Class 09: Structural Bioinformatics (pt. 1)

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PDB Data Base

Download a CSV file from the PDB site (accessible from :Analyze” > “PDB Statistics” > “by Experimental Method and Molecular Type”).

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

```
           Molecular.Type   X.ray     EM    NMR Integrative Multiple.methods
1          Protein (only) 176,204 20,299 12,708         342              218
2 Protein/Oligosaccharide  10,279  3,385     34           8               11
3              Protein/NA   9,007  5,897    287          24                7
4     Nucleic acid (only)   3,066    200  1,553           2               15
5                   Other     173     13     33           3                0
6  Oligosaccharide (only)      11      0      6           0                1
  Neutron Other   Total
1      83    32 209,886
2       1     0  13,718
3       0     0  15,222
4       3     1   4,840
5       0     0     222
6       0     4      22
```

```
stats$Total
```

```
[1] "209,886" "13,718"  "15,222"  "4,840"   "222"     "22"
```

if these were characters then use the following code

```
stats$Total <- as.numeric(gsub(",", "", stats$Total))
n.total <- sum(stats$Total)
n.total
```

```
[1] 243910
```

> Q1. What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy. Give your answer two significant figures.

```
stats$X.ray <- as.numeric(gsub(",", "", stats$X.ray))
n.xray <- sum(stats$X.ray)
```

```r
percent_xray <- n.xray/n.total * 100
percent_xray <- signif(percent_xray, 2)
percent_xray
```

```
[1] 81
```

There are `percent_xray` percent X ray strcutures in the PDB.

```r
stats$EM <- as.numeric(gsub(",", "", stats$EM))
n.em <- sum(stats$EM)
percent_em <- n.em/n.total * 100
percent_em <- signif(percent_em, 2)
percent_em
```

```
[1] 12
```

There are `percent_em` percent EM structures in the PDB.

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

```r
round( stats$Total[1]/n.total * 100, 2)
```

```
[1] 86.05
```

Exploring PDB Structures

> 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 over 100 HIV-protease strcutures in the current PDB.

Package for structural bioinformatics

```r
library(bio3d)

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

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

```r
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 object?

There are 196 amino acid residues in this PDB object.

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

Water is a non-protien residue.

> Q9: How many protein chains are in this structure?

There are 2 protien chains in this structure.

