

Class09: Structural Bioinformatics Pt 1

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The PDB database

The main repository for biomolecular structure data is the Protein Data Bank (PDB)
<https://www.rcsb.org>

Lets have a quick look at the composition of this database

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

	Molecular.Type	X.ray	EM	NMR	Integrative	Multiple.methods
1	Protein (only)	176,378	20,438	12,709	342	221
2	Protein/Oligosaccharide	10,284	3,396	34	8	11
3	Protein/NA	9,007	5,931	287	24	7
4	Nucleic acid (only)	3,077	200	1,554	2	15
5	Other	174	13	33	3	0
6	Oligosaccharide (only)	11	0	6	0	1
	Neutron	Other	Total			
1	83	32	210,203			
2	1	0	13,734			
3	0	0	15,256			
4	3	1	4,852			
5	0	0	223			
6	0	4	22			

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

```
as.numeric(sub(",","",stats$X.ray))
```

```
[1] 176378 10284 9007 3077 174 11
```

This is annoying lets try a different import function from the **readr** package

```
library(readr)

stats<-read_csv("Data Export Summary.csv")

Rows: 6 Columns: 9
-- Column specification -----
Delimiter: ","
chr (1): Molecular Type
dbl (4): Integrative, Multiple methods, Neutron, Other
num (4): X-ray, EM, NMR, Total

i Use `spec()` to retrieve the full column specification for this data.
i Specify the column types or set `show_col_types = FALSE` to quiet this message.

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) 176378 20438 12709      342            221   83
2 Protein/Oligosacch~ 10284  3396   34        8             11    1
3 Protein/NA       9007   5931   287       24             7    0
4 Nucleic acid (only) 3077    200  1554       2            15    3
5 Other            174     13   33        3             0    0
6 Oligosaccharide (o~ 11      0    6         0             1    0
# i 2 more variables: Other <dbl>, Total <dbl>
```

Percent X.ray

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

[1] 81.43

Percent EM

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

[1] 12.27

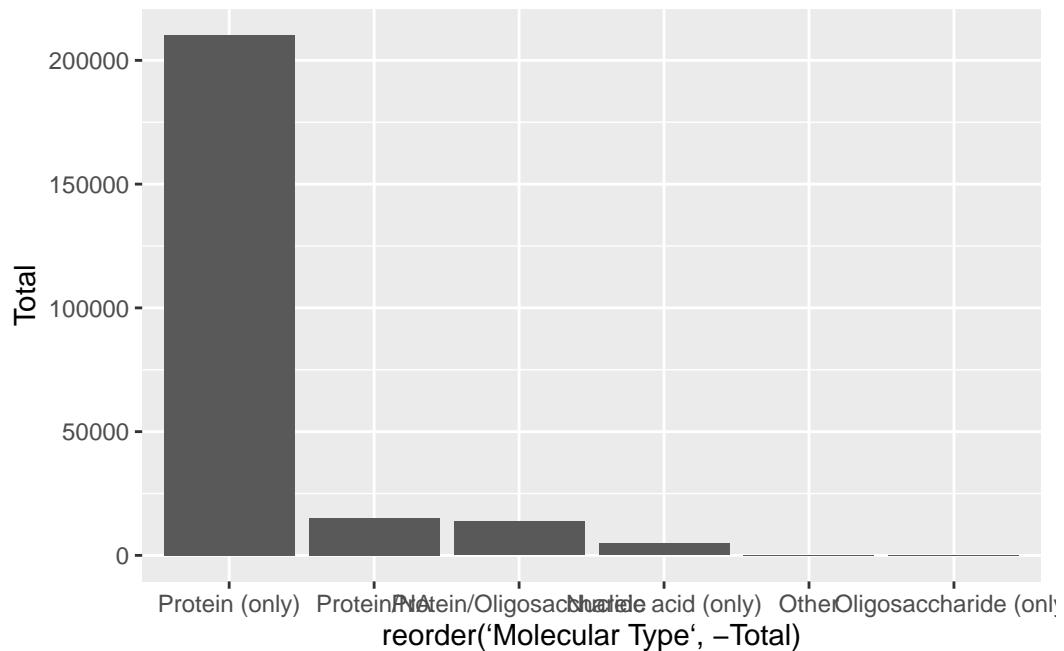
Q2: What proportion of structures in the PDB are protein?

```
n.protein <-stats$Total[1]
n.protein/n.total
```

