Class 10: Structural Bioinformatics Pt.1

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1. Introduction to the RCSB Protein Data Bank (PDB)

Reading the data first

```
pdbstats <- read.csv("pdb.csv", row.names=1)
head(pdbstats)
```

```
                        X.ray     EM    NMR Multiple.methods Neutron Other
Protein (only)        161,663 12,592 12,337              200      74    32
Protein/Oligosaccharide 9,348  2,167     34                8       2     0
Protein/NA              8,404  3,924    286                7       0     0
Nucleic acid (only)     2,758    125  1,477               14       3     1
Other                     164      9     33                0       0     0
Oligosaccharide (only)     11      0      6                1       0     4
                        Total
Protein (only)        186,898
Protein/Oligosaccharide 11,559
Protein/NA              12,621
Nucleic acid (only)      4,378
Other                      206
Oligosaccharide (only)      22
```

The pdbstats df has numbers with commas in them which may be an issue.

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

I can make a function to use for converting columns into integers.

```
x = '22,000'
sum(as.numeric(gsub(",", "", x)))
```

```
[1] 22000
```

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

Apply across all columns

```
totals <- apply(pdbstats, 2, commasum)
round(totals / totals['Total'] * 100, 2)
```

```
          X.ray              EM             NMR Multiple.methods
          84.54            8.72            6.57            0.11
        Neutron           Other           Total
           0.04            0.02          100.00
```

93.2% resolved by Xray(84.5%) and EM(8.7%)

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

```
round(commasum(pdbstats['Protein (only)','Total']) / commasum(pdbstats[,'Total'])* 100, 2)
```

```
[1] 86.65
```

86.65%

2. Visualizing the HIV-1 protease structure

We will learn the basics of Mol* (mol-star). https://molstar.org/viewer/

We will play with the PDB code 1HSG

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

We see one atom per water molecule because Oxygen is large enough to be visible at this scale but Hydrogen is too small.

> 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.
>
> Discussion Topic: Can you think of a way in which indinavir, or even larger ligands and substrates, could enter the binding site?

Larger ligands can enter the binding site since the flexible flaps of the protein are dynamic and can open to allow the protein to enter and bind to the active site.

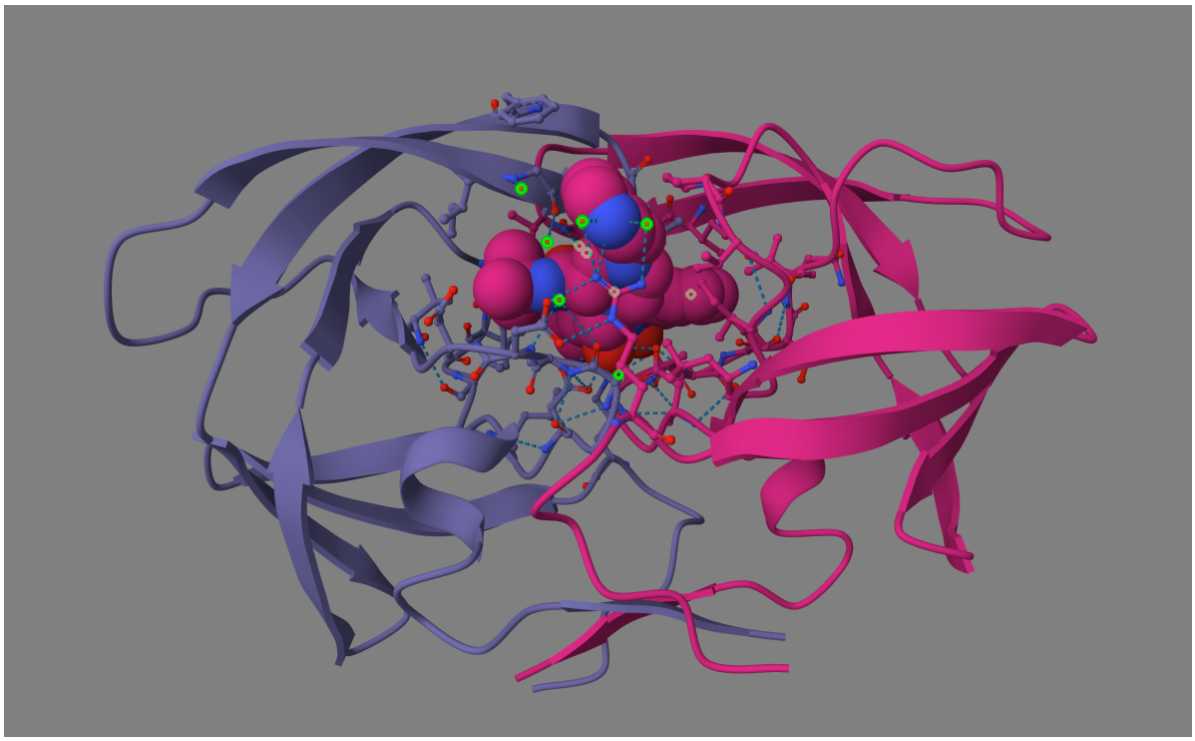


Figure 1: 1HSG with a bound inhibitor

Show the ASP 25 residues

Back to R and working with PDB structures

Predict the dynamics and flexibility of a protein.

