Lab 10 2.6 - Structural Bioinformatics (Pt. 1)

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The PDB Database

The main repository of biomolecular structure data is called the PDB (Protein Data Bank) found at: https://www.rcsb.org/

Let's see what this databse contains. I went to PDB > Analyze > PDB Statistics > By experimental 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.

```r
pdbstats$X.ray
```

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

The quotation marks around them indicates that they are characters due to the commas; therefore, we can't do quantitative analysis with them.

I can fix this by raplcing ",", for nothing " " with the `sub()` function:

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

```
[1] 191374
```

Or I can use the **readr** package and the `read_csv()` function. The underscore in `read_csv` respects the commas in the values.

```r
library (readr)
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.
```

```r
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 lower case and don't have spaces in them.

```r
colnames(pdbstats)
```

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

```r
library(janitor)
```

```
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 number of X-ray structures.

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

```
[1] 191374
```

Total number of structures.

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

```
[1] 231029
```

Percent of X-ray structures.

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

```
[1] 82.83549
```

Percent of EM structures.

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

```
[1] 10.75017
```

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

Take

```
#Take the total of the first three rows that represent protein structures which is present i
sum(df[1:3,8])/sum(df$total)
```

```
[1] 0.9791585
```

> 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?

There are 2298 HIV-protease structures in the current PDB.

Section 2 - Using Mol*

The main Mol* homepage at: https://molstar.org/viewer/. We can input our own PDB files or just give it a PDB database accession code (4 letter PDB code).

`![](file_name)` is the code to insert an image.

Figure 1: Molecular view of 1HSG

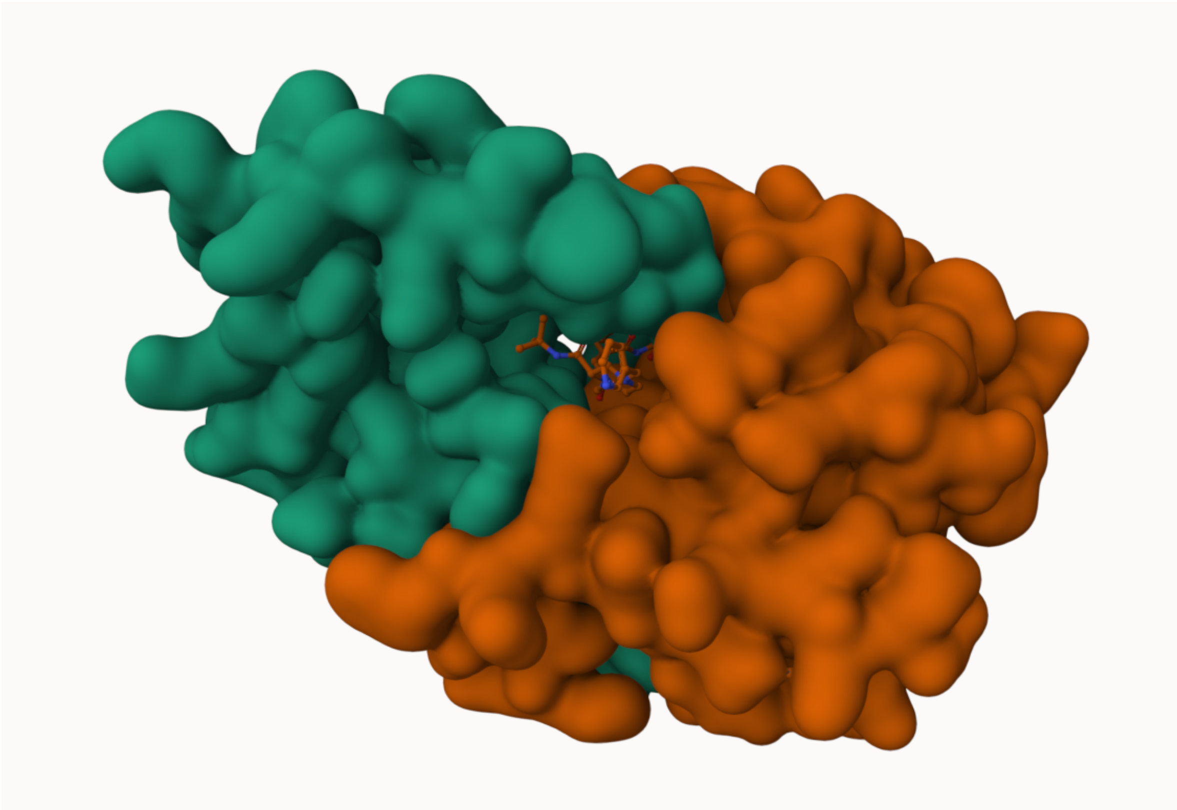


Figure 2: Surface representation showing binding cavity

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

Water normally has 2 hydrogens and 1 oxygen. However, the structure only shows the singular oxygen atom in the structure.

> 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.

The critical conserved water molecule is in residue number 308 and is shown in the image below.

