Class 10: Structural Bioinformatics pt 1

Destiny (A16340362)

#The PDB Database

First lets see what's in the PDB database- the main resposity of protein structures

Downloaded composition stats from: https://www.rcsb.org/

For context: Release 2023_04 of 12-Sept-2023

```
stats <- read.csv("PDBstats.csv", row.name=1)
stats
```

```
                          X.ray     EM    NMR Multiple.methods Neutron Other
Protein (only)          158,844 11,759 12,296              197      73    32
Protein/Oligosaccharide   9,260  2,054     34                8       1     0
Protein/NA                8,307  3,667    284                7       0     0
Nucleic acid (only)       2,730    113  1,467               13       3     1
Other                       164      9     32                0       0     0
Oligosaccharide (only)       11      0      6                1       0     4
                          Total
Protein (only)          183,201
Protein/Oligosaccharide  11,357
Protein/NA               12,265
Nucleic acid (only)       4,327
Other                       205
Oligosaccharide (only)       22
```

```
x <-  stats$X.ray
x
```

```
[1] "158,844" "9,260"   "8,307"   "2,730"   "164"     "11"
```

`gsub()` is for pattern replacement, first thing is what you want to replace

```r
as.numeric(gsub(",", "", x))
```

```
[1] 158844   9260   8307   2730    164     11
```

```r
rm.comma <- function(x) {
  as.numeric(gsub(",", "", x))
}
```

```r
rm.comma(stats$EM)
```

```
[1] 11759  2054  3667   113     9     0
```

I can use the `apply()` to fix the whole table

```r
pdbstats <- apply(stats, 2, rm.comma)
rownames(pdbstats) <- rownames(stats)
head(pdbstats)
```

```
                          X.ray    EM   NMR Multiple.methods Neutron Other
Protein (only)           158844 11759 12296              197      73    32
Protein/Oligosaccharide    9260  2054    34                8       1     0
Protein/NA                 8307  3667   284                7       0     0
Nucleic acid (only)        2730   113  1467               13       3     1
Other                       164     9    32                0       0     0
Oligosaccharide (only)       11     0     6                1       0     4
                          Total
Protein (only)           183201
Protein/Oligosaccharide   11357
Protein/NA                12265
Nucleic acid (only)        4327
Other                       205
Oligosaccharide (only)       22
```

> Q1: What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy.

```r
totals <- apply(pdbstats, 2, sum)
totals
```

```
           X.ray              EM             NMR Multiple.methods
          179316           17602           14119              226
         Neutron           Other           Total
              77              37          211377
```

```
round(totals/totals["Total"]* 100, 2)
```

```
           X.ray              EM             NMR Multiple.methods
           84.83            8.33            6.68             0.11
         Neutron           Other           Total
            0.04            0.02          100.00
```

> Q2: What proportion of structures in the PDB are protein?

```
round(pdbstats[, "Total"] / sum(pdbstats[,"Total"]) *100, 2)
```

```
      Protein (only) Protein/Oligosaccharide              Protein/NA
               86.67                    5.37                    5.80
 Nucleic acid (only)                   Other  Oligosaccharide (only)
                2.05                    0.10                    0.01
```

> Q3: Type HIV in the PDB website search box on the home page and determine how many HIV-1 protease structures are in the current PDB? SKIPPED

> Q4: Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure?

There is a 2 Angstrom structure and hydrogen is not visible at this resolution, You need 1 Angstrom or better to see such a small atoms

> Q5: There is a critical "conserved" water molecule in the binding site. Can you identify this water molecule? What residue number does this water molecule have

water HOH 308

Here is a lovely figure of HIP-Pr with the catalytic ASP residues, the MK1 compound and the all important water 308

> Q6: Generate and save a figure clearly showing the two distinct chains of HIV-protease along with the ligand. You might also consider showing the catalytic residues ASP 25 in each chain and the critical water (we recommend "Ball & Stick" for these side-chains). Add this figure to your Quarto document.

##The bio3d package for structueral bioinformatics

```
library(bio3d)

pdb <- read.pdb("1hsg")
```

