Class 10: Structural Bioinformatics pt.1

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The PDB database

The main repository of biomolecular structure data is called the PDB found at: https://www.rcsb.org/

Let's see what this database contains. I went to PDB > Analyze > PDB Statistics > By Exp method and molecular type.

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

```
           Molecular.Type   X.ray     EM    NMR Multiple.methods Neutron Other
1          Protein (only) 169,563 16,774 12,578              208      81    32
2 Protein/Oligosaccharide   9,939  2,839     34                8       2     0
3              Protein/NA   8,801  5,062    286                7       0     0
4     Nucleic acid (only)   2,890    151  1,521               14       3     1
5                   Other     170     10     33                0       0     0
6  Oligosaccharide (only)      11      0      6                1       0     4
    Total
1 199,236
2  12,822
3  14,156
4   4,580
```

```
5     213
6      22
```

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

```
pdbstats$X.ray
```

```
[1] "169,563" "9,939"   "8,801"   "2,890"   "170"     "11"
```

The comma in these numbers is causing them to be read as character rather than numeric.

I can fix this by replacing "," for nothing " " with the `sub()` function:

```
x <- pdbstats$X.ray
sum( as.numeric( sub(",", "", x) ) )
```

```
[1] 191374
```

Or I can use the **readr** package and the `read_csv()` function.

```
library(readr)
pdbstats <- read_csv("Data Export Summary.csv")
```

```
Rows: 6 Columns: 8
-- Column specification --------------------------------------------------------
Delimiter: ","
chr (1): Molecular Type
dbl (3): 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.
```

```
pdbstats
```

```
# A tibble: 6 x 8
  `Molecular Type`   `X-ray`    EM   NMR `Multiple methods` Neutron Other  Total
  <chr>                <dbl> <dbl> <dbl>                <dbl>   <dbl> <dbl>  <dbl>
1 Protein (only)      169563 16774 12578                  208      81    32 199236
2 Protein/Oligosacc~    9939  2839    34                    8       2     0  12822
3 Protein/NA            8801  5062   286                    7       0     0  14156
4 Nucleic acid (onl~    2890   151  1521                   14       3     1   4580
5 Other                  170    10    33                    0       0     0    213
6 Oligosaccharide (~      11     0     6                    1       0     4     22
```

I want to clean the column names so they are all lower case and don't have any spaces in them.

```
colnames(pdbstats)
```

```
[1] "Molecular Type"   "X-ray"            "EM"               "NMR"             
[5] "Multiple methods" "Neutron"          "Other"            "Total"           
```

```
library(janitor)
```

```

Attaching package: 'janitor'

The following objects are masked from 'package:stats':

    chisq.test, fisher.test
```

```
df <- clean_names(pdbstats)
```

Total number of X-ray structures.

```
sum(df$x_ray)
```

```
[1] 191374
```

Total number of structures:

```
sum(df$total)
```

```
[1] 231029
```

```
(sum(df$x_ray)/sum(df$total))*100
```

```
[1] 82.83549
```

Percent of EM structures structures:

```
(sum(df$em)/sum(df$total))*100
```

```
[1] 10.75017
```

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

```
df_protein_total <- df[1:3, 8]
df_protein_total
```

```
# A tibble: 3 x 1
   total
   <dbl>
1 199236
2  12822
3  14156
```

```
(sum(df_protein_total)/sum(df$total))*100
```

```
[1] 97.91585
```

2. Using Mol*

The main Mol* homepage at: https://molstar.org/viewer/ We can input our own PDB files or just hive it a PDB database accession code (4 letter PDB code).

