Class10: Structural Bioinformatics (p1)

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The PDB Database

The main repository of biomolecular structure data is called the Protein Data Bank (PDB for short). It is the second oldest database (after GenBank).

What is currently in the PDB? We can access current composition stats here

```
stats <- read.csv("Data Export Summary (1).csv")
head(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
```

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

```
x <- stats$X.ray
# Substitute comma for nothing
y <- gsub(",", "", stats$X.ray)

# Convert to numeric
sum(as.numeric(y))
```

```
[1] 193952
```

Turn this snippet into a function so I can use it any time I have this comma problem (i.e. the other columns of this `stats` table)

```
comma.sum <- function(x) {
  # Substitute comma for nothing
y <- gsub(",", "", x)

# Convert to numeric and sum
return( sum(as.numeric(y)) )
}
```

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

```
xray.sum/total.sum * 100
```

```
[1] 82.37223
```

```
em.sum/total.sum * 100
```

```
[1] 11.30648
```

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

```
total.num <- as.numeric(gsub(",", "", stats$Total))
sum(total.num[1:3])/total.sum
```

```
[1] 0.9791046
```

> 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

2. Visualizing with Mol-star

Explore the HIV-1 protease structure with PDB code: `1HSG` Mol-star homepage at: https://molstar.org/viewer/.

