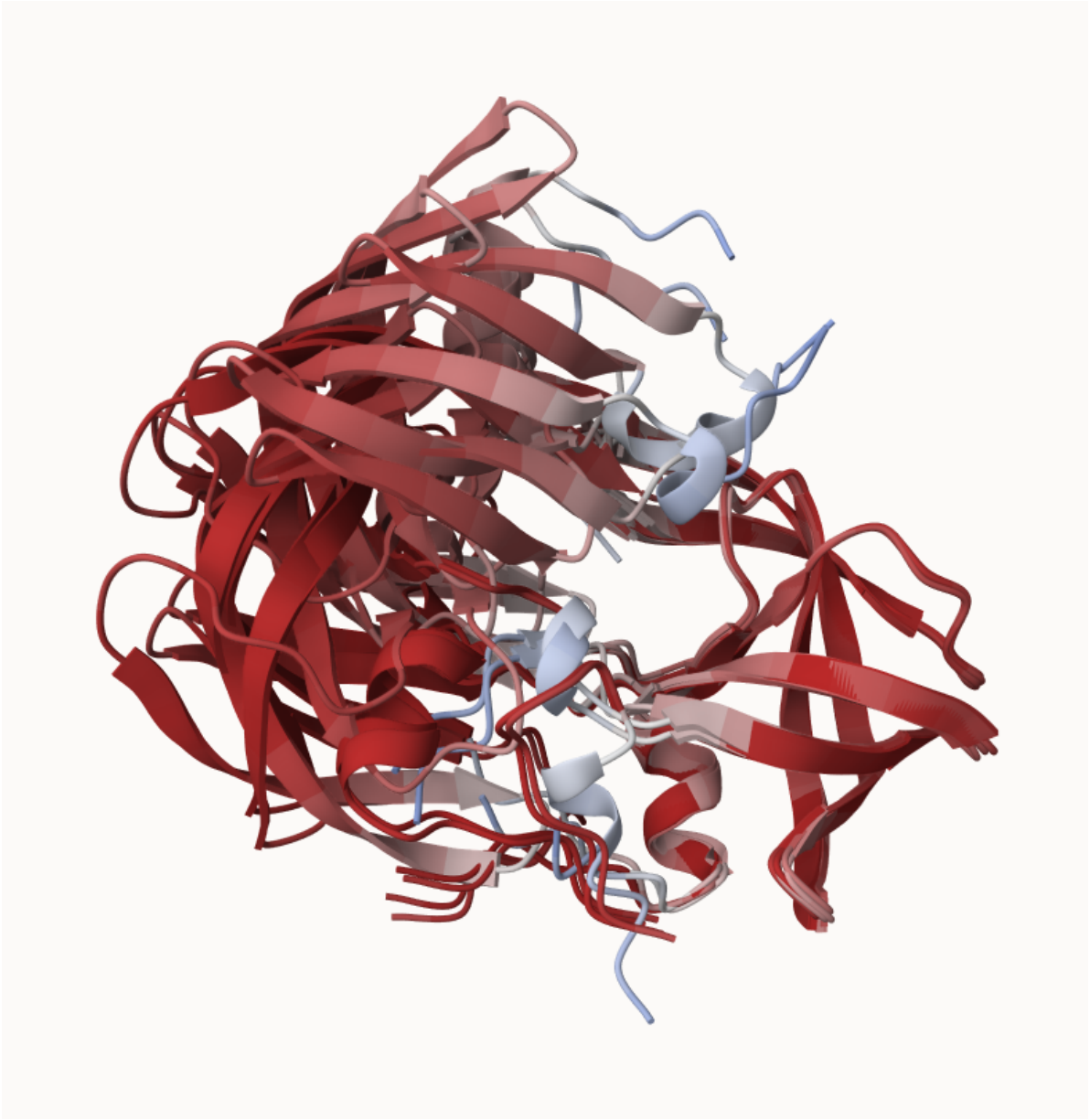
```
 core size 94 of 198  vol = 30.175
 core size 93 of 198  vol = 22.974
 core size 92 of 198  vol = 14.316
 core size 91 of 198  vol = 9.184
 core size 90 of 198  vol = 5.133
 core size 89 of 198  vol = 3.603
 core size 88 of 198  vol = 2.705
 core size 87 of 198  vol = 2.032
 core size 86 of 198  vol = 1.404
 core size 85 of 198  vol = 1.211
 core size 84 of 198  vol = 1.073
 core size 83 of 198  vol = 0.925
 core size 82 of 198  vol = 0.788
 core size 81 of 198  vol = 0.651
 core size 80 of 198  vol = 0.528
 core size 79 of 198  vol = 0.486
 FINISHED: Min vol ( 0.5 ) reached
```