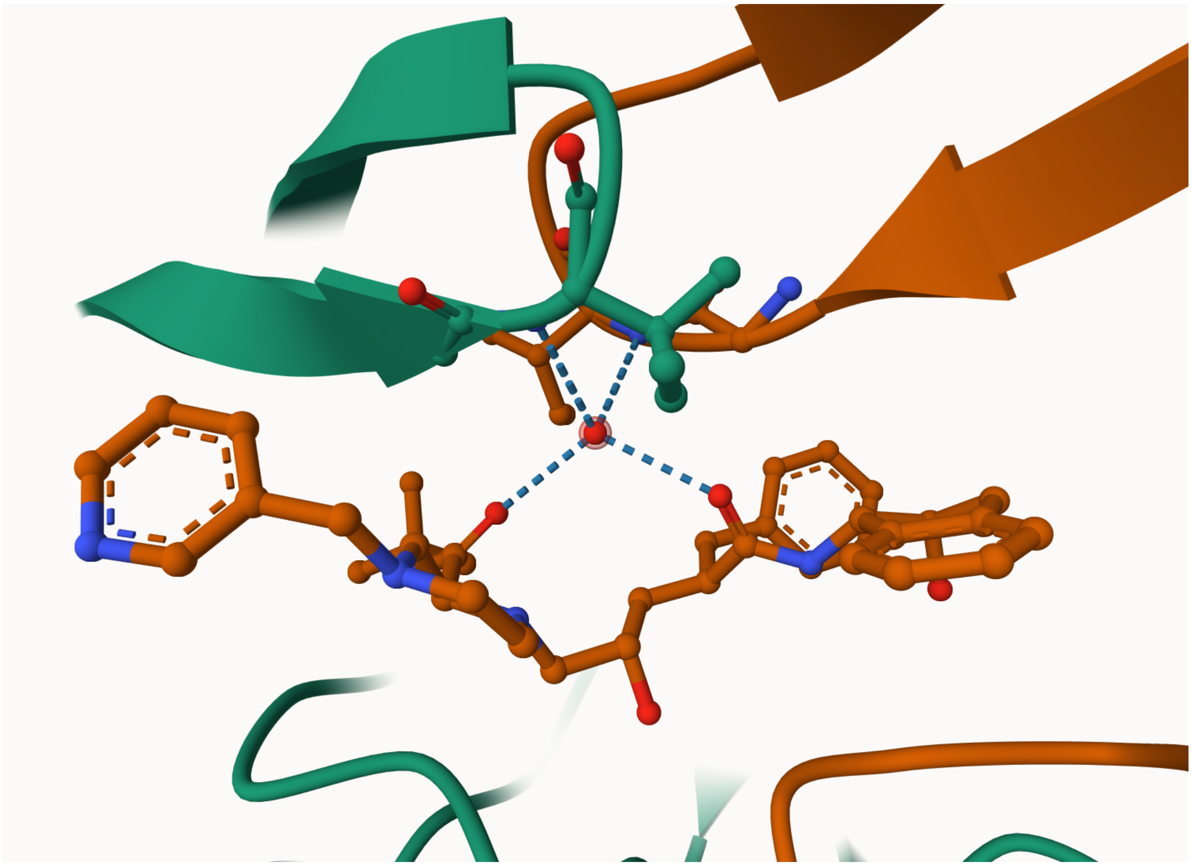


Figure 3: Water 308 in the binding molecule

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 4: The Important Asp-25 Amino Acid

Section 3 - Introduction to Bio3D in R

We can use the **bio3d** package for structural bioinformatics to read PDB data into R.

```
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
```

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

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

```
[1] 198
```

Q8. Name one of the two non-protein residues?

MK1

Q9. How many protein chains are in this structure?

There are two chains: chain A and B.

Looking at the `pdb` object in more detail.

```r
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 bio3d package. It requires the **r3dmol** package that we need to install with `install.packages("r3dmol")` as well as `install.packages("shiny")`.

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

Section 4 - Predicting Functional Dynamics

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

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

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

```
adk
```

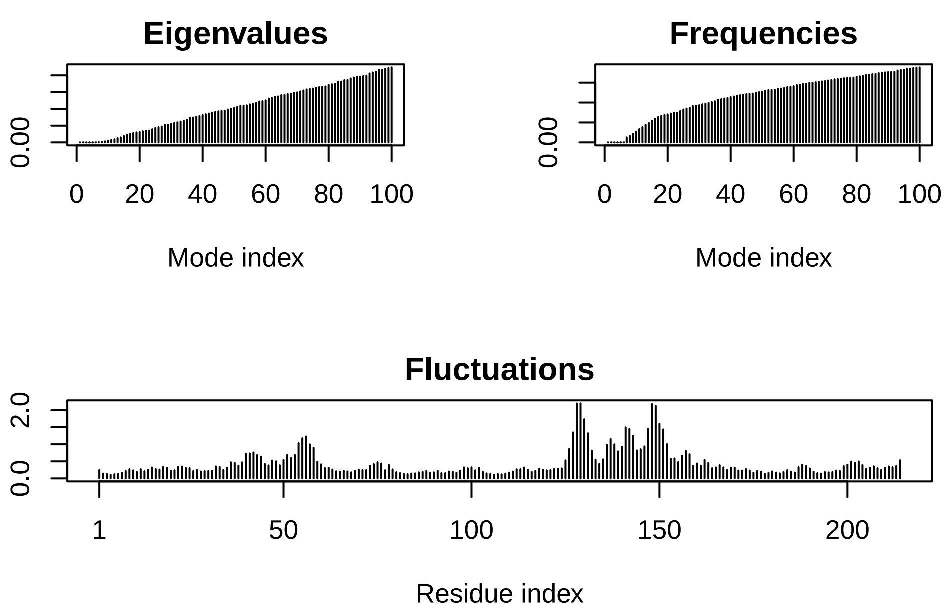
```

 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 0.012 seconds.
 Diagonalizing Hessian...   Done in 0.26 seconds.
```

```r
plot(m)
```



Write out a trajectory of the predicted molecular motion

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

Insert the above data file into mol* to look at its animated action.

This is the the downloaded animated file, but it is not rendered into the PDF document `ADK_M7.PDB_animate-trajectory.mp4`.