[1] 0.860465

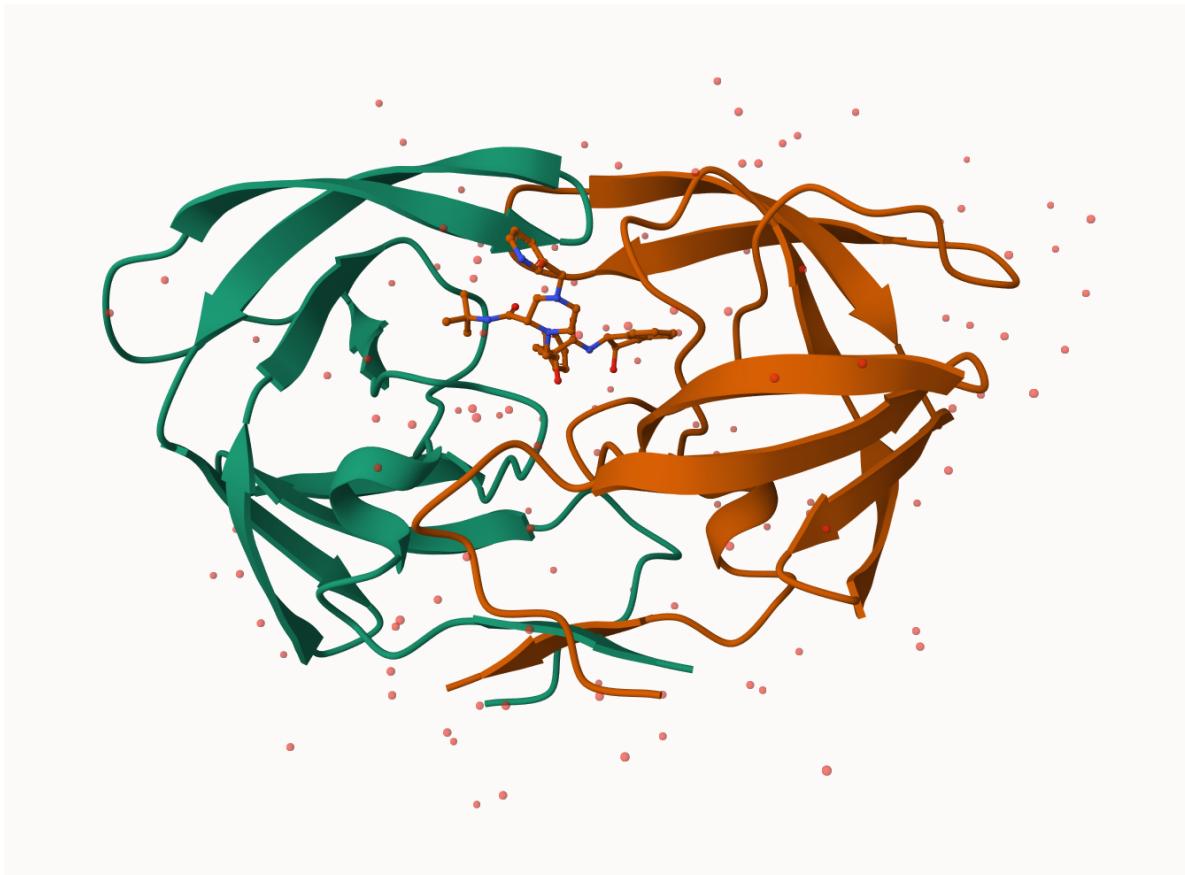
Q3: Make a bar plot overview.

```
library(ggplot2)
ggplot(stats)+
  aes(reorder(`Molecular Type`,-Total),Total)+
  geom_col()
```



Visualizing structure data

The Mol* viewer is embedded in many bioinformatics websites. The homepage is <https://molstar.org>
I can insert any figure or image file using markdown format



Notice inside square brackets you can put caption



Figure 1: The catalytic ASP2

```
##Bio3D package for structural bioinformatics
```

We can use the bio3d package to read and analyze biomolecular data in R:

```
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:
PQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWPKMIGGGFIKVRQYD
QILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNFPQITLWQRPLVTIKIGGQLKE
ALLDTGADDTVLEEMSLPGRWPKMIGGGFIKVRQYDQILIEICGHKAIGTVLVGPTP
VNIIGRNLLTQIGCTLNF

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

