Class 10: Structural Bionformatics 1

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PDB database

The main repository of biomolecular structure data is called the [Protein Data Bank] (https://www.rcsb.org/) (PDB for short). It is the second oldest database (after GenBank).

```r
result <- 202990/252188522*100
result
```

```
[1] 0.08049137
```

~~~
::: {.cell}

```{.r .cell-code}
stats <- read.csv("Data Export Summary .csv")
stats
~~~

```
           Molecular.Type   X.ray     EM    NMR Multiple.methods Neutron Other
1          Protein (only) 171,959 18,083 12,622              210      84    32
2 Protein/Oligosaccharide  10,018  2,968     34               10       2     0
3              Protein/NA   8,847  5,376    286                7       0     0
```

```
4     Nucleic acid (only)   2,947     185  1,535                14       3     1
5                   Other     170      10     33                 0       0     0
6  Oligosaccharide (only)      11       0      6                 1       0     4
    Total
1 202,990
2  13,032
3  14,516
4   4,685
5     213
6      22
```

:::

```
x <- as.numeric(stats$xray)
```

```
x <- as.numeric(stats$xray)
x <- stats$X.ray
#Substitute coma for nothing
as.numeric( gsub(",","",stats$X.ray))
```

```
[1] 171959  10018   8847   2947    170     11
```

```
y <- gsub (",","",x)
```

Turn this into a function for any input x. Turn this snippet into a function so I can use it any time I have this commma problem (i.e the other columns of this `stats` table) >Q1: What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy? According to the results below, it was determined at 93.6787%

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

comma.sum <- function(x) { y <- gsub (“,”,“ “,x) sum(as.numeric(y))

comma.sum <- function(x) { x <- as.character(x) y <- gsub(“,”, “ “, x) y_numeric <- as.numeric(y) sum(y_numeric, na.rm = TRUE)

```r
xray.sum <- comma.sum(stats$X.ray)
em.sum <- comma.sum(stats$EM)
total.sum <- comma.sum(stats$Total)
xray.prop <- xray.sum / total.sum
```

```r
f <- as.numeric(xray.sum/total.sum*100)
```

```r
g <- em.sum/total.sum *100
```

```r
f+g
```

```
[1] 93.6787
```

> Q2: What proportion of structures in the PDB are protein? When considering only the protein only row of the dataframe, it yielded that 86.2107% of the structures were only composed of protein structures. When considering the rows that had protein elements in it, as in not just only protein, but also considering those structures with combinations of protein and nucleic acid and oligosaccharides, this yielded a much higher proportion of structures at 97.91046%.

```r
z<- as.numeric(stats[which(stats$Type == "Protein (only)"), ])
```

```r
a <- as.numeric(gsub(",", "", stats[1, 8]))
```

```r
r <- gsub(",", "", stats$Total)
numeric_total <- as.numeric(r)
b <- sum(numeric_total, na.rm = TRUE)
b
```

```
[1] 235458
```

```r
a/b*100
```

```
[1] 86.2107
```

```r
a <- as.numeric(gsub(",", "", stats[1, 8]))
e <- as.numeric(gsub(",", "", stats[2, 8]))
f <- as.numeric(gsub(",", "", stats[3, 8]))
(a+e+f)/b *100
```