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

```
pdb
```

```

 Call:  read.pdb(file = "1hsg")

   Total Models#: 1
     Total Atoms#: 1686,  XYZs#: 5058  Chains#: 2  (values: A B)

     Protein Atoms#: 1514  (residues/Calpha atoms#: 198)
     Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)

     Non-protein/nucleic Atoms#: 172  (residues: 128)
     Non-protein/nucleic resid values: [ HOH (127), MK1 (1) ]

   Protein sequence:
      PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGIGGFIKVRQYD
      QILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFPQITLWQRPLVTIKIGGQLKE
      ALLDTGADDTVLEEMSLPGRWKPKMIGGIGGFIKVRQYDQILIEICGHKAIGTVLVGPTP
      VNIIGRNLLTQIGCTLNF

+ attr: atom, xyz, seqres, helix, sheet,
        calpha, remark, call
```

```
head(pdb$atom)
```

```
  type eleno elety  alt resid chain resno insert      x      y     z o     b
1 ATOM     1     N <NA>   PRO     A     1   <NA> 29.361 39.686 5.862 1 38.10
2 ATOM     2    CA <NA>   PRO     A     1   <NA> 30.307 38.663 5.319 1 40.62
3 ATOM     3     C <NA>   PRO     A     1   <NA> 29.760 38.071 4.022 1 42.64
4 ATOM     4     O <NA>   PRO     A     1   <NA> 28.600 38.302 3.676 1 43.40
5 ATOM     5    CB <NA>   PRO     A     1   <NA> 30.508 37.541 6.342 1 37.87
6 ATOM     6    CG <NA>   PRO     A     1   <NA> 29.296 37.591 7.162 1 38.40
  segid elesy charge
1  <NA>     N   <NA>
2  <NA>     C   <NA>
3  <NA>     C   <NA>
4  <NA>     O   <NA>
5  <NA>     C   <NA>
6  <NA>     C   <NA>
```

#Predicting functional motions of a single structure

Lets finish today with a bioinformatics calculation to predict the functional motions of a PDK structure

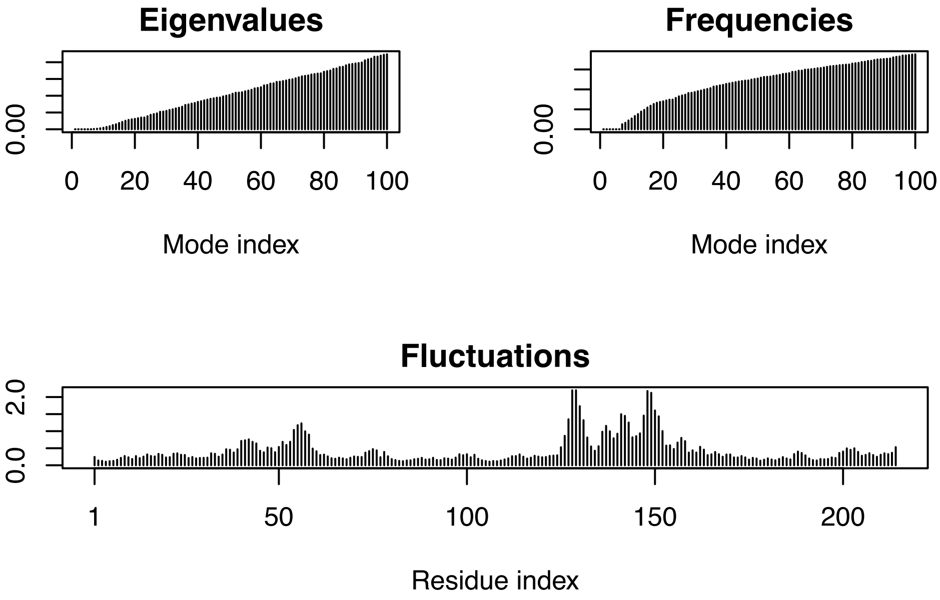
```
adk <- read.pdb("6s36")
```

```
  Note: Accessing on-line PDB file
   PDB has ALT records, taking A only, rm.alt=TRUE
```

```
m <- nma(adk)
```

```
Building Hessian...        Done in 0.016 seconds.
Diagonalizing Hessian...   Done in 0.286 seconds.
```

```
plot(m)
```



```
mktrj(m, file="adk_m7.pdb")
```

Class 11: Comparative analysis of structures

Destiny (A16340362)

We need some packages for todays class. These include `bio3d` and `msa`

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

`BiocManager::install("msa")` all entered in the R "brain" console

```r
library(bio3d)

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

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

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

```r
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 sequences

```
#b <- blast.pdb(aa)
```

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

```
#attributes(b)
#head(b$hit.tbl)
```

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

```
 [1] "1AKE_A" "6S36_A" "6RZE_A" "3HPR_A" "1E4V_A" "5EJE_A" "1E4Y_A" "3X2S_A"
 [9] "6HAP_A" "6HAM_A" "4K46_A" "3GMT_A" "4PZL_A"
```

Side note: Let's annotate these structures (in other words, find out what they are, what species they're from. stuff about the experiement they were solved in, etc.)

For this use the `pdb.annotate()`

```
anno <- pdb.annotate(hits$pdb.id)
```

```
#attributes(anno)
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         ligandId
1AKE_A       2.00 Adenylate kinase Adenylate kinase (ADK)              AP5
6S36_A       1.60             <NA> Adenylate kinase (ADK) CL (3),NA,MG (2)
6RZE_A       1.69             <NA> Adenylate kinase (ADK)    NA (3),CL (2)
3HPR_A       2.00             <NA> Adenylate kinase (ADK)              AP5
1E4V_A       1.85 Adenylate kinase Adenylate kinase (ADK)              AP5
5EJE_A       1.90             <NA> Adenylate kinase (ADK)           AP5,CO
                                             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
                                       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 INHIB
6S36_A
6RZE_A
3HPR_A
1E4V_A
5EJE_A                                                                                  Crys
                                                    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.