Use the identified core atom positions as a basis for a more suitable superposition:

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

```
# 80 positions (cumulative volume <= 0.5 Angstrom^3)
  start end length
1    10  25     16
2    27  48     22
3    53  94     42
```

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

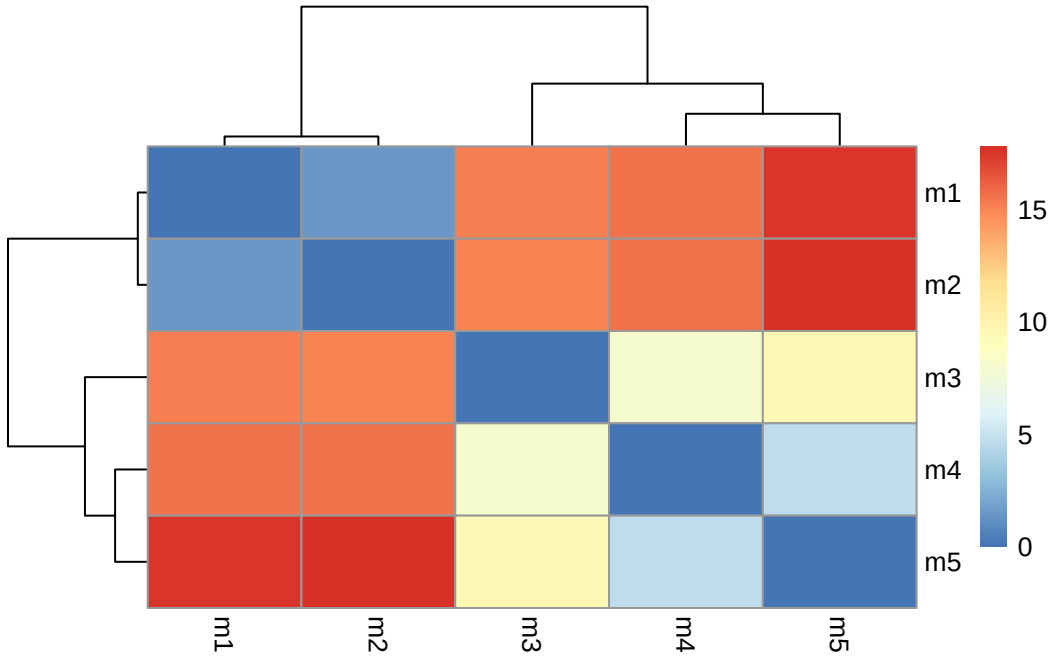


```
rd <- rmsd(xyz)
```

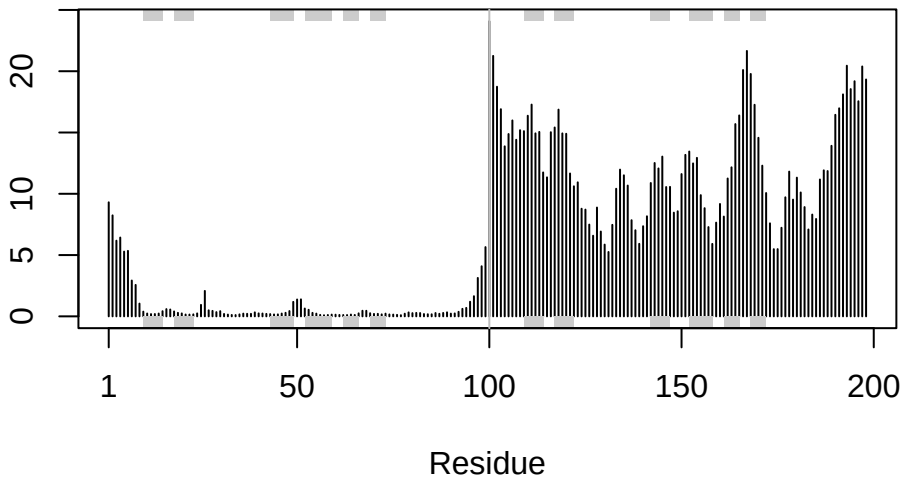
```
Warning in rmsd(xyz): No indices provided, using the 198 non NA positions