```
[1] 97.91046
```

> 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? (Skip Question 3) We were told to skip this question 3 even though it is part of the rubric.

2. Visualizing with Mol-Star

Explore the HIV-1 protease structure with PDB code: `1HSG`

>Q4: Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure? We only see one atom per water molecule in this structure because the Hydrogen atoms are comparatively very small compared to the much larger Oxygen atoms, thus the mol star website only depicts the larger oxygen structure when displaying a water molecule. >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? This water molecule can be identified as water 301. This water was key for inhibition and designing residues for hydrogen binding for more effective blocking of the 1HSG protein activity.

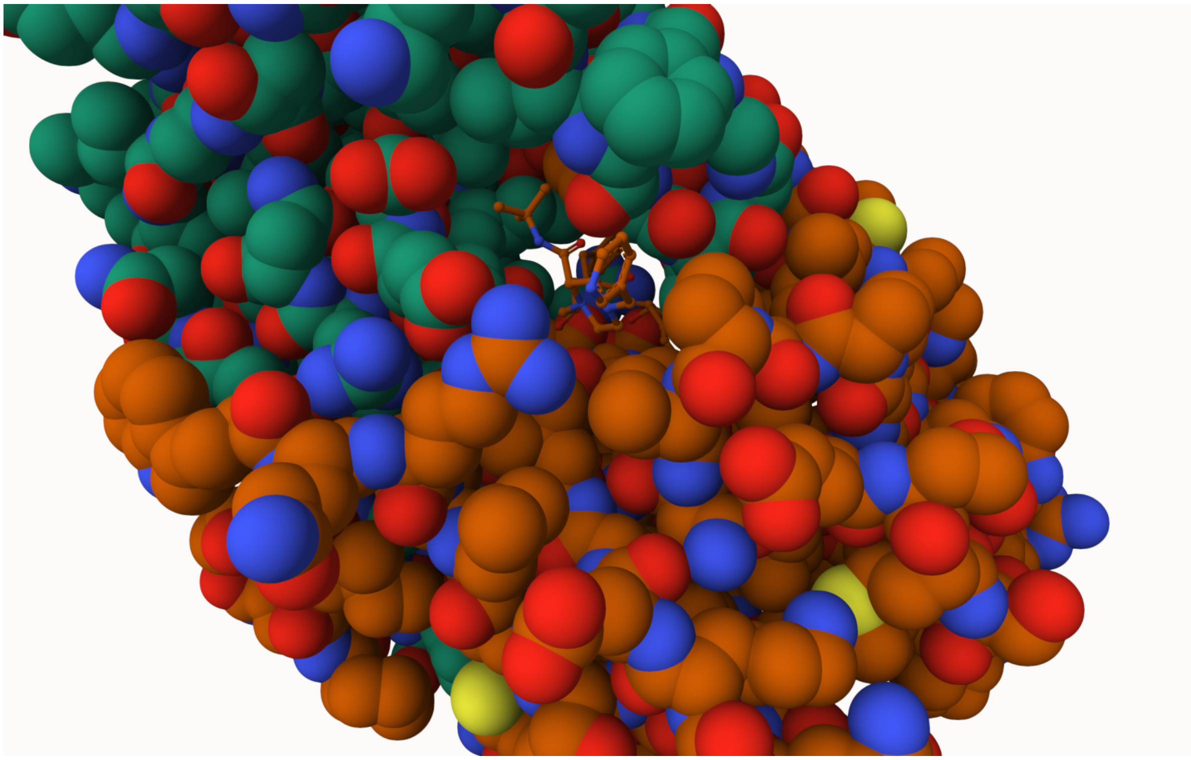


Figure 1: Figure2. Ligand Clearly Shown in Ball and Stick format with rest of protein in spacefill representation

Paste ligand as ball and stick model in spacefill model with rest of protein.

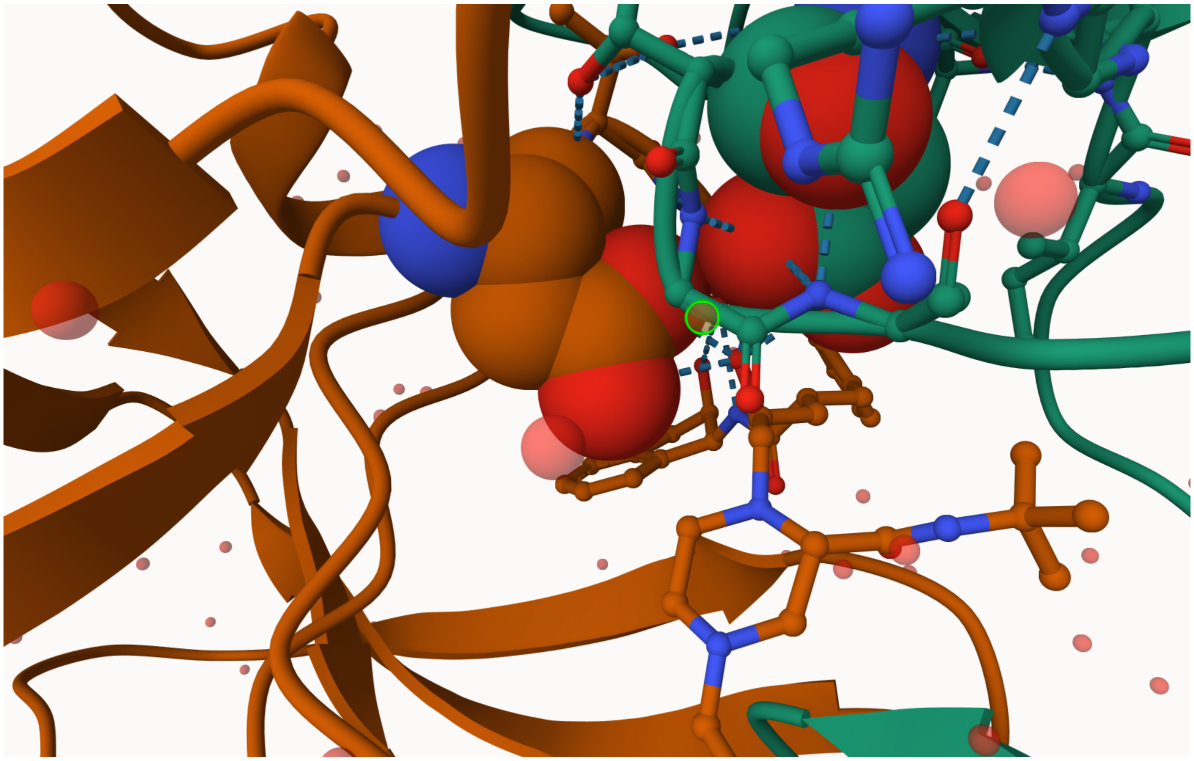


Figure 2: Figure 3: Key water and Aspartate Residues

3: Using the Bio3D package in R

The Bio 3D package is focused on structural bionformatics analysis and allows us to read and analyze PDB (and related) data.