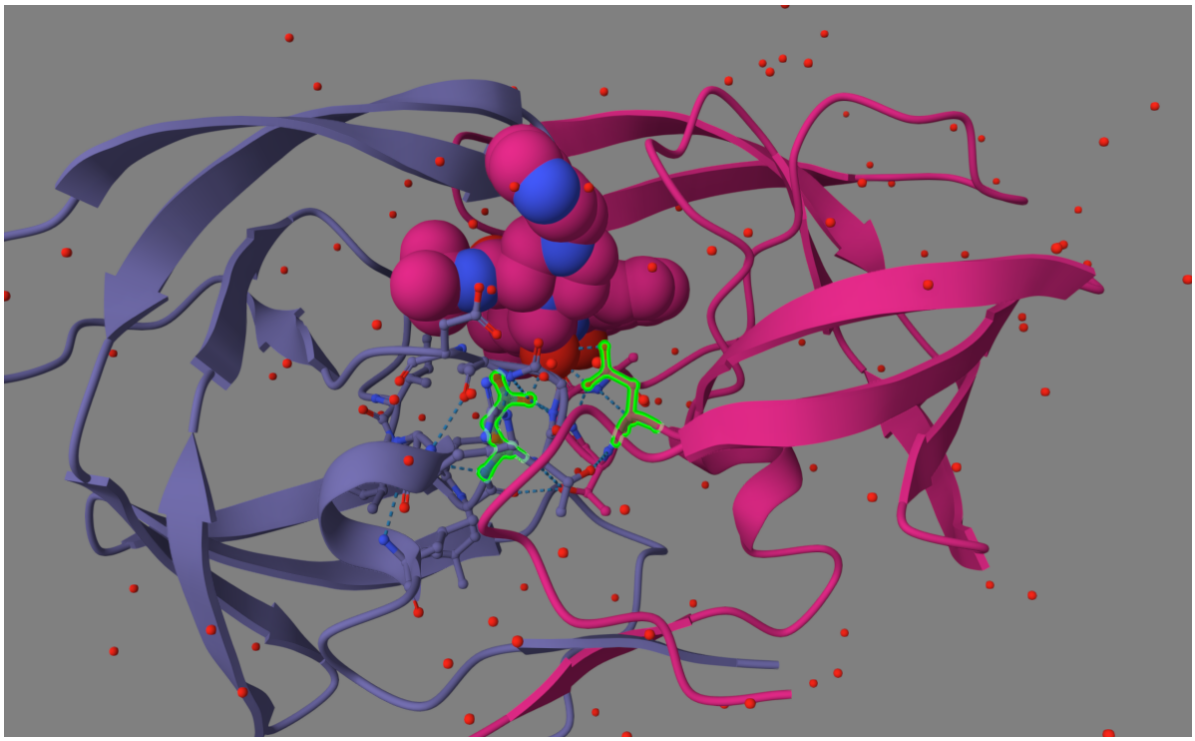


Figure 2: Asp25 residues in each protein of the homodimer

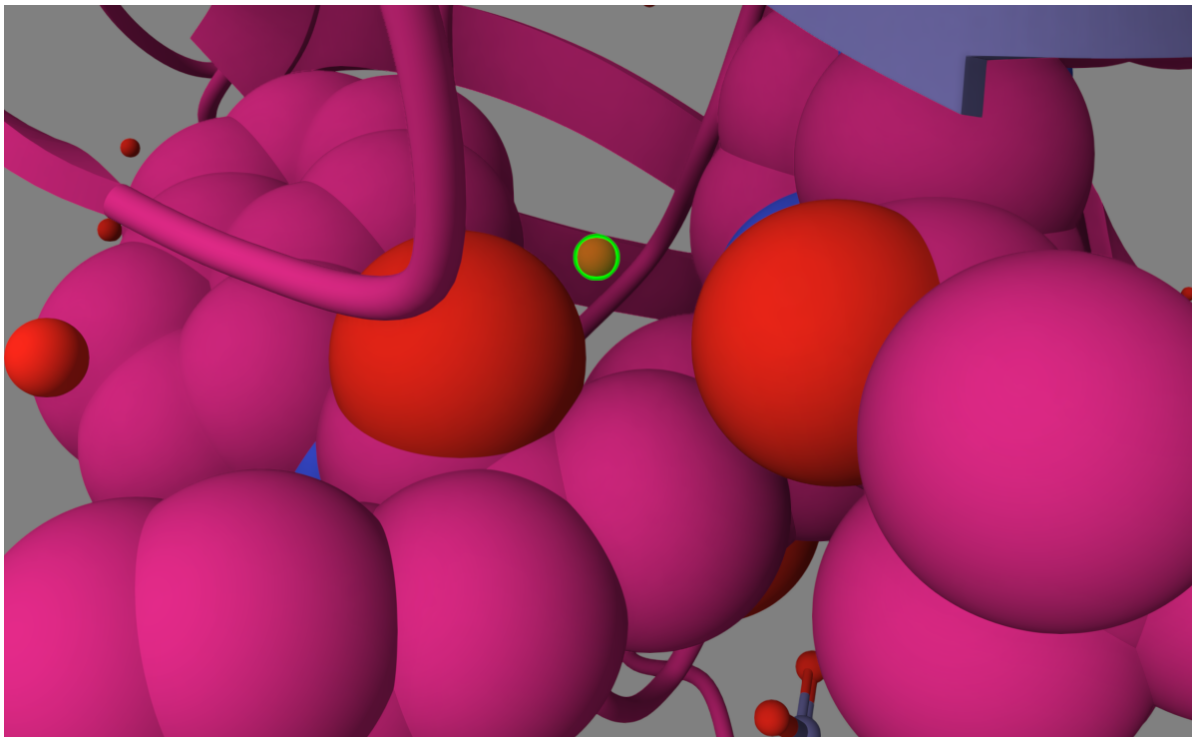


Figure 3: Critical H2O

```
#install.packages("bio3d")
library(bio3d)

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

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

```
hiv
```

```
 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 obj

198 amino acid residues.

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

H2O.

Q9: How many protein chains are in this structure?

2 protein chains in this structure.

```
head(hiv$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>
```

Here we will do a Normal Mode Analysis (NMA) to predict functional motions of a kinase.