```

```
# Change the names for easy reference
colnames(rd) <- paste0("m",1:5)
```

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




```
rf <- rmsf(xyz)

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



Predicted Alignment Error (PAE) for domains

```
library(jsonlite)

# Listing of all PAE JSON files
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"
```

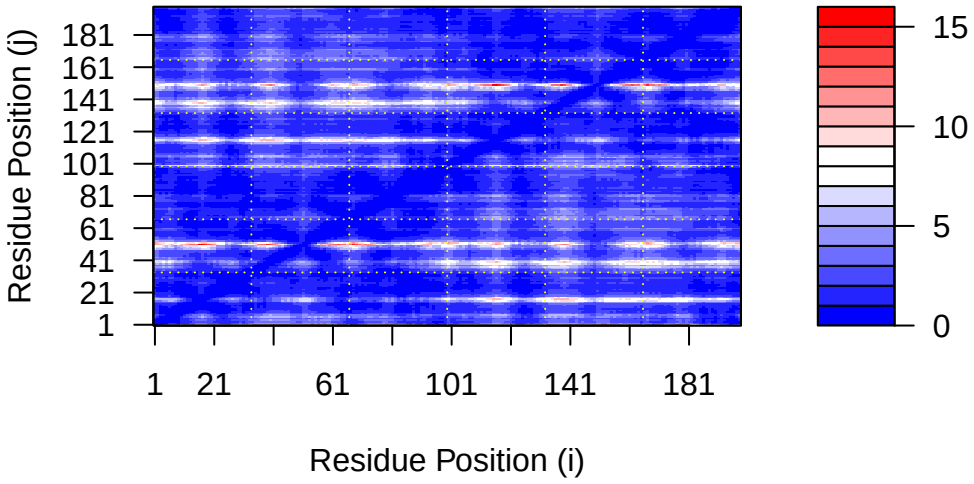
```
# Per-residue pLDDT scores
#  same as B-factor of PDB..
head(pae1$plddt)
```