```r
library(bio3d)
```

```r
pdb <- read.pdb("1HSB")
```

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

```r
pdb
```

```


 Call:  read.pdb(file = "1HSB")
```

```
  Total Models#: 1
   Total Atoms#: 3327,  XYZs#: 9981  Chains#: 3  (values: A B C)

   Protein Atoms#: 3057  (residues/Calpha atoms#: 374)
   Nucleic acid Atoms#: 0  (residues/phosphate atoms#: 0)

   Non-protein/nucleic Atoms#: 270  (residues: 270)
   Non-protein/nucleic resid values: [ HOH (270) ]

  Protein sequence:
    GSHSMRYFYTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW
    DRNTRNVKAQSQTDRVDLGTLRGYYNQSEAGSHTIQMMYGCDVGSDGRFLRGYRQDAYDG
    KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQWRAYLEGTCVEWLRRYLENGKETLQ
    RTDAPKTHMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQT...<cut>...VAAR

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

```
attributes(pdb)
```

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

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

We can see atom data with pdb$atom

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

```
  type eleno elety  alt resid chain resno insert      x      y       z o     b
1 ATOM     1     N <NA>   GLY     A     1   <NA> 50.037 51.776 100.904 1 21.82
2 ATOM     2    CA <NA>   GLY     A     1   <NA> 48.980 50.885 100.440 1 20.81
3 ATOM     3     C <NA>   GLY     A     1   <NA> 49.326 49.556 101.036 1 20.29
4 ATOM     4     O <NA>   GLY     A     1   <NA> 50.362 49.487 101.707 1 20.54
5 ATOM     5     N <NA>   SER     A     2   <NA> 48.350 48.668 100.941 1 19.63
6 ATOM     6    CA <NA>   SER     A     2   <NA> 48.486 47.273 101.301 1 18.77
  segid elesy charge
1  <NA>     N   <NA>
2  <NA>     C   <NA>
3  <NA>     C   <NA>
```

```
4  <NA>     O   <NA>
5  <NA>     N   <NA>
6  <NA>     C   <NA>
```

> Q7: How many amino acid residues are there in this pdb object? 198 Q8: Name one of the two non-protein residues? HOH Q9:How many protein chains are in this structure? 2 A and B

```
head(pdbseq(pdb) )
```

```
  1   2   3   4   5   6 
"G" "S" "H" "S" "M" "R" 
```

Molecular Visualization in R

We can make quick 3D viz with `view.pdb()` function:

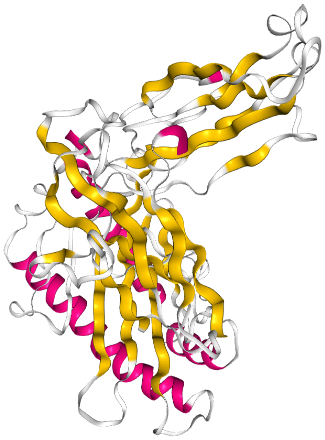
```
#install.packages("pak")
#pak::pak("bioboot/bio3dview")
#install.packages("NGLVieweR")
#install.packages()

#library(bio3dview)
#library(NGLvieweR)

#view.pdb(pdb) |>
  #setSpin()
```

```
#install.packages("pak")
#pak::pak("bioboot/bio3dview")
#install.packages("NGLVieweR")
```

```
library(bio3dview)
library(NGLVieweR)
view.pdb(pdb, backgroundColor="pink", colorScheme="sse")
```

```
PhantomJS not found. You can install it with webshot::install_phantomjs(). If it is installe
```