Let’s first use the Mol* viewer to explore this structure

My first view of HIV-Pr

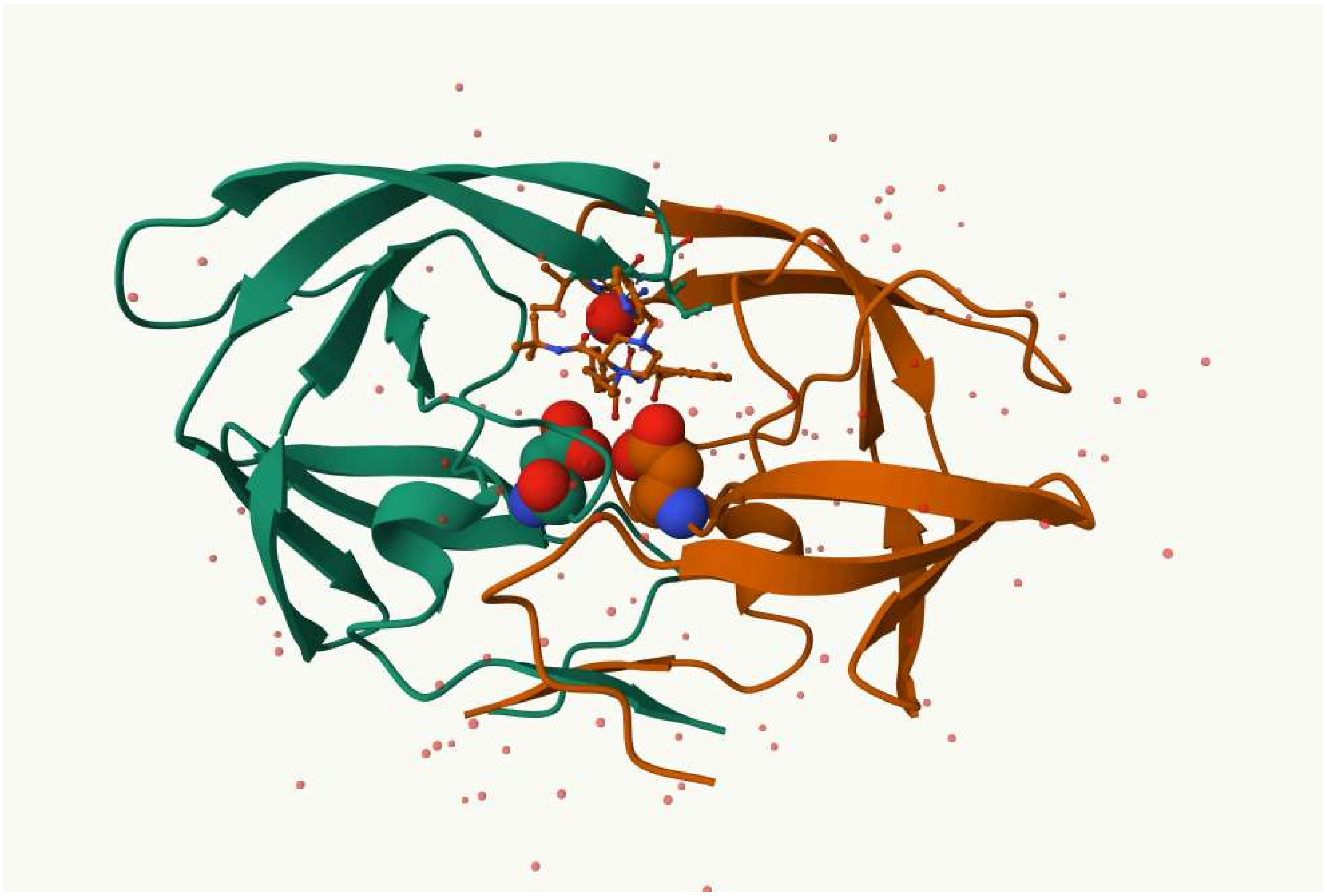
> Q4. Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure?

The atom that is visualized is the oxygen atom due to the relatively small size of hydrogen.

> 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

Water Molecule 308

> 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.