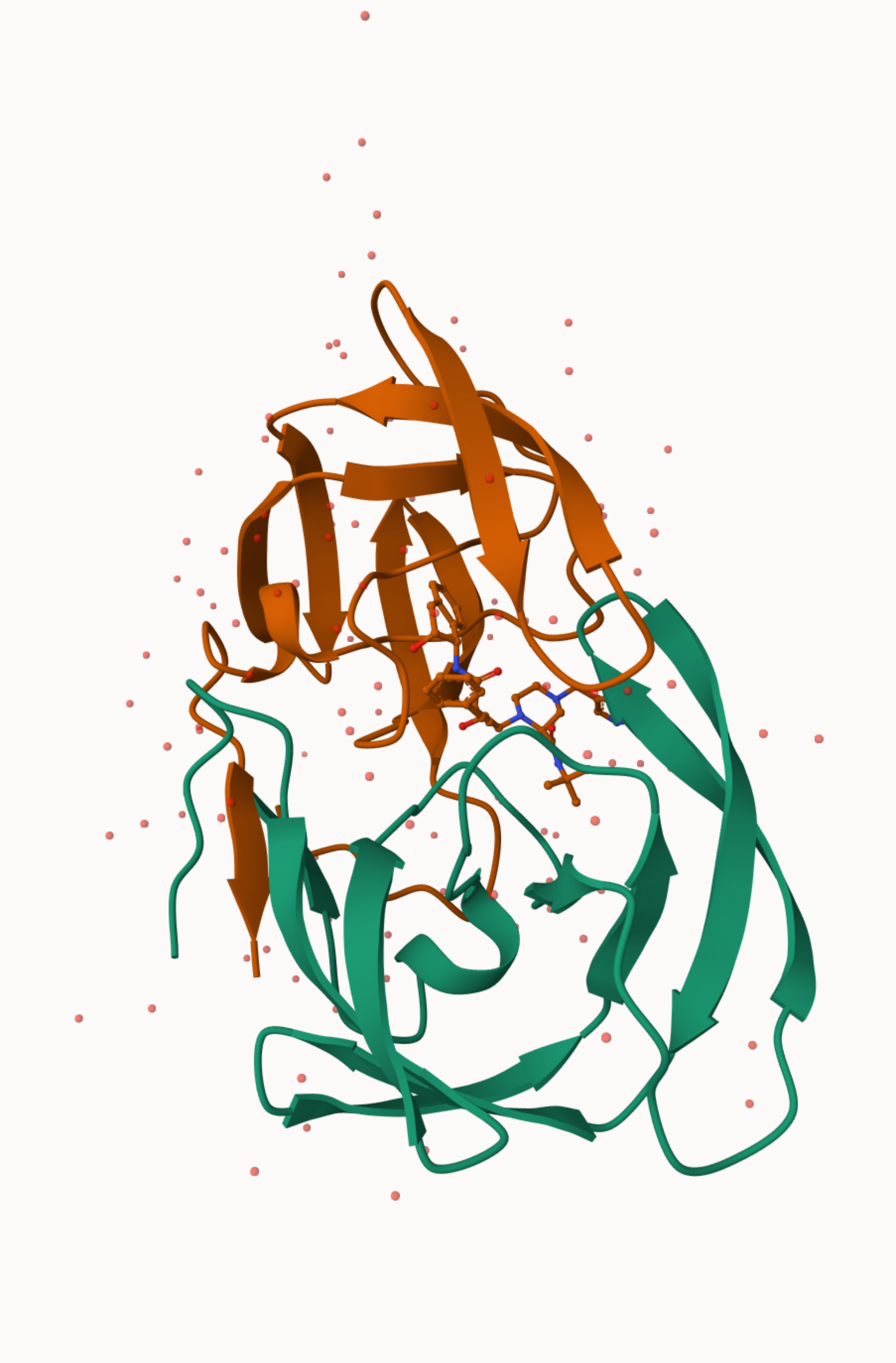

Figure 1: Molecular view of HSG

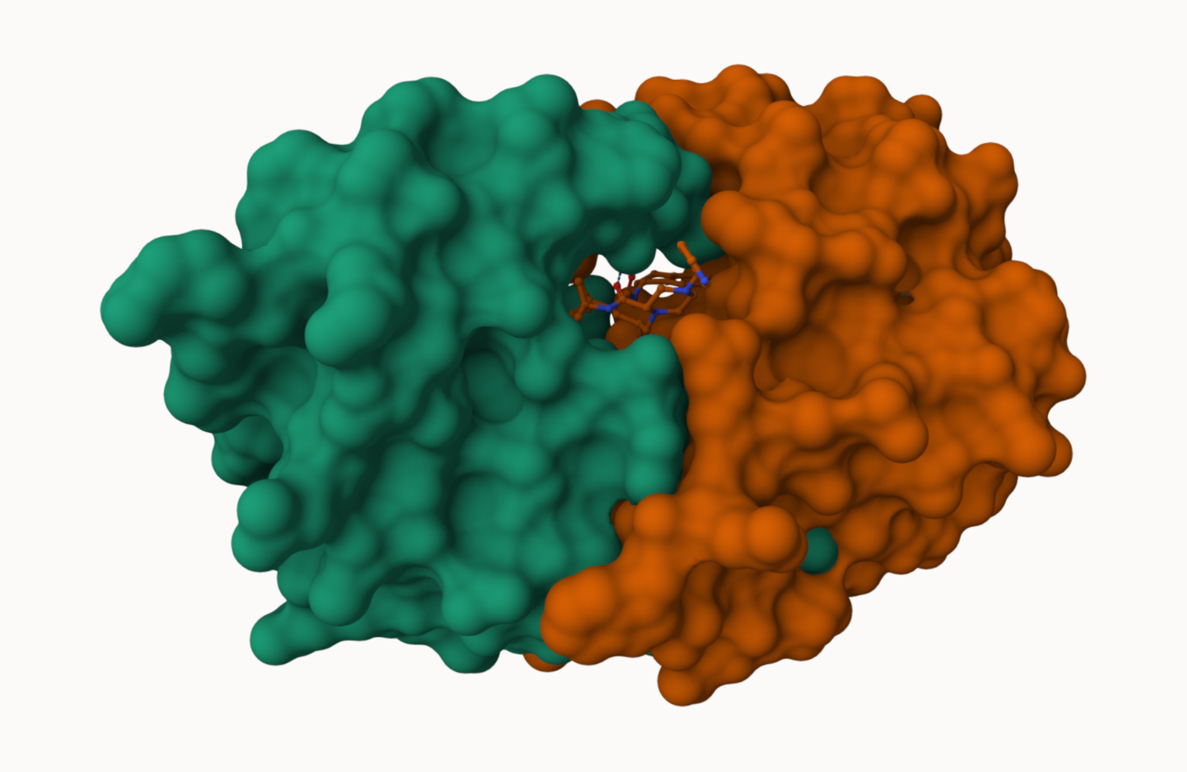

Figure 2: 1HSG side view

Introduction to Bio3D in R

We can use the **bio3d** package for structural bioinformatics to read PDB data into R.

```
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
```

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

To conserve space and make the display visually appealing.

