Class 10: Structural Bioinformatics pt. 1

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1. The PDB database

The main repository of bio molecular structure data is called the PDB found at http://www.rcsb.org/

Let's see what this database contains. I went to PDB > Analyze > PDB Statistics > By Exp method and molecular type.

```
pdbstats <- read.csv("Data Export Summary.csv")
pdbstats
```

```
           Molecular.Type   X.ray     EM    NMR Multiple.methods Neutron Other
1          Protein (only) 169,563 16,774 12,578              208      81    32
2 Protein/Oligosaccharide   9,939  2,839     34                8       2     0
3              Protein/NA   8,801  5,062    286                7       0     0
4     Nucleic acid (only)   2,890    151  1,521               14       3     1
5                   Other     170     10     33                0       0     0
6  Oligosaccharide (only)      11      0      6                1       0     4
    Total
1 199,236
2  12,822
3  14,156
4   4,580
```

```
5      213
6       22
```

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

```
pdbstats$X.ray
```

```
[1] "169,563" "9,939"   "8,801"   "2,890"   "170"     "11"
```

The comma in these numbers is causing them to be read as characters rather than numeric.

I can fix this by replacing “,” for nothing ” with the `sub()` function:

```
x <- pdbstats$X.ray
sum( as.numeric( sub(",", "", x)))
```

```
[1] 191374
```

Or I can use the **readr** package and the `read_csv()`

```
library("readr")
```

```
Warning: package 'readr' was built under R version 4.3.3
```

```
pdbstats <- read_csv("Data Export Summary.csv")
```

```
Rows: 6 Columns: 8
-- Column specification --------------------------------------------------------
Delimiter: ","
chr (1): Molecular Type
dbl (3): Multiple methods, Neutron, Other
num (4): X-ray, EM, NMR, Total

i Use `spec()` to retrieve the full column specification for this data.
i Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

```
pdbstats
```

```
# A tibble: 6 x 8
  `Molecular Type`   `X-ray`    EM   NMR `Multiple methods` Neutron Other  Total
  <chr>                <dbl> <dbl> <dbl>              <dbl>   <dbl> <dbl>  <dbl>
1 Protein (only)      169563 16774 12578                208      81    32 199236
2 Protein/Oligosacc~    9939  2839    34                  8       2     0  12822
3 Protein/NA            8801  5062   286                  7       0     0  14156
4 Nucleic acid (onl~    2890   151  1521                 14       3     1   4580
5 Other                  170    10    33                  0       0     0    213
6 Oligosaccharide (~      11     0     6                  1       0     4     22
```

I want to clean the column names so they are all lowercase and don't have spaces.

```r
colnames(pdbstats)
```

```
[1] "Molecular Type"   "X-ray"            "EM"               "NMR"             
[5] "Multiple methods" "Neutron"          "Other"            "Total"           
```

```r
library("janitor")
```

```
Warning: package 'janitor' was built under R version 4.3.3
```

```

Attaching package: 'janitor'

The following objects are masked from 'package:stats':

    chisq.test, fisher.test
```

```r
df <- clean_names(pdbstats)
df
```

```
# A tibble: 6 x 8
  molecular_type         x_ray    em   nmr multiple_methods neutron other  total
  <chr>                  <dbl> <dbl> <dbl>            <dbl>   <dbl> <dbl>  <dbl>
1 Protein (only)        169563 16774 12578              208      81    32 199236
2 Protein/Oligosacchar~   9939  2839    34                8       2     0  12822
3 Protein/NA              8801  5062   286                7       0     0  14156
4 Nucleic acid (only)     2890   151  1521               14       3     1   4580
5 Other                    170    10    33                0       0     0    213
6 Oligosaccharide (onl~     11     0     6                1       0     4     22
```

Total # of X-ray structures