```
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>										

Lets get 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"
```

Lets trim to chain A and get just its sequence

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

Lets blast

```
#this code saves your results so that every time you render it does not have to rerun this b
blast<-blast.pdb(chainA.seq)
```

```
Searching ... please wait (updates every 5 seconds) RID = GABWZN6W014
.....
Reporting 249 hits
```

```
head(blast$hit.tbl)
```

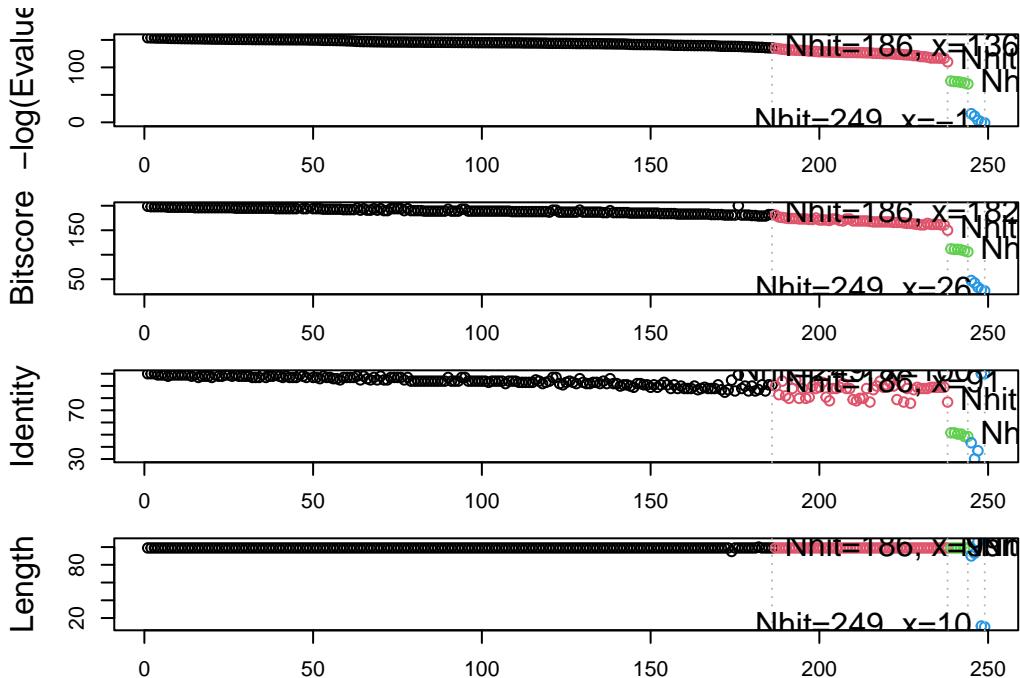
	queryid	subjectids	identity	alignmentlength	mismatches	gapopens	q.start	q.end	s.start	s.end	evalue	bitscore	positives	mlog.evalue	pdb.id	acc	
1	Query_536831	1W5V_A	100.00		99	0	0		99	12	110	1.38e-67	199	100	153.9511	1W5V_A	1W5V_A
2	Query_536831	2FDE_A	100.00		99	0	0		99	2	100	1.70e-67	198	100	153.7426	2FDE_A	2FDE_A
3	Query_536831	1AJV_A	100.00		99	0	0		99	1	99	1.99e-67	198	100	153.5851	1AJV_A	1AJV_A
4	Query_536831	2R38_A	98.99		99	1	0		99	1	99	2.50e-67	198	100	153.3569	2R38_A	2R38_A
5	Query_536831	2R3T_A	98.99		99	1	0		99	1	99	2.50e-67	198	100	153.3569	2R3T_A	2R3T_A
6	Query_536831	1HXB_A	98.99		99	1	0		99	1	99	2.50e-67	198	100	153.3569	1HXB_A	1HXB_A

Plot a quick overview of blast results

```
hits<-plot(blast)
```

```
* Possible cutoff values:    135 110 69 -2
Yielding Nhits:          186 238 244 249