```
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
```

```
  |
  |                                                                      |   0%
  |
  |=====                                                                 |   8%
  |
  |===========                                                           |  15%
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  |===========================================================           |  85%
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  |=================================================================     |  92%
  |
  |======================================================================| 100%
```

Now we have all these related structures we can Align and superimpose

```r
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
```

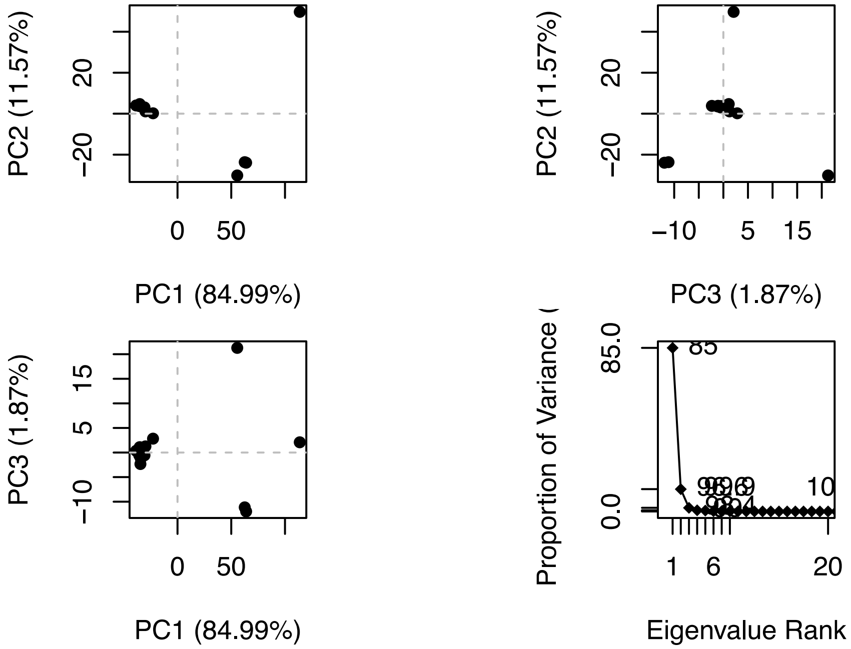
```
pdbs
```

```
                                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

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



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

Custom analysis of resulting models

```
results_dir <- "hivpr_dimer_23119"
```

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

```
library(bio3d)

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

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
```

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

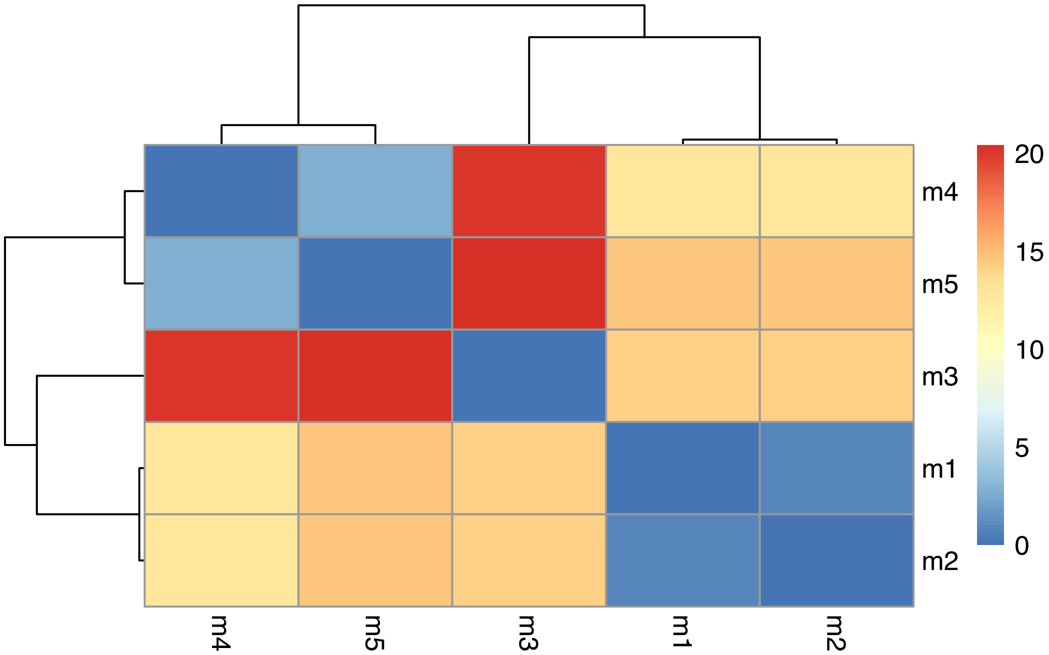
```
Warning in rmsd(pdbs): No indices provided, using the 198 non NA positions
```

```r
range(rd)
```

```
[1]  0.000 20.431
```

```r
library(pheatmap)
```