```
sum(df$x_ray)
```

```
[1] 191374
```

Total # of structures

```
sum(df$total)
```

```
[1] 231029
```

% of X-ray structures

```
sum(df$x_ray) / sum(df$total) * 100
```

```
[1] 82.83549
```

% of EM structures

```
sum(df$em) / sum(df$total) * 100
```

```
[1] 10.75017
```

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

```
sum(df$total[1:3]) / sum(df$total) * 100
```

```
[1] 97.91585
```

> 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? (unanswered)

When searching HIV and adding HIV-1 and protease as sub searches you get a result of 24,695 structures.

2. Using Mol*

The main Mol* homepage https://molstar.org/viewer/ We can input our own PDB files or just give it a PDB database accession code (4 letter PDB code). We can use this markdown code to insert an image

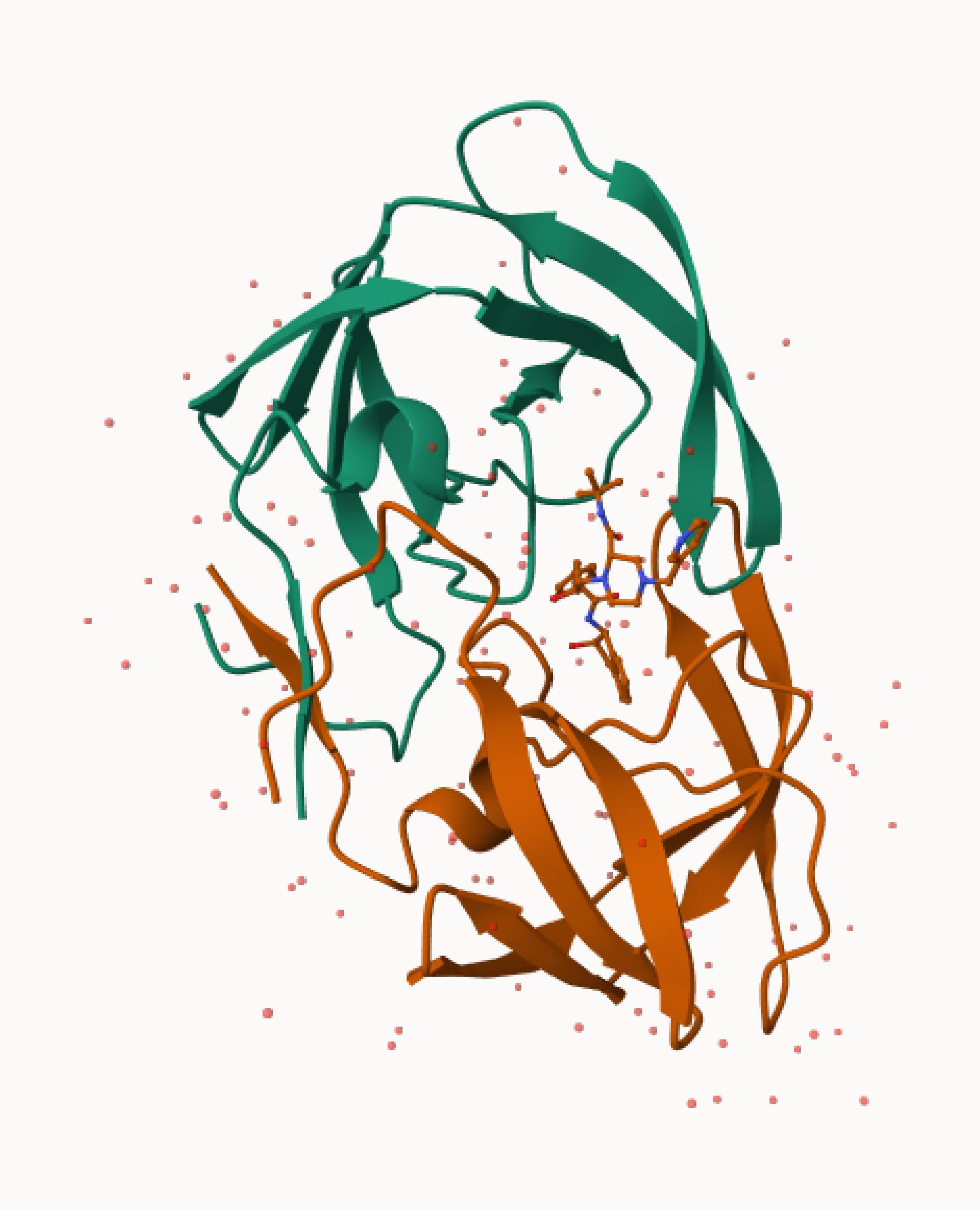
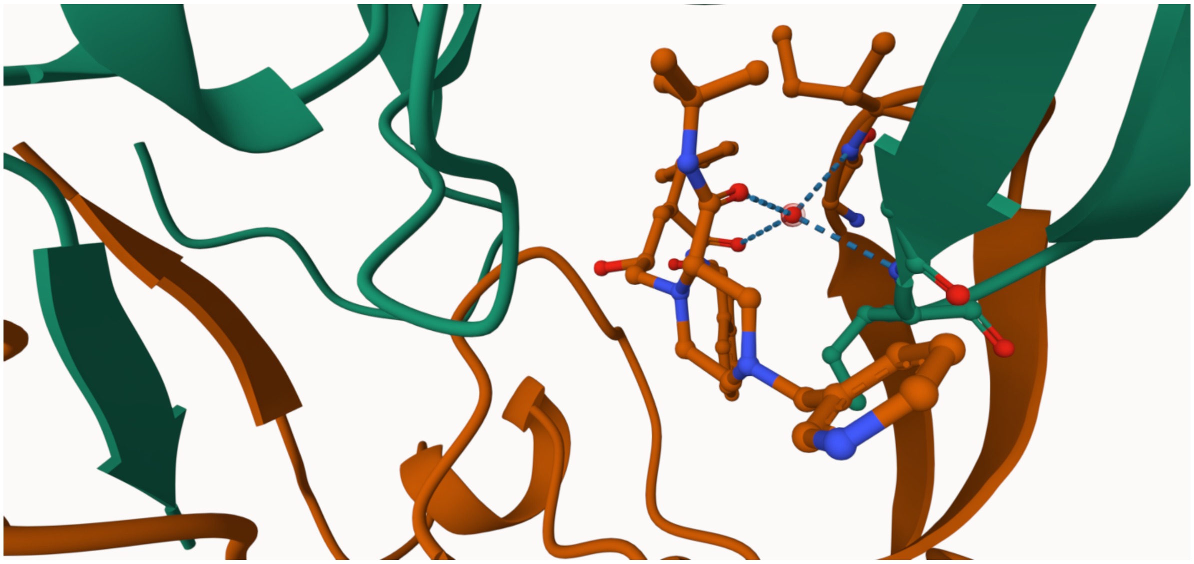


Figure 1: Molecular view of 1HSG