* Chosen cutoff value of:   69
Yielding Nhits:          244
```



```
hits$pdb.id
```

```
[1] "1W5V_A" "2FDE_A" "1AJV_A" "2R38_A" "2R3T_A" "1HXB_A" "1BV9_A" "1AAQ_A"
[9] "1AXA_A" "1HVS_A" "1ZP8_A" "2QHC_A" "1A8G_A" "204L_A" "5COK_A" "1TCX_A"
[17] "2Z54_A" "1D4S_A" "1BV7_A" "1BWA_A" "1A9M_A" "2FLE_A" "1ODY_A" "1GNN_A"
[25] "1GNM_A" "5YRS_B" "1HEF_E" "10DX_A" "4QGI_A" "1BVE_A" "2AZ8_A" "1A30_A"
[33] "6DH6_A" "6DHO_A" "2I4D_A" "600S_A" "1RL8_A" "5YRS_A" "1ZSF_A" "2Q64_A"
[41] "6DH3_A" "2NPH_A" "2Q63_A" "1LZQ_A" "1FB7_A" "1G6L_A" "1HIV_A" "600U_A"
[49] "1HVC_A" "2I4V_A" "2AZ9_A" "600T_A" "2P3B_B" "5KAO_A" "2WLO_A" "6OPT_A"
[57] "1IZI_A" "1MRX_A" "2PYM_A" "2PYN_A" "1DMP_A" "4K4P_A" "1LV1_A" "1AID_A"
[65] "1LV1_A" "1ZBG_A" "3TKG_A" "1HVC_A" "5YOK_A" "1G6L_A" "1FGC_C" "3K4V_A"
[73] "3KT5_A" "3KT5_A" "4QLH_A" "4QLH_A" "2F3K_A" "4Q5M_A" "2AOC_A" "3B80_A"
[81] "3VF5_A" "2AVQ_A" "1DW6_C" "1KZK_A" "2HS1_A" "1K6C_A" "1MTB_A" "4Q1X_A"
[89] "4Q1W_A" "4Q5M_A" "3D1X_A" "2AVM_A" "3PWM_A" "3KT2_A" "3KT2_A" "1SDV_A"
[97] "3JWV_A" "3OY4_A" "1A94_A" "2HS2_A" "4EJ8_A" "2FGU_A" "2AVV_A" "3JW2_A"
[105] "3BVA_A" "1FFF_C" "3S43_B" "2NXD_A" "1FG6_C" "1EBK_C" "4Q1Y_A" "3EL4_A"
[113] "1F7A_A" "1K2B_A" "2FGV_A" "1Z8C_A" "2G69_A" "3EL9_A" "30XV_A" "1BDR_A"
[121] "3N3I_A" "3N3I_A" "30XW_A" "3S43_A" "3EM3_A" "3CYW_A" "5KQX_A" "2B60_A"
[129] "7DOZ_A" "1K2C_A" "1MT7_A" "3EM4_A" "4QJ9_A" "1BDL_A" "3LZS_A" "5T84_A"
[137] "4DQB_A" "7DOZ_A" "4QJ2_A" "3LZV_A" "1SGU_A" "2FXE_A" "1BDQ_A" "3U71_A"
[145] "2R5P_A" "4OBD_A" "7MAS_A" "3IXO_A" "3D3T_A" "5YOJ_A" "3LZU_A" "4NJS_A"
[153] "3EKP_A" "1B6J_A" "3EKQ_A" "2RKF_A" "1C6X_A" "7MAR_A" "4DQF_A" "1RPI_A"
```

```
[161] "3OU1_B" "3PJ6_A" "2P3A_A" "60GQ_A" "30Q7_A" "5KR1_A" "30QD_A" "4RVI_A"
[169] "30QA_A" "1B6K_A" "30UD_B" "6MK9_A" "3S09_A" "1Q9P_A" "6I45_A" "7SEP_A"
[177] "4NJT_A" "3BXR_A" "4YOA_A" "4DQC_A" "2FDD_A" "2RKG_A" "4DQH_A" "2P3C_A"
[185] "4EP2_A" "4EP2_A" "4EQO_A" "4NPT_A" "6OPU_A" "4NPU_A" "3U7S_A" "3HAW_A"
[193] "2AZB_A" "3TTP_A" "3HBO_A" "3GGU_A" "7N6T_A" "60PV_A" "4EQO_A" "60PX_A"
[201] "204N_A" "5T2E_A" "3UCB_A" "3KA2_A" "3FSM_A" "60PW_A" "2AZC_A" "3FSM_A"
[209] "3HLO_A" "2P3D_A" "3T3C_A" "7MYP_A" "6054_X" "60PY_A" "4Z4X_A" "60PZ_A"
[217] "2JE4_A" "1DAZ_C" "7MAP_A" "7MAQ_A" "1K1U_A" "2B7Z_A" "3MWS_A" "1K1T_A"
[225] "8DCH_A" "3I2L_A" "6P9A_A" "2FXD_A" "2J9J_A" "3DCK_A" "2J9J_B" "3NXE_A"
[233] "2040_A" "2040_A" "3NXE_A" "3KA2_A" "3HLO_A" "5B18_A" "1SIP_A" "2SAM_A"
[241] "1AZ5_A" "1SIV_A" "1HII_A" "1IVP_A"
```

Prediction of functional motions

We can run a Normal Mode Analysis (NMA) to predict large scale motions/flexibility/dynamics of any biomolecule that we can read into R

Lets look at ADK and chain A only!