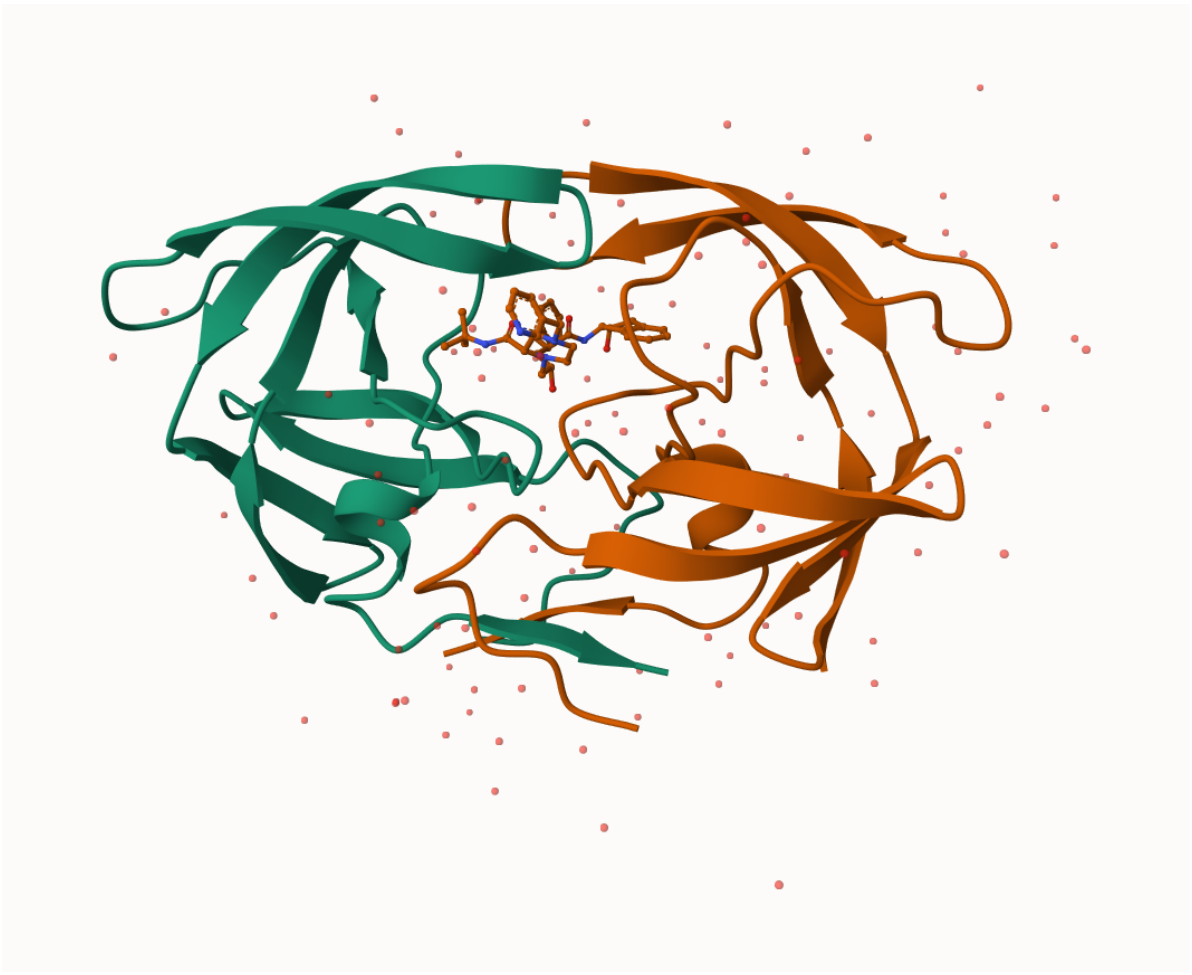


Figure 1: Figure 1. A first view of HIV-Pr

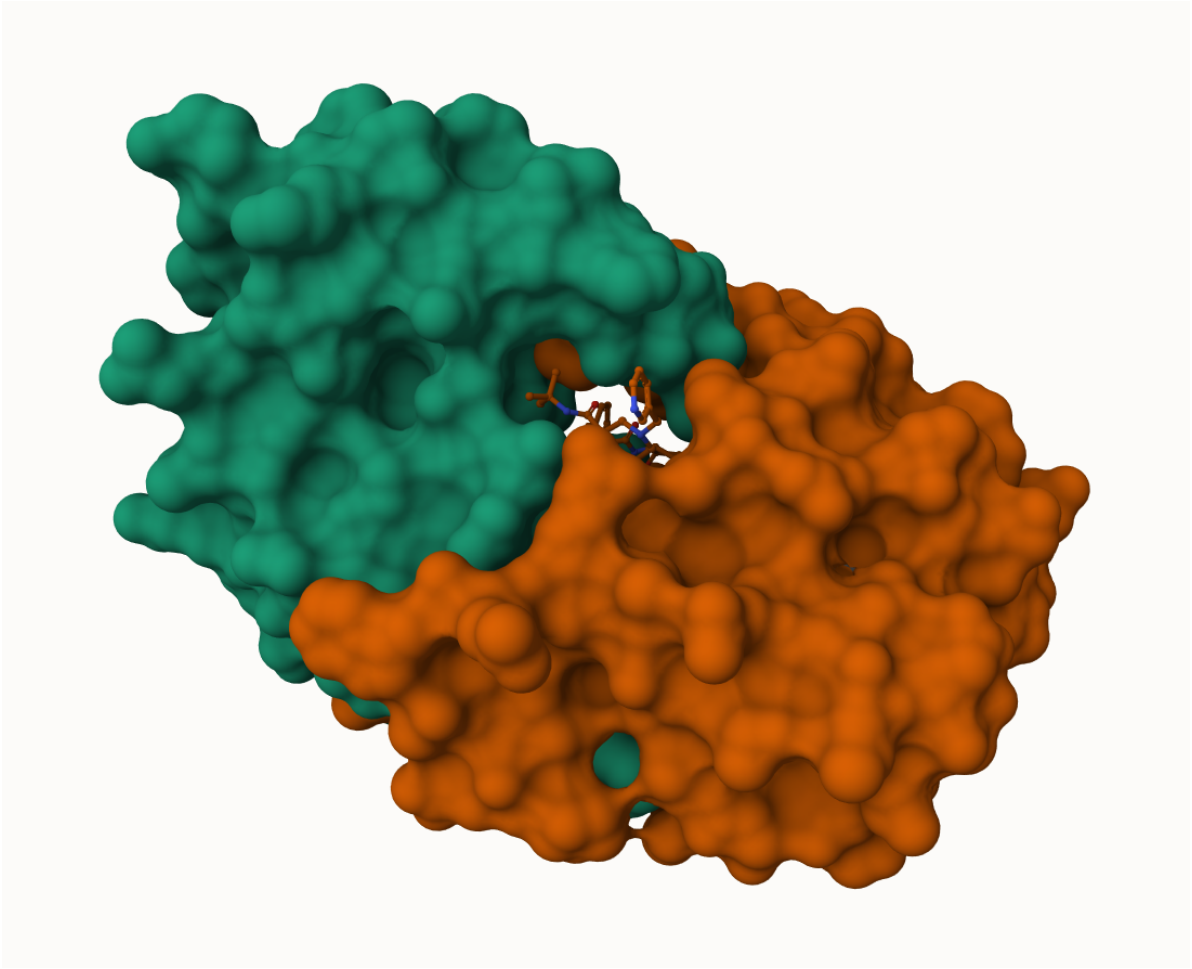


Figure 2: Figure 2. Molecular surface showing binding cavity

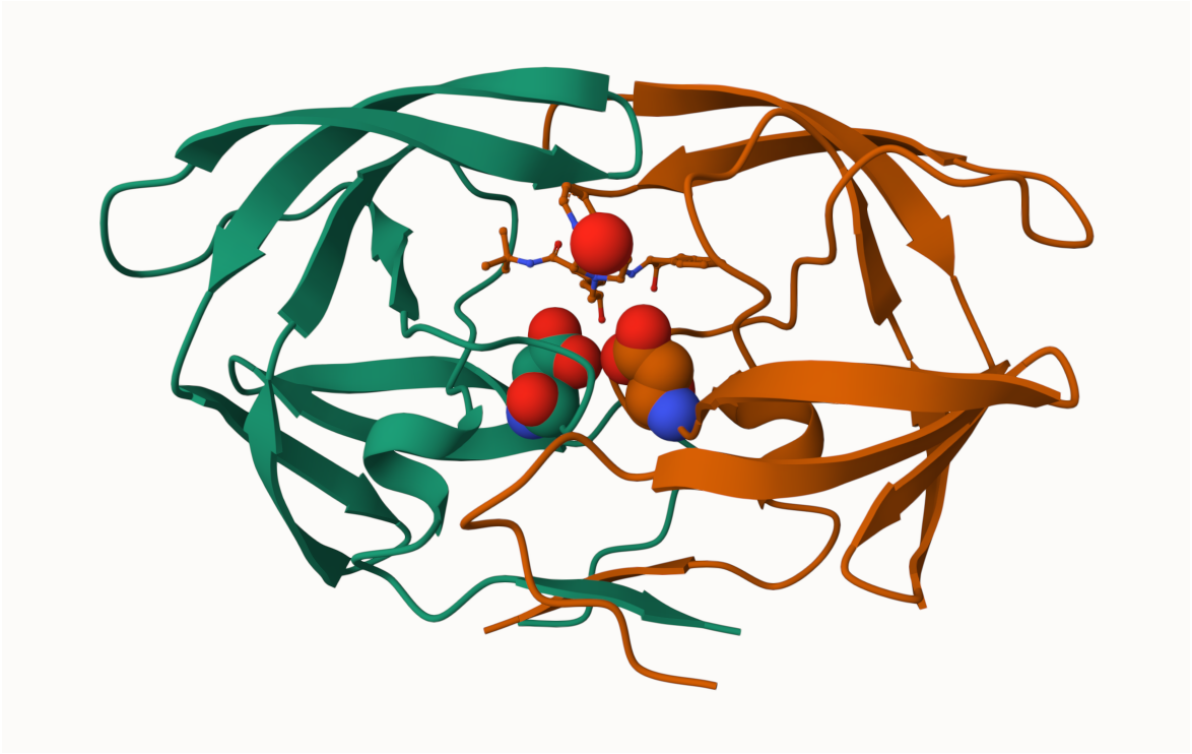


Figure 3: Figure 3. The catatilically important ASP 25 and drug interacting HOH 308 water molecule

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

Yes, I can identify it; and this water molecule has the residue number 308.

3. Using the bio3d package in R

The Bio3D package is focused on structural bioinformatics analysis and allows us to read and analyze PDB (and related) data.

```
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
```

```
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>   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>
```

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

```
  1   2   3   4   5   6
"P" "Q" "I" "T" "L" "W"
```

Molecular Visualization in R

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

```
library(bio3dview)
library(NGLVieweR)

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