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

By having water represented only as one atom compared to three we are able to see our protein stucture clearly. If water were repsrented how it truly is, we wouldn't be able to see our protein.

> 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



> 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.

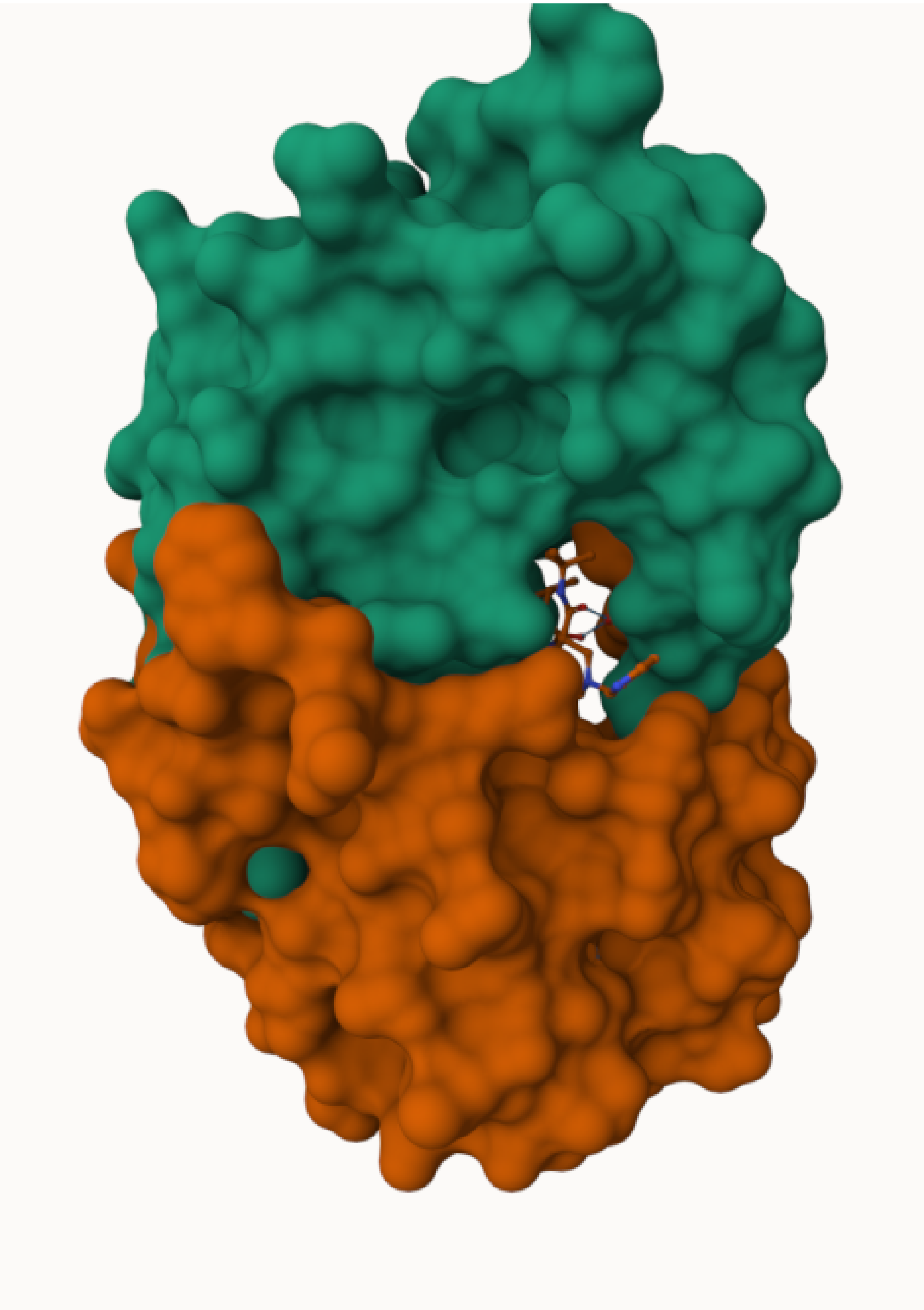
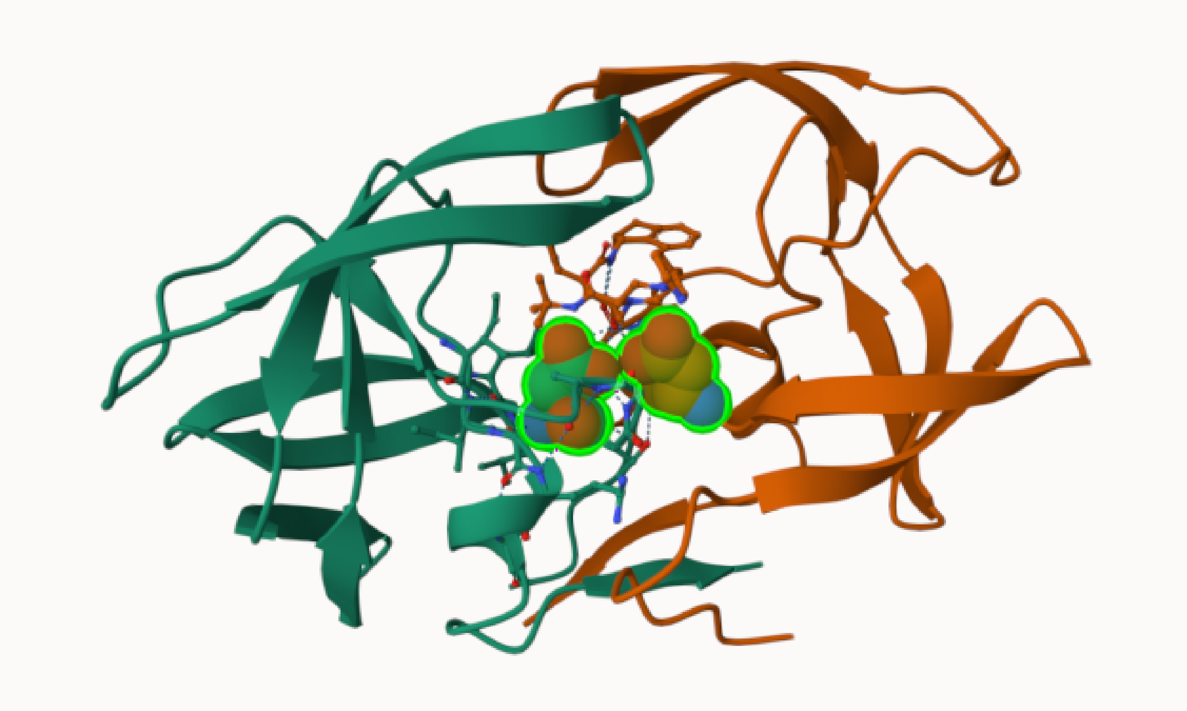


Figure 2: Molecular Surface of HSG