```
adk <-read.pdb("1ake")
```

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

```
adk_A<-trim.pdb(adk,chain="A")
adk_A
```

```
Call: trim.pdb(pdb = adk, chain = "A")

Total Models#: 1
Total Atoms#: 1954, XYZs#: 5862 Chains#: 1 (values: A)

Protein Atoms#: 1656 (residues/Calpha atoms#: 214)
Nucleic acid Atoms#: 0 (residues/phosphate atoms#: 0)

Non-protein/nucleic Atoms#: 298 (residues: 242)
Non-protein/nucleic resid values: [ AP5 (1), HOH (241) ]

Protein sequence:
MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMRLRAAVKSGSELGKQAKDIMDAGKLVT
```

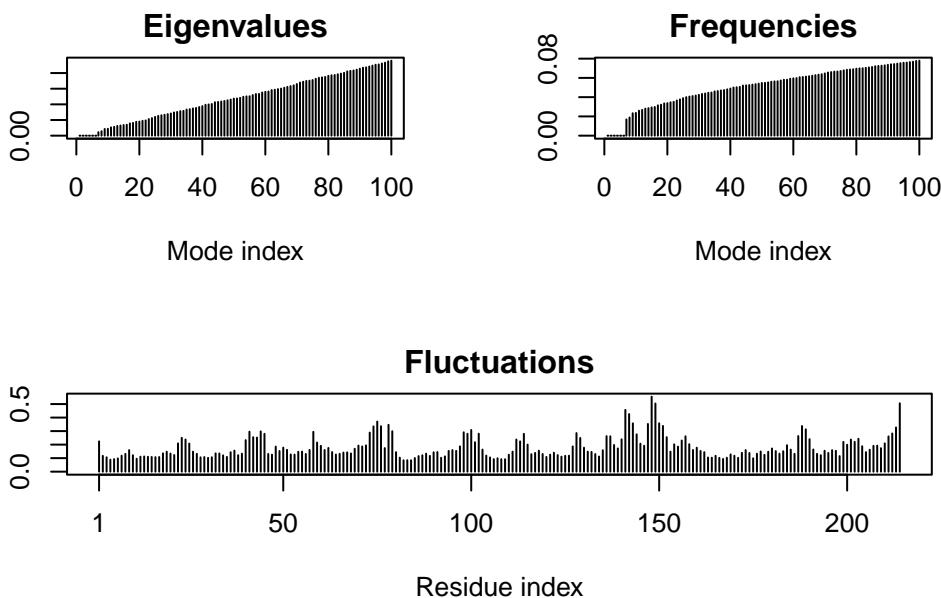
```
DELVIALVKERIAQEDCRNGFLLDGFPR TIPQADAMKEAGINV D YVLEFDVPDELIVDRI  
VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTRKDDQEETVRKRLVEYHQMTAPLIG  
YY SKEAEAGNTKYAKVDGTPVAEVRA DLEKILG
```

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

```
m<-nma(adk_A)
```

```
Building Hessian...      Done in 0.008 seconds.  
Diagonalizing Hessian... Done in 0.169 seconds.
```

```
plot(m)
```



Lets write out a “trajectory” of predicted motion

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

Play with 3D viewing in R

We can use the new **bio3dview** package, which is not yet on CRAN, to render interactive 3D views in R and HTML quarto output reports.

To install from GitHub we can use the **pak** package

```
library(bio3dview)
#view.pdb(adk)
```