```
[1] 92.50 96.56 96.94 96.62 97.69 96.00
```

For PAE values the lower the better

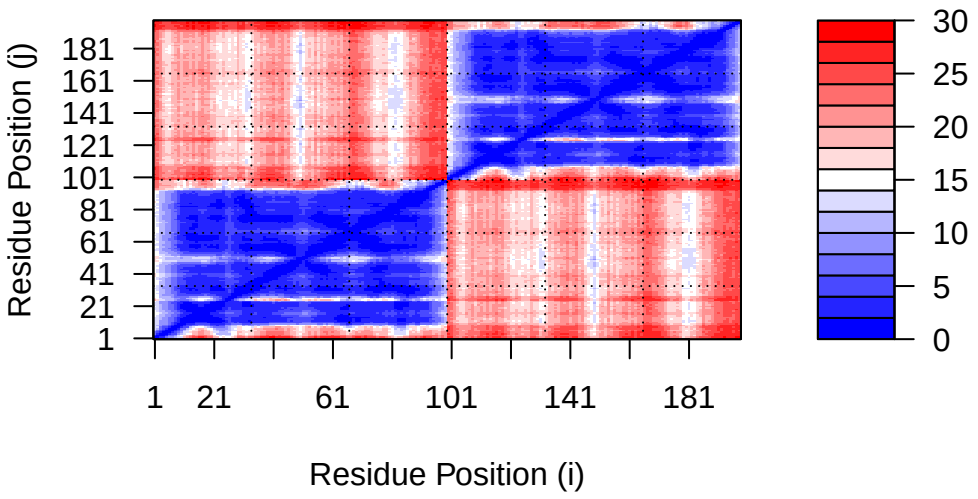
Plot these with ggplot or with functions from the Bio3D package:

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

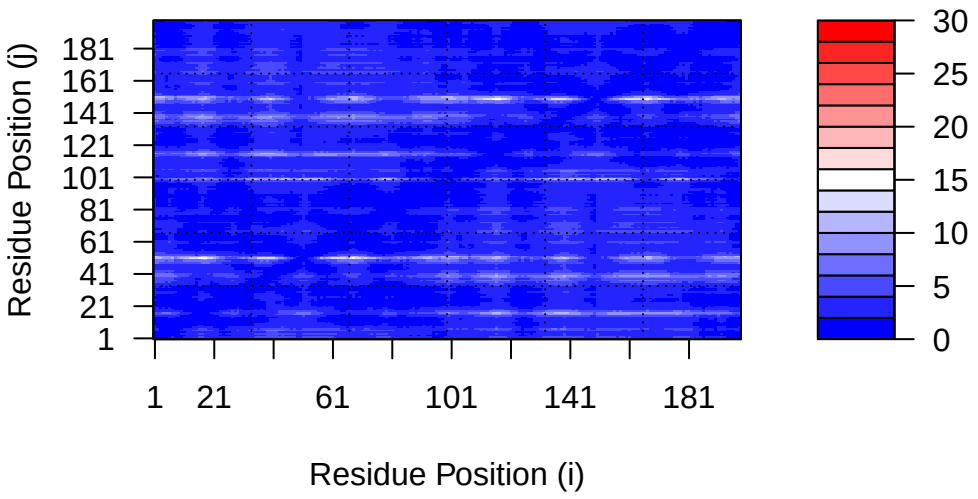


Plot with `plot.dmat()` function

```
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))
```



The residue conservation from alignment file

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

```
[1] "hivpr_dimer_23119//hivpr_dimer_23119.a3m"
```

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

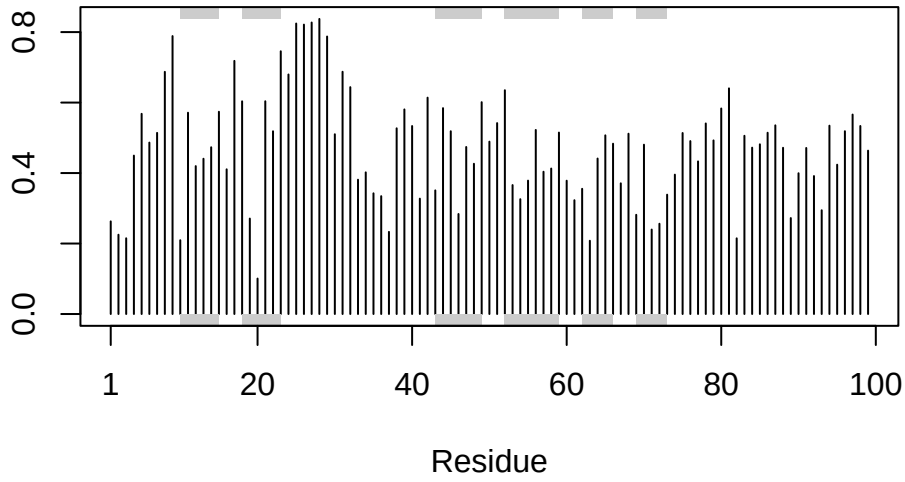
```
[1] " ** Duplicated sequence id's: 101 **"
[2] " ** Duplicated sequence id's: 101 **"
```

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

```
[1] 5378  132
```

Score residue conservation in the alignment with the `conserv()` function.

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




```
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")
```