> Q7: [Optional] As you have hopefully observed HIV protease is a homodimer (i.e. it is composed of two identical chains). With the aid of the graphic display can you identify secondary structure elements that are likely to only form in the dimer rather than the monomer?

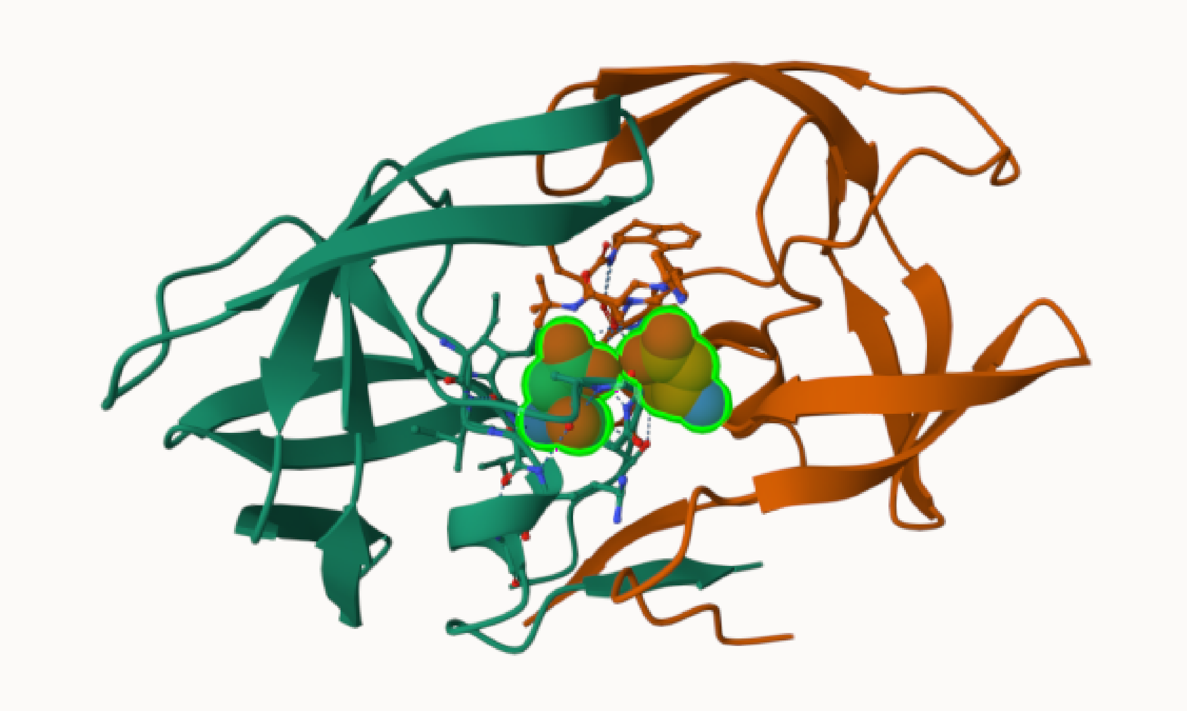


Figure 3: The important ASP25 amino-acids

3. Introduction to Biod3D in R

We can use the **bio3D** package for structural bioinformatics to read PDC data into R.