```
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:
```

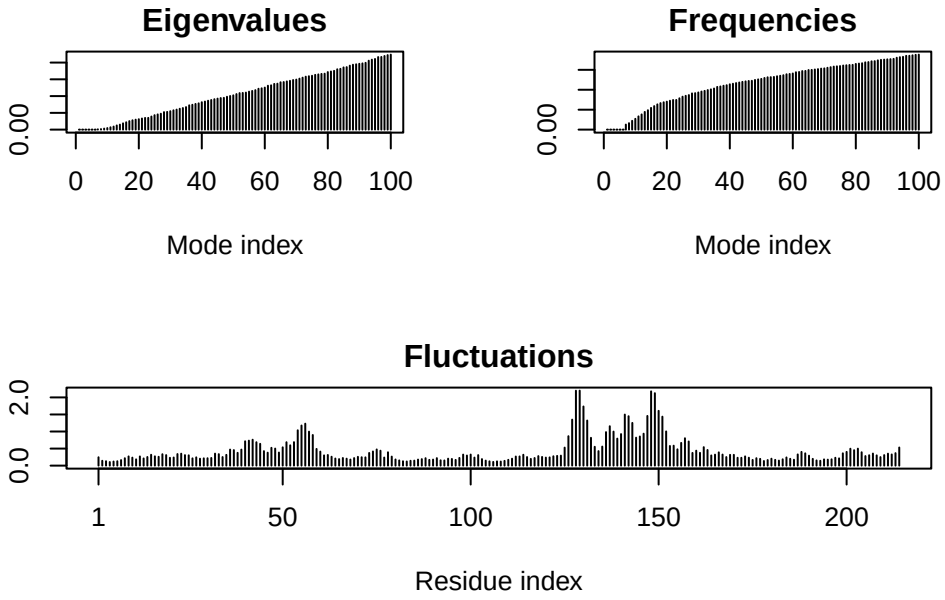
```
      MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
      DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVDYVLEFDVPDELIVDKI
      VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      YYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG

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

```
modes <- nma(adk)
```

```
 Building Hessian...        Done in 0.051 seconds.
 Diagonalizing Hessian...   Done in 0.55 seconds.
```

```
plot(modes)
```



Make a movie called a trajectory of the predicted morions:

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