> 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

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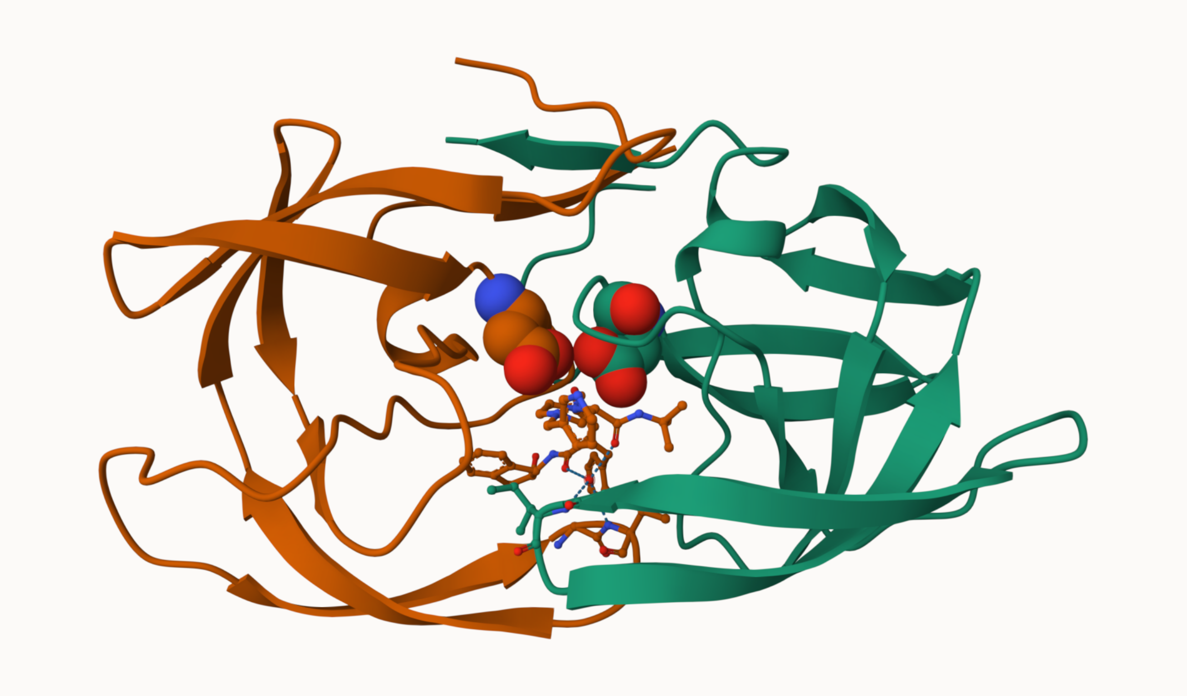
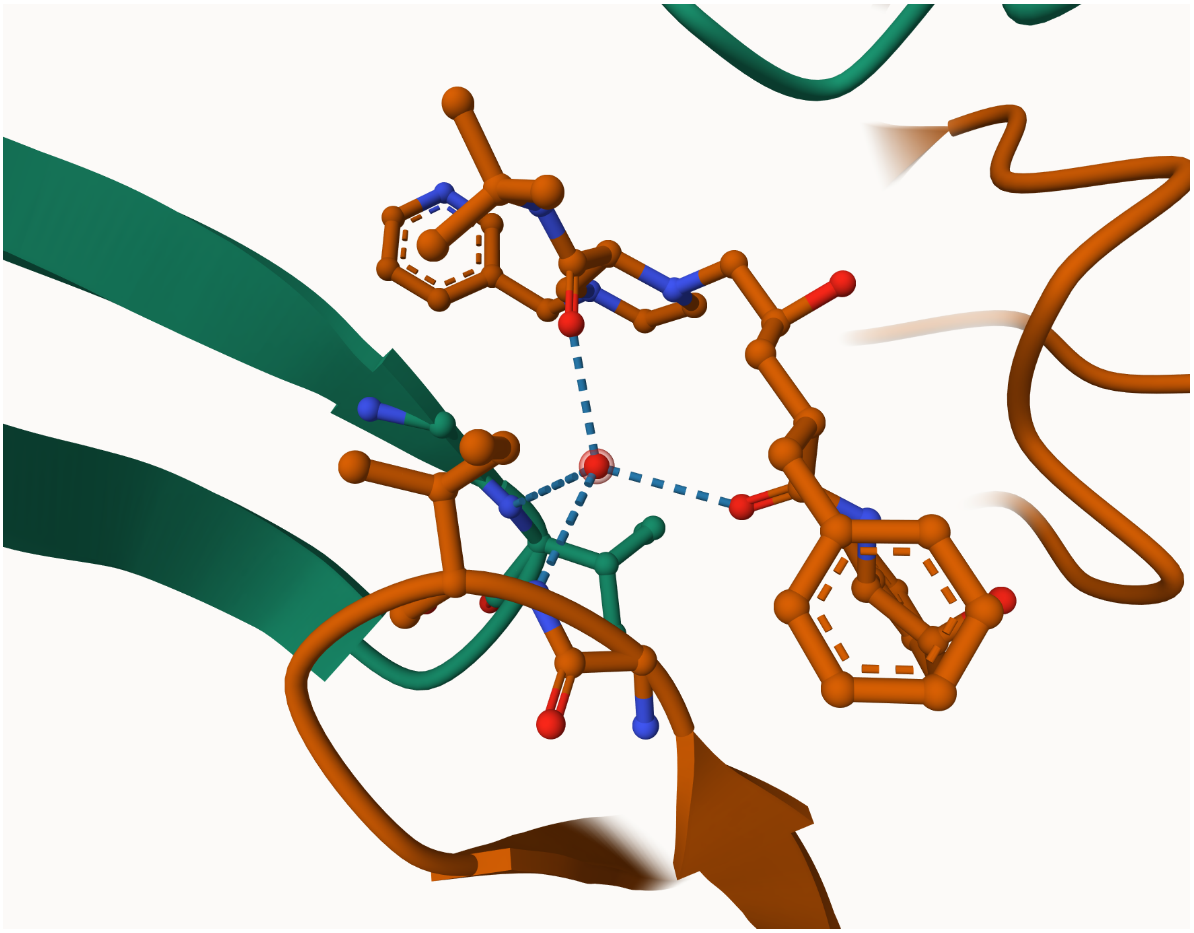
> Q6: Generate and save a figure clearly showing the two distinct chains of HIV-protease along with the ligand. You might also consider showing the catalytic residues ASP 25 in each chain and the critical water (we recommend "Ball & Stick" for these side-chains). Add this figure to your Quarto document.





Q7: How many amino acid residues are there in this pdb object?

```
length( pdbseq(pdb) )
```

```
[1] 198
```

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

MK1

Q9: How many protein chains are in this structure?

2 chains A and B

Looking at the `pdb` object in more detail

```
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>
```

Let's try a new function not yet in the bio3d package. It requires the **r3dmol** and the **shiny** package that we need to install with `install.packages("r3dmol")` and `install.packages("shiny")`.

```
source("https://tinyurl.com/viewpdb")
#view.pdb(pdb, backgroundColor = "pink")
```

4. Predicting functional dynamics

We can use the `nma()` function in bio3d to predict the large-scale functional motions of biomolecules.

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

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