```
library(bio3d)
```

```
Warning: package 'bio3d' was built under R version 4.3.3
```

```
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
```

> Q7: How many amino acid residues are there in this pdb object?

```
length(pdbseq(pdb))
```

```
[1] 198
```

> Q8: Name one of the two non-protein residues?

MK1

> Q9: How many protein chains are in this structure?

2 chains A and B

Looking at the `pdb` object in more details

```
attributes(pdb)
```

```
$names
[1] "atom"   "xyz"    "seqres" "helix"  "sheet"  "calpha" "remark" "call"  

$class
[1] "pdb" "sse"
```

```r
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>
```

Let’s try a new function not yet in the bio3D package. It requires the **r3dmol** and **shiny** packages we need to install with `install.packages()`

```r
library(r3dmol)
```

```
Warning: package 'r3dmol' was built under R version 4.3.3
```

```r
library(shiny)
```

```
Warning: package 'shiny' was built under R version 4.3.3
```

```r
source("https://tinyurl.com/viewpdb")
#view.pdb(pdb, backgroundColor="black")
```

4. Predicting functional dynamics

We can use the `nma()` function in bio3d to predict the large scale functional motions of molecules

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

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

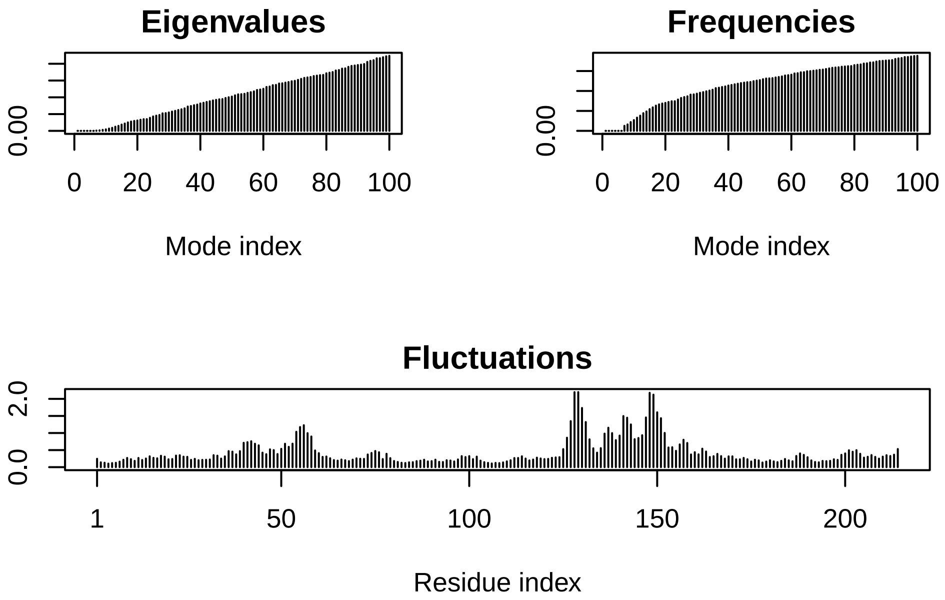
```r
adk
```

```
 Call:  read.pdb(file = "6s36")

   Total Models#: 1
     Total Atoms#: 1898,  XYZs#: 5694  Chains#: 1  (values: A)

     Protein Atoms#: 1654  (residues/Calpha atoms#: 214)
     Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)

     Non-protein/nucleic Atoms#: 244  (residues: 244)
     Non-protein/nucleic resid values: [ CL (3), HOH (238), MG (2), NA (1) ]

   Protein sequence:
      MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
      DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDKI
      VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG

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

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

```
 Building Hessian...         Done in 0.03 seconds.
 Diagonalizing Hessian...    Done in 0.51 seconds.
```

```r
plot(m)
```



Write out a trajectory of the predicted molecular motion:

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