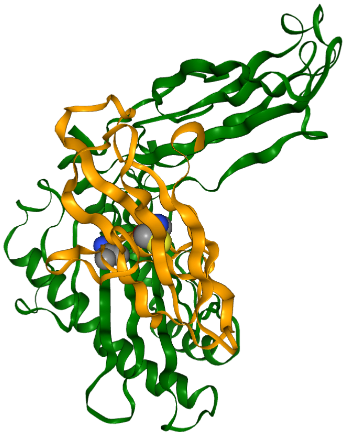
```
file:////private/var/folders/m8/ndytkmz55395lwskyz8gkrsh0000gn/T/RtmpiAw5rp/file15a617a3c3068
```



```r
sel <- atom.select(pdb, resno=25)

view.pdb(pdb, cols=c("green","orange"),
           highlight=sel,
        highlight.style="spacefill") |>
 setRock()
```

```
Warning in view.pdb(pdb, cols = c("green", "orange"), highlight = sel,
highlight.style = "spacefill"): Not enough distinct cols for each chain,
recycling
```

```
file:////private/var/folders/m8/ndytkmz55395lwskyz8gkrsh0000gn/T/RtmpiAw5rp/file15a611bcc583/
```



Predicting Functional motions of a single structure

We can finish off today with a bionformatics prediction of the functional motions of a protein.

We will run a Normal Mode Analysis (NMA)

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

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

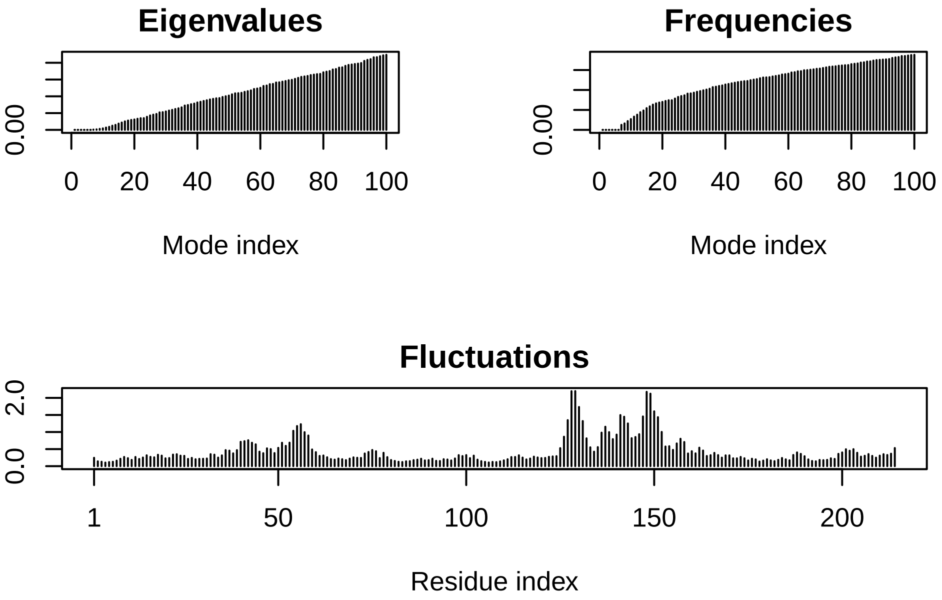
```r
adk
```

```


 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)
```

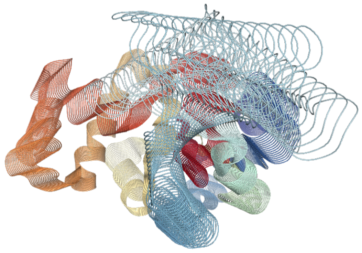
```
 Building Hessian...        Done in 0.014 seconds.
 Diagonalizing Hessian...   Done in 0.277 seconds.
```

```
plot(m)
```



```
view.nma(m)
```

```
file:////private/var/folders/m8/ndytkmz55395lwskyz8gkrsh0000gn/T/RtmpiAw5rp/file15a6167692df
```



```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
```

> Q10. Which of the packages above is found only on BioConductor and not CRAN? msa

> Q11. Which of the above packages is not found on BioConductor or CRAN?: bio3d-view

> Q12. True or False? Functions from the devtools package can be used to install packages from GitHub and BitBucket? TRUE
>
> Q13. How many amino acids are in this sequence, i.e. how long is this sequence? 214

We can write out a trajectory of the predicted dynamics and view this in Molstar.

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