Class09: Structural Bioinformatics Part 1

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The PDB Database

The main database for structural biology is called the PDB (Protein Data Bank). Let's have a look at what it contains:

Download a CSV file from the PDB site (accessible from "Analyze" > "PDB Statistics" > "by Experimental Method and Molecular Type". Move this CSV file into your RStudio project and use it to answer the following questions:

```
pdbtable <- read.csv("DataExportSummary.csv")
pdbtable
```

```
           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
```

```
pdbtable$Total
```

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

```
# sum(pdbtable[,"X.ray"]) not working because they are characters, not numeric.
pdbtable$Total
```

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

```
sub(",", "---", pdbtable$Total)
```

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

```
library(readr)
stats <- read_csv("DataExportSummary.csv")
stats
```

```
# A tibble: 6 x 9
  `Molecular Type`    `X-ray`    EM   NMR Integrative `Multiple methods` Neutron
  <chr>                 <dbl> <dbl> <dbl>       <dbl>               <dbl>   <dbl>
1 Protein (only)       176204 20299 12708         342                 218      83
2 Protein/Oligosacch~   10279  3385    34           8                  11       1
3 Protein/NA             9007  5897   287          24                   7       0
4 Nucleic acid (only)    3066   200  1553           2                  15       3
5 Other                   173    13    33           3                   0       0
6 Oligosaccharide (o~      11     0     6           0                   1       0
# i 2 more variables: Other <dbl>, Total <dbl>
```

```
stats$Total
```

```
[1] 209886  13718  15222   4840    222     22
```

Q1: What percentage of structures in the PDB are solved by X-Ray and Electron Microscopy. Give to 2 sig figs.

```
n.xray <- sum(stats$`X-ray`) #Add `` in X-ray
n.total <- sum(stats$Total)
round(n.xray/n.total*100, 2) # Use round(number,2)
```

```
[1] 81.48
```

```
n.em <- sum(stats$EM)
round(n.em/n.total*100, 2)
```

```
[1] 12.22
```

Around 81.48% of structures in the PDB are solved by X-Ray and 12.22% are solved by Electron Microscopy.

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

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

```
  Total
1 86.05
```

```
# or stats$Total[1]
```

86.05% are protein (only).

> 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?

In PDB website, there are 4865 structures for HIV and 1150 for HIV-1 protease.

Exploring PDB structures

Package for structural bioinformatics.

```
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
```