#view.pdb(pdb, backgroundColor = "pink", colorScheme = "sse")
```

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

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

Predicting functional motions of a single structure

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

We will run a Normal Mode Analysis (NMA)

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

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

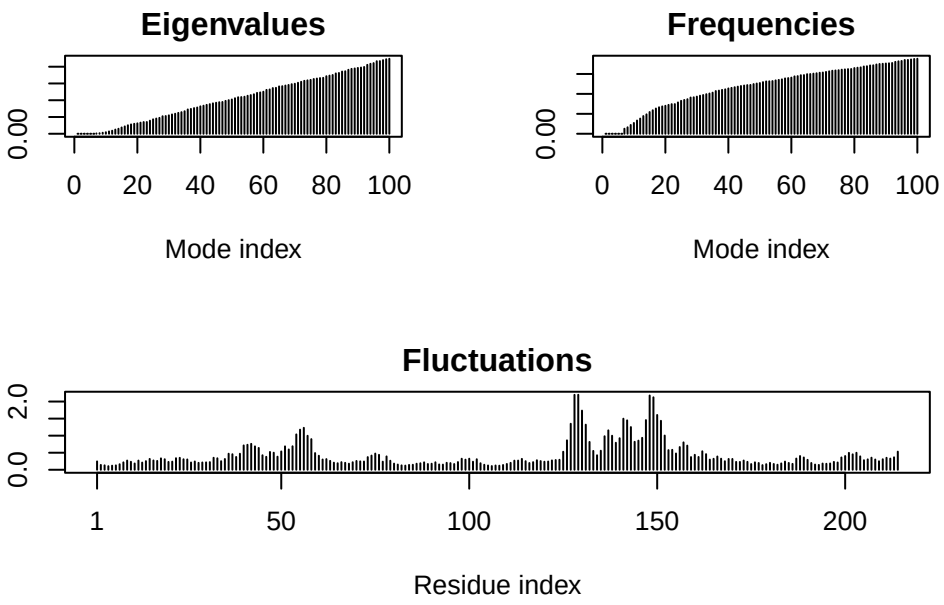
```
adk
```

```
 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
```

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

```
 Building Hessian...        Done in 0.012 seconds.
 Diagonalizing Hessian...   Done in 0.266 seconds.
```

```
plot(m)
```




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

We can write out a trajectory of the predicted dynamics and view this in Mol-star

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

```
202990/252188522 * 100
```

```
[1] 0.08049137
```

So we only know 0.8% of the structures. Tiny coverage of structure based.