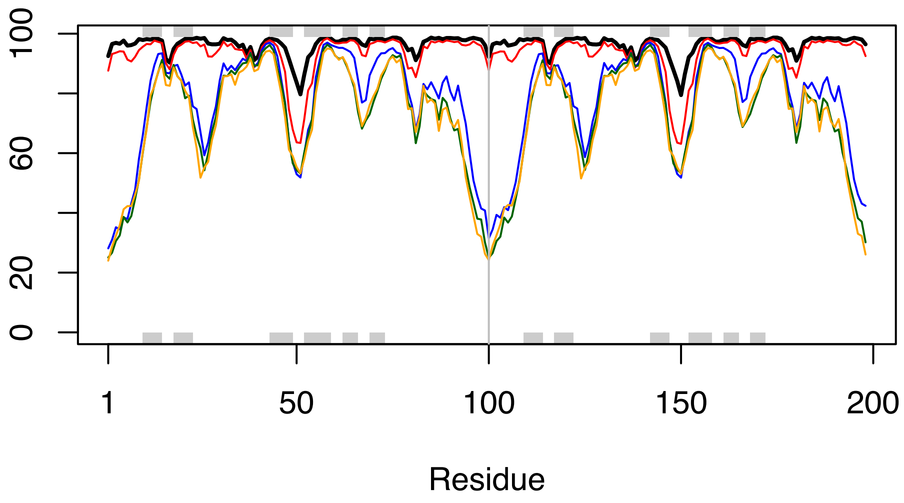
```
colnames(rd) <- paste0("m",1:5)
rownames(rd) <- paste0("m",1:5)
pheatmap(rd)
```



```
# 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")
```