PDB Objects in R

```
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>
```

Extract the sequence

```
pdbseq(hiv)
```

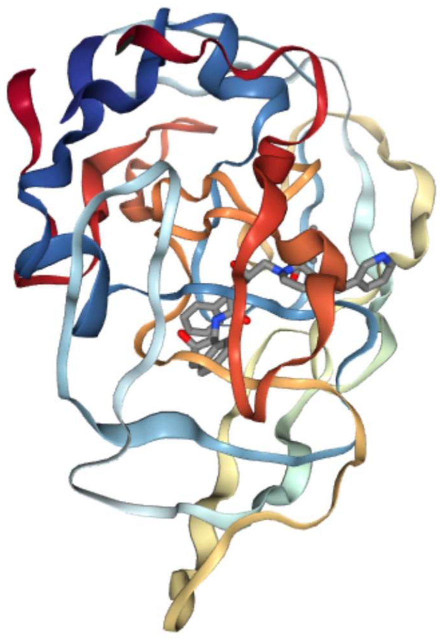
```
  1   2   3   4   5   6   7   8   9  10  11  12  13  14  15  16  17  18  19  20 
"P" "Q" "I" "T" "L" "W" "Q" "R" "P" "L" "V" "T" "I" "K" "I" "G" "G" "Q" "L" "K" 
 21  22  23  24  25  26  27  28  29  30  31  32  33  34  35  36  37  38  39  40 
"E" "A" "L" "L" "D" "T" "G" "A" "D" "D" "T" "V" "L" "E" "E" "M" "S" "L" "P" "G" 
 41  42  43  44  45  46  47  48  49  50  51  52  53  54  55  56  57  58  59  60 
"R" "W" "K" "P" "K" "M" "I" "G" "G" "I" "G" "G" "F" "I" "K" "V" "R" "Q" "Y" "D" 
 61  62  63  64  65  66  67  68  69  70  71  72  73  74  75  76  77  78  79  80 
"Q" "I" "L" "I" "E" "I" "C" "G" "H" "K" "A" "I" "G" "T" "V" "L" "V" "G" "P" "T" 
 81  82  83  84  85  86  87  88  89  90  91  92  93  94  95  96  97  98  99   1 
"P" "V" "N" "I" "I" "G" "R" "N" "L" "L" "T" "Q" "I" "G" "C" "T" "L" "N" "F" "P" 
  2   3   4   5   6   7   8   9  10  11  12  13  14  15  16  17  18  19  20  21 
"Q" "I" "T" "L" "W" "Q" "R" "P" "L" "V" "T" "I" "K" "I" "G" "G" "Q" "L" "K" "E" 
 22  23  24  25  26  27  28  29  30  31  32  33  34  35  36  37  38  39  40  41 
"A" "L" "L" "D" "T" "G" "A" "D" "D" "T" "V" "L" "E" "E" "M" "S" "L" "P" "G" "R" 
 42  43  44  45  46  47  48  49  50  51  52  53  54  55  56  57  58  59  60  61 
"W" "K" "P" "K" "M" "I" "G" "G" "I" "G" "G" "F" "I" "K" "V" "R" "Q" "Y" "D" "Q" 
 62  63  64  65  66  67  68  69  70  71  72  73  74  75  76  77  78  79  80  81 
"I" "L" "I" "E" "I" "C" "G" "H" "K" "A" "I" "G" "T" "V" "L" "V" "G" "P" "T" "P" 
 82  83  84  85  86  87  88  89  90  91  92  93  94  95  96  97  98  99 
"V" "N" "I" "I" "G" "R" "N" "L" "L" "T" "Q" "I" "G" "C" "T" "L" "N" "F" 
```

```
chainA_seq <- pdbseq (trim.pdb(hiv, chain = "A"))
```

I can interactively view these PDB objects in R with the new **bio3dview** package. This is not yet on CRAN.

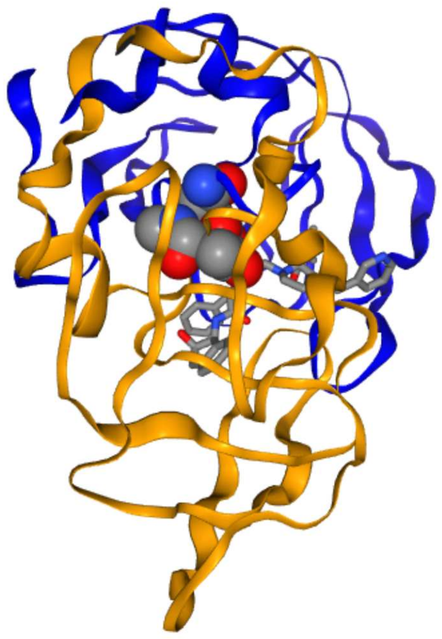
To install this I can set up **pak** package and use it to install **bio3dview** from GitHub. In my console I first run,

```
library(bio3dview)

view.pdb(hiv)
```



Change some settings

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

view.pdb (hiv, highlight = sel,
          highlight.style = "spacefill",
          colorScheme = "chain",
          col = c("blue","orange"),
          backgroundColor = "pink")
```



Predict Protein Flexibility

We can run a bioinformatics calculation to preduct protein dynamics - i.e. functional motions.

We will use the `nma()` function:

```
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 0.02 seconds.
 Diagonalizing Hessian...   Done in 0.17 seconds.
```

Generate a “trajectory” of predicted motion

```r
mktrj(m, file = "ADK_nma.pdb")
```

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