Class 09: Structural Bioinformatics

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

```
db <- read.csv("PDB.csv")
db
```

```
          Molecular.Type   X.ray    EM    NMR Multiple.methods Neutron Other
1          Protein (only) 152,809 9,421 12,117              191      72    32
2 Protein/Oligosaccharide   9,008 1,654     32                7       1     0
3              Protein/NA   8,061 2,944    281                6       0     0
4     Nucleic acid (only)   2,602    77  1,433               12       2     1
5                   Other     163     9     31                0       0     0
6  Oligosaccharide (only)      11     0      6                1       0     4
    Total
1 174,642
2  10,702
3  11,292
4   4,127
5     203
6      22
```

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

```
gsub(",","",db$Total)
```

```
[1] "174642" "10702"  "11292"  "4127"   "203"    "22"
```

```
gsub(",","",db$EM)
```

```
[1] "9421" "1654" "2944" "77"   "9"    "0"
```

```
gsub(",","",db$X.ray)
```

```
[1] "152809" "9008"   "8061"   "2602"   "163"    "11"
```

```
sum(as.numeric( gsub(",","",db$X.ray) ))
```

```
[1] 172654
```

I am doing the same thing over and over, time to write a function.

```
sumcomma <- function(x) {
  # substitute comma for it to become numeric
  sum(as.numeric( gsub(",","",x) ))
}
```

For X-ray:

```
sumcomma(db$X.ray) / sumcomma(db$Total)
```

```
[1] 0.8590264
```

For EM:

```
round( sumcomma(db$EM) / sumcomma(db$Total), 2 )
```

```
[1] 0.07
```

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

```
round( sumcomma(db$Total[1]) / sumcomma(db$Total), 2)
```

```
[1] 0.87
```

```
# first value in the Total column
```

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

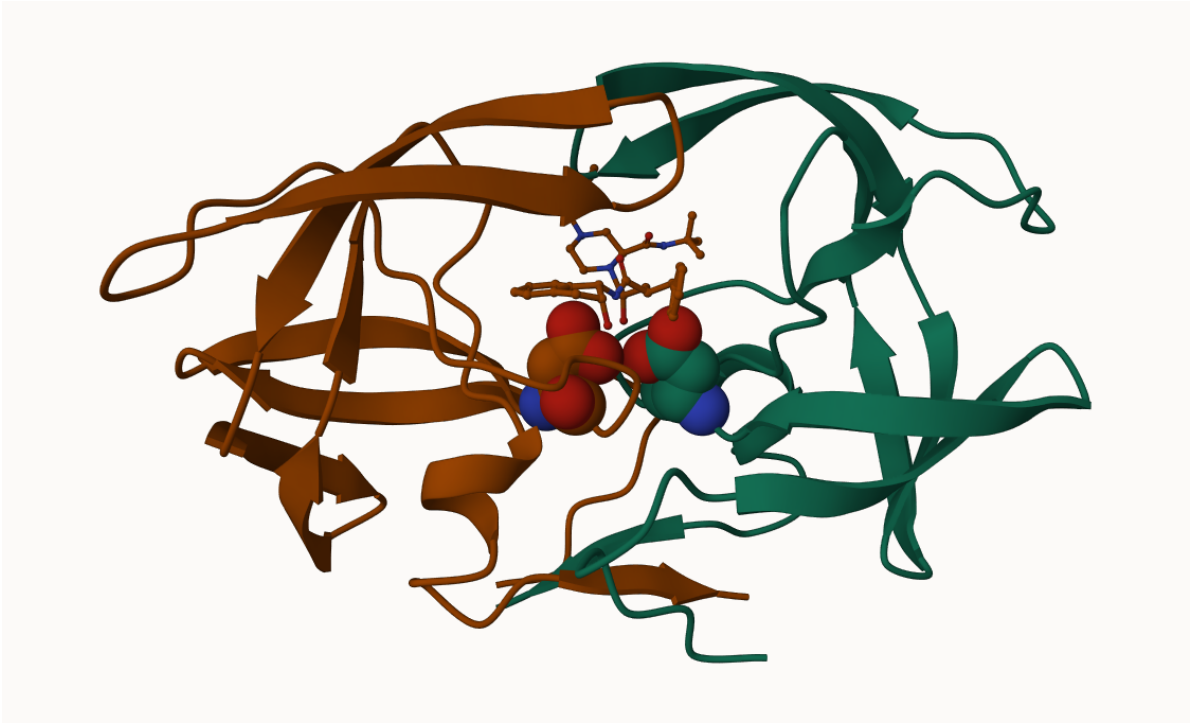


Figure 1: HIV-PR Structure from MERK with a bound drug

2. Visualizing the HIV-1 protease structure

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

Hydrogen is the smallest element and could not be captured by this x-ray crystalography.

> 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

HOH308

> 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?

3. Introduction to Bio3D in R

We can use the `bio3d` package to read and perform bioinformatics calculation on PDB structures.

```
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?

198

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

HOH

Q9: How many protein chains are in this structure?

2

```
attributes(pdb)
```

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

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

```
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>
```

Read an ADK structure

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

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

```
adk
```

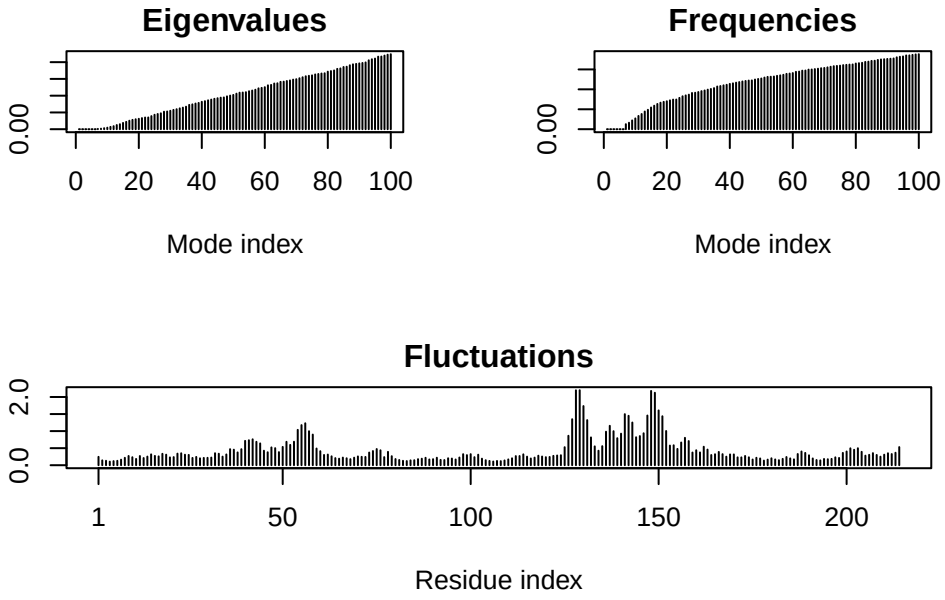
```
 Call:  read.pdb(file = "6s36")

   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
```

Perform a flexiblity prediction with a technique called NMA (normal mode analysis)

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

```
Building Hessian...         Done in 0.062 seconds.
Diagonalizing Hessian...    Done in 0.759 seconds.
```

```
plot(m)
```



Write out a "movie" of the motion for viewing in Molstart

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