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

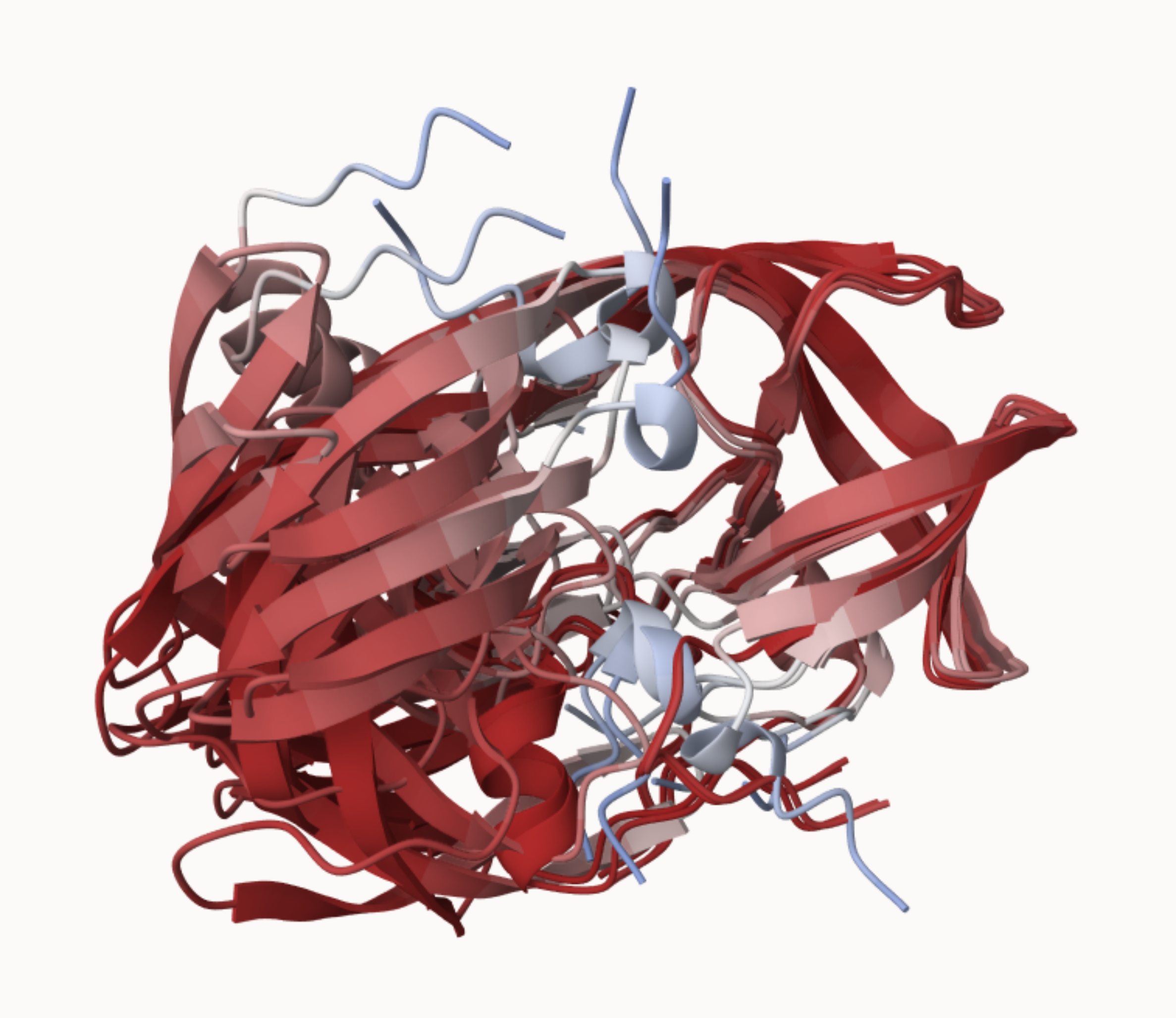
```
core size 197 of 198  vol = 6154.856
core size 196 of 198  vol = 5399.691
core size 195 of 198  vol = 5074.812
core size 194 of 198  vol = 4802.535
core size 193 of 198  vol = 4520.271
core size 192 of 198  vol = 4305.376
core size 191 of 198  vol = 4089.806
core size 190 of 198  vol = 3886.157
core size 189 of 198  vol = 3758.332
core size 188 of 198  vol = 3620.19
core size 187 of 198  vol = 3496.708
core size 186 of 198  vol = 3389.995
core size 185 of 198  vol = 3320.123
core size 184 of 198  vol = 3258.693
core size 183 of 198  vol = 3208.601
core size 182 of 198  vol = 3156.745
core size 181 of 198  vol = 3141.677
core size 180 of 198  vol = 3136.582
core size 179 of 198  vol = 3155.527
core size 178 of 198  vol = 3185.368
core size 177 of 198  vol = 3204.492
core size 176 of 198  vol = 3211.981
core size 175 of 198  vol = 3234.994
core size 174 of 198  vol = 3244.062
core size 173 of 198  vol = 3237.844
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 = 2928.271
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 = 2636.515
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 = 1632.172
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 = 1367.705
core size 145 of 198  vol = 1302.596
core size 144 of 198  vol = 1251.985
core size 143 of 198  vol = 1207.975
core size 142 of 198  vol = 1167.112
core size 141 of 198  vol = 1118.27
core size 140 of 198  vol = 1081.663
core size 139 of 198  vol = 1029.749
core size 138 of 198  vol = 981.765
core size 137 of 198  vol = 944.445
core size 136 of 198  vol = 899.223
core size 135 of 198  vol = 859.402
core size 134 of 198  vol = 814.693
core size 133 of 198  vol = 771.861
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 = 324.739
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 = 128.923
core size 104 of 198  vol = 114.054
core size 103 of 198  vol = 100.936
core size 102 of 198  vol = 90.43
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 = 14.976
```

```
 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
```

```
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
```

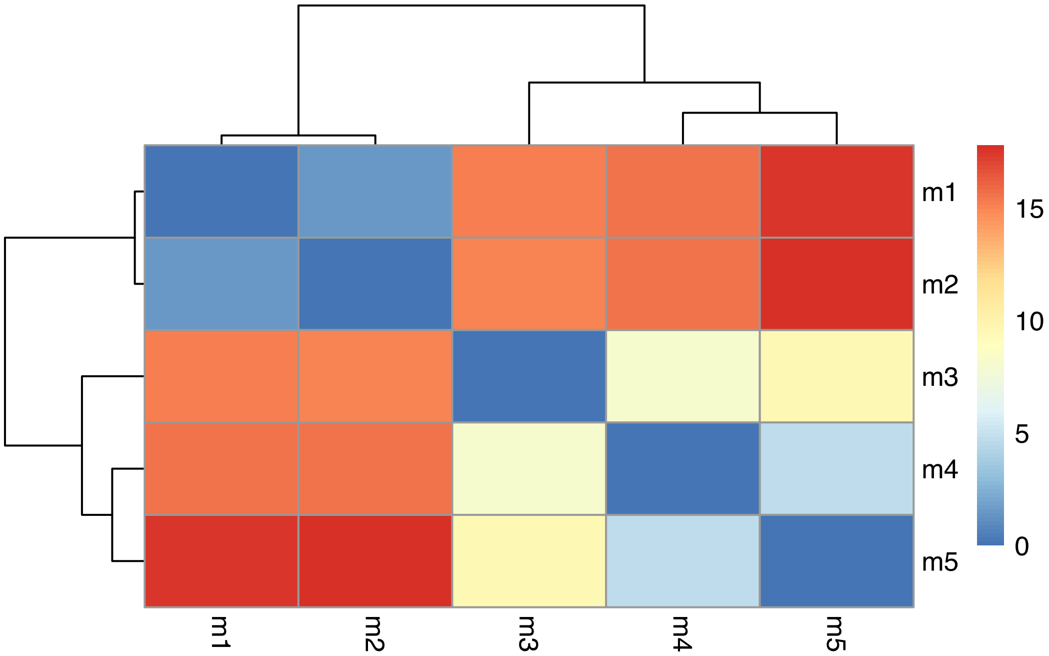
```
xyz <- pdbfit(pdbs, core.inds, outpath="corefit_structures")
```