Let's first use the Mol* viewer to explore this structure. molstar.org

Figure 1: My first view of HIV-Protease

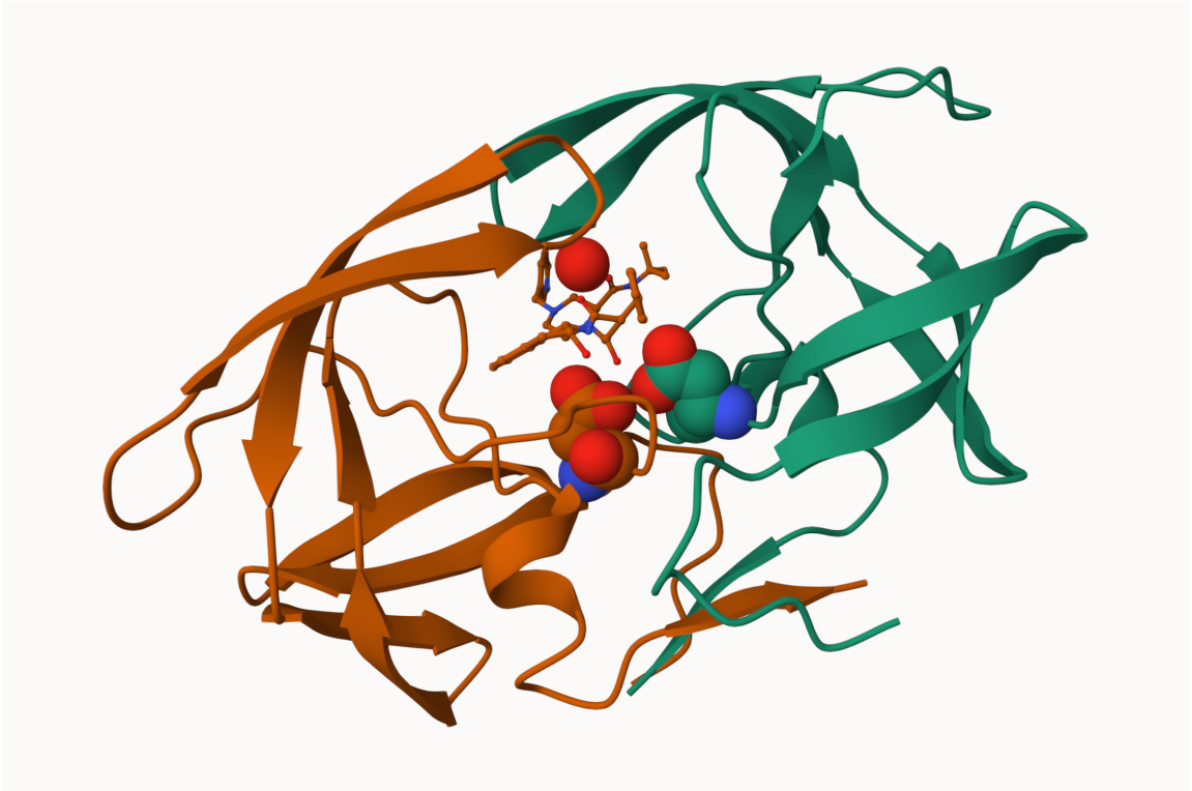
> Q4: Water molecules normally have 3 atoms. Why do we see just one atom per water molecule in this structure?

It's for simplification. Now it's easier to view.

> 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 is important for binding with ligand. The residue number is HOH 308.

And a view of the ligand (ball and stick) with catalytic ASP25 amino-acids (spacefill) and the all important active site water molecules (spacefill):



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"
```

Predict protein flexibility

We can run a bioinformatics calculation to predict 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
```

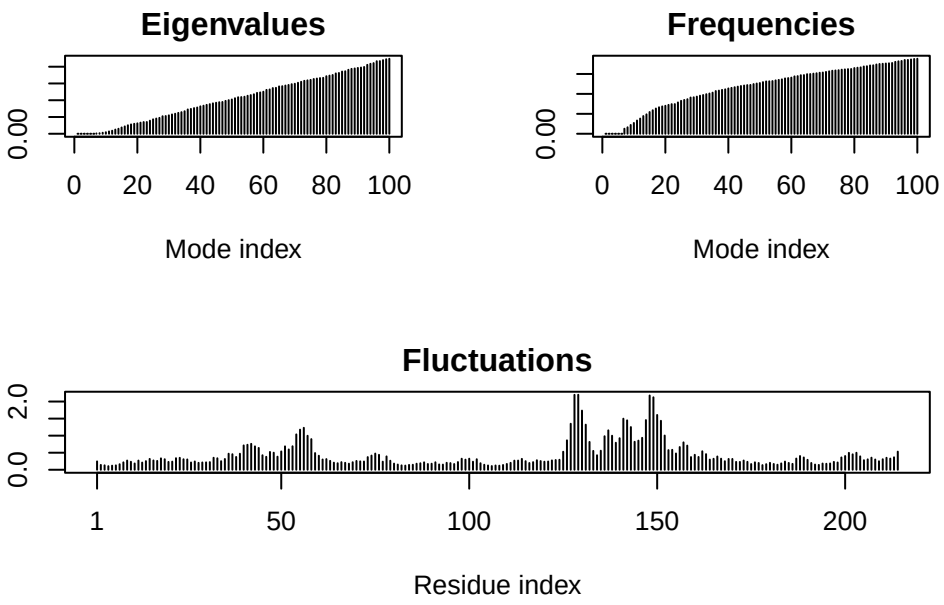
```
adk
```

```
 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
```

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

```
 Building Hessian...        Done in 0.045 seconds.
 Diagonalizing Hessian...   Done in 0.269 seconds.
```

```
plot(m)
```



Generate a "trajectory" of predicted motion

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