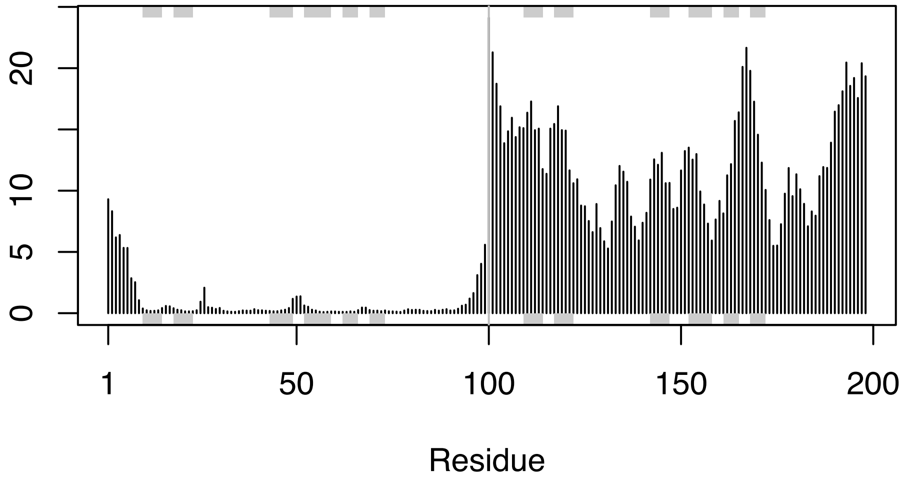
```r
rd <- rmsd(xyz)
```

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

```r
# 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 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
```

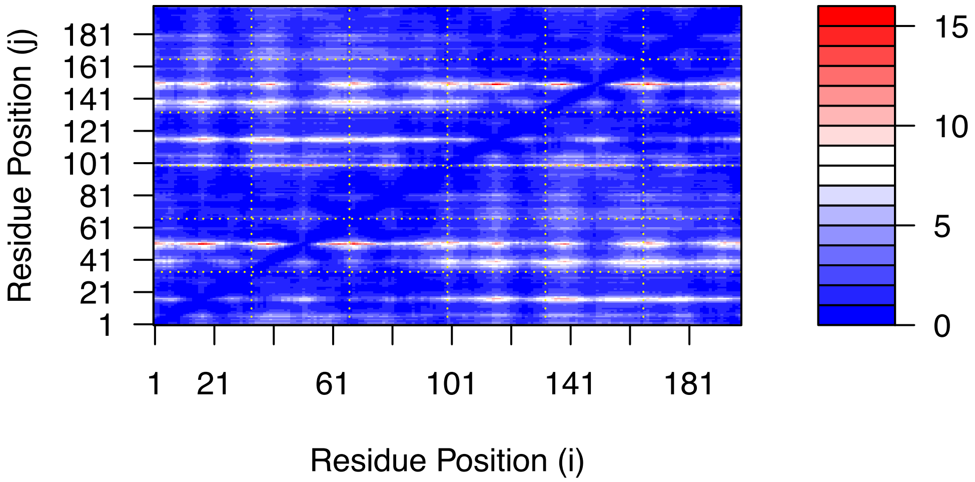
```
pae1$max_pae
```

```
[1] 15.54688
```

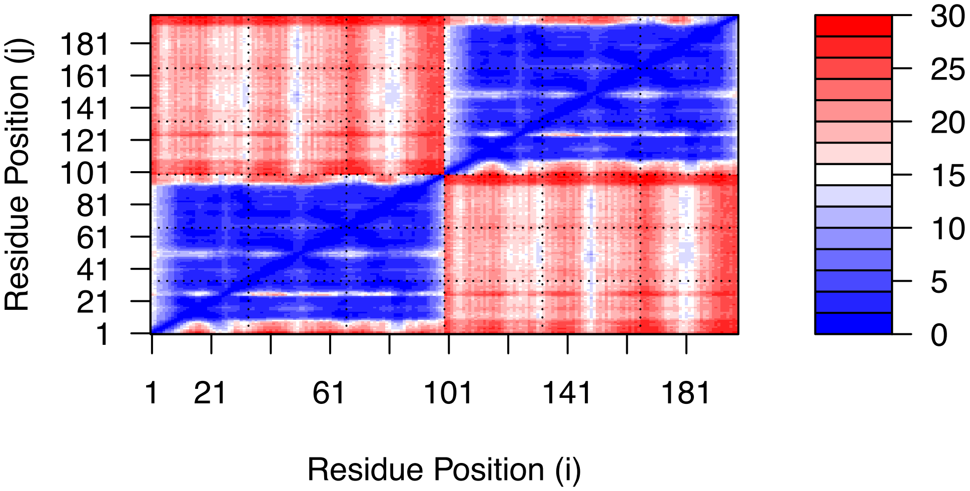
```
pae5$max_pae
```

```
[1] 29.29688
```

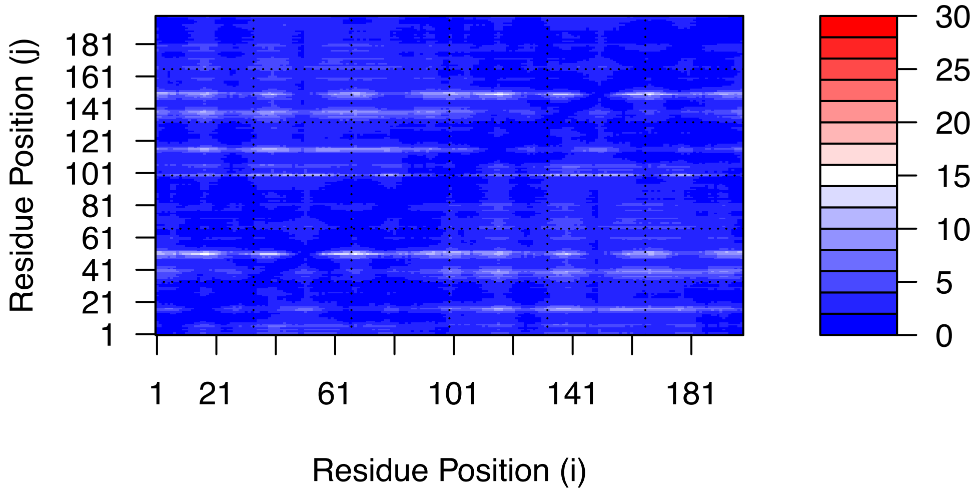
```
plot.dmat(pae1$pae,
          xlab="Residue Position (i)",
          ylab="Residue Position (j)")
```



```
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))
```



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"
```

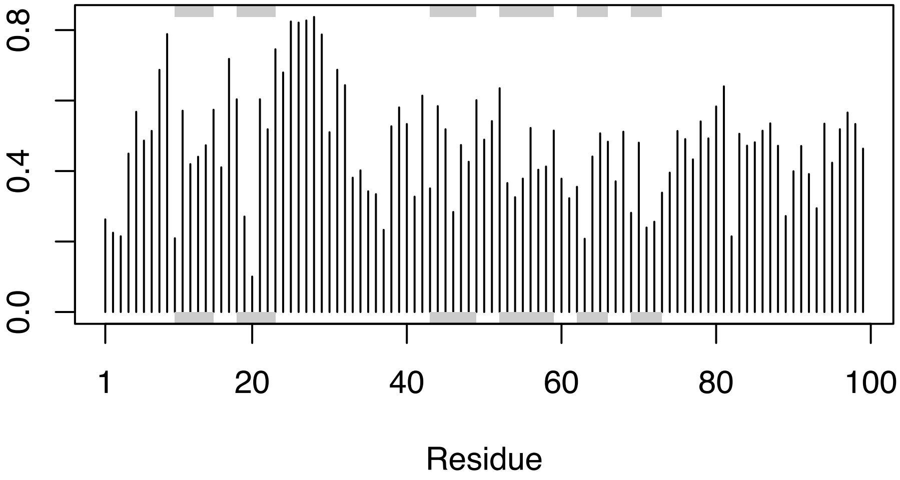
```
aln <- read.fasta(aln_file[1], to.upper = TRUE)
```

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

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

```
[1] 5378  132
```

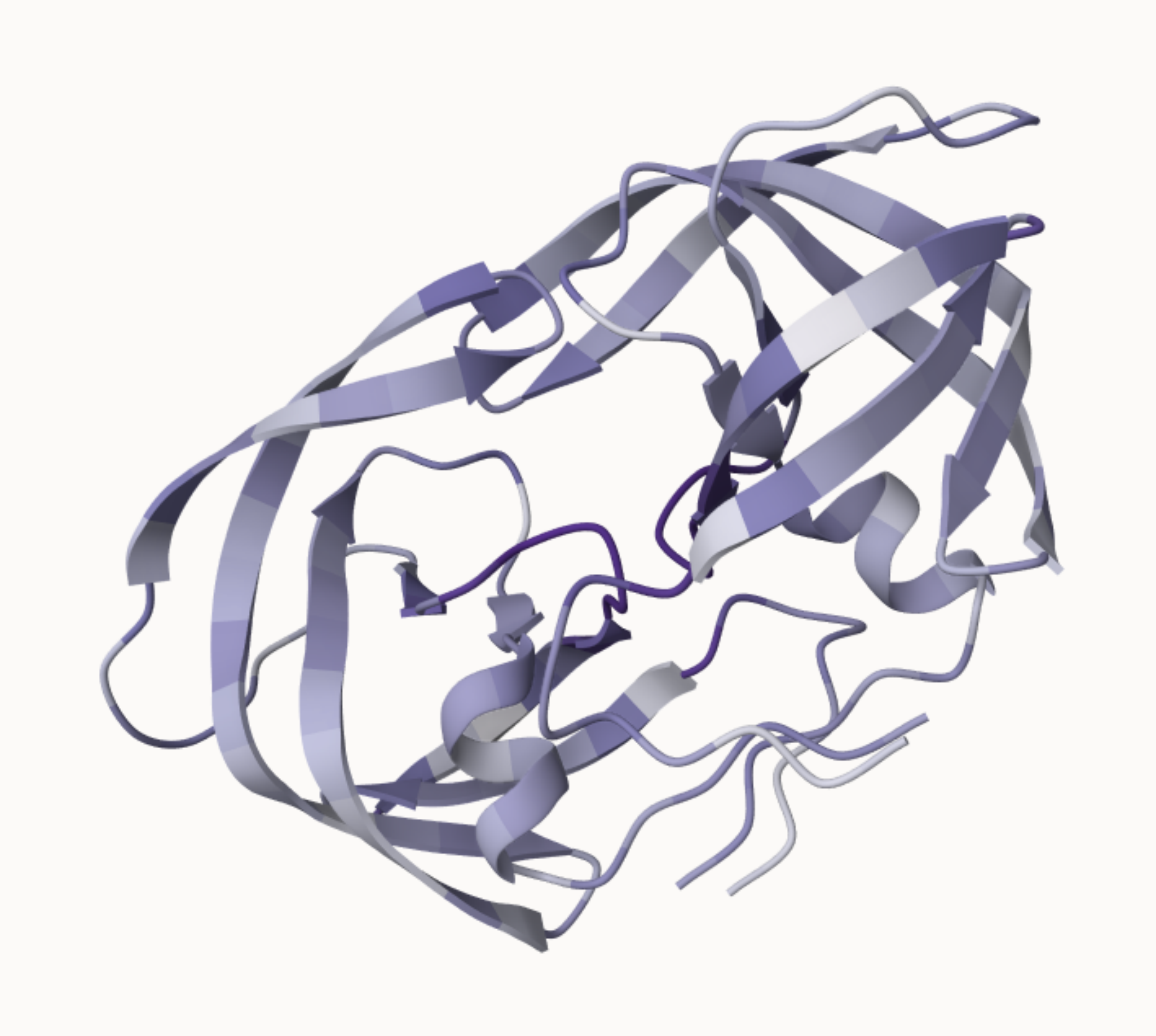
```
sim <- conserv(aln)
plotb3(sim[1:99], sse=trim.pdb(pdb, chain="A"))
```



```
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")
```



```
sessionInfo()
```

```
R version 4.3.1 (2023-06-16)
Platform: aarch64-apple-darwin20 (64-bit)
Running under: macOS Sonoma 14.1

Matrix products: default
BLAS:   /Library/Frameworks/R.framework/Versions/4.3-arm64/Resources/lib/libRblas.0.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/4.3-arm64/Resources/lib/libRlapack.dylib;

locale:
[1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
```

```
time zone: America/Los_Angeles
tzcode source: internal

attached base packages:
[1] stats     graphics  grDevices utils     datasets  methods   base

other attached packages:
[1] jsonlite_1.8.7  pheatmap_1.0.12 bio3d_2.4-4

loaded via a namespace (and not attached):
 [1] crayon_1.5.2            httr_1.4.7              cli_3.6.1
 [4] knitr_1.45              rlang_1.1.1             xfun_0.41
 [7] glue_1.6.2              S4Vectors_0.40.1        colorspace_2.1-0
[10] RCurl_1.98-1.13         Biostrings_2.70.1       htmltools_0.5.7
[13] stats4_4.3.1            scales_1.2.1            rmarkdown_2.25
[16] grid_4.3.1              munsell_0.5.0           evaluate_0.23
[19] bitops_1.0-7            fastmap_1.1.1           lifecycle_1.0.3
[22] yaml_2.3.7              IRanges_2.36.0          GenomeInfoDb_1.38.0
[25] compiler_4.3.1          RColorBrewer_1.1-3      Rcpp_1.0.11
[28] XVector_0.42.0          digest_0.6.33           R6_2.5.1
[31] GenomeInfoDbData_1.2.11 curl_5.1.0              parallel_4.3.1
[34] gtable_0.3.4            tools_4.3.1             zlibbioc_1.48.0
[37] msa_1.34.0              BiocGenerics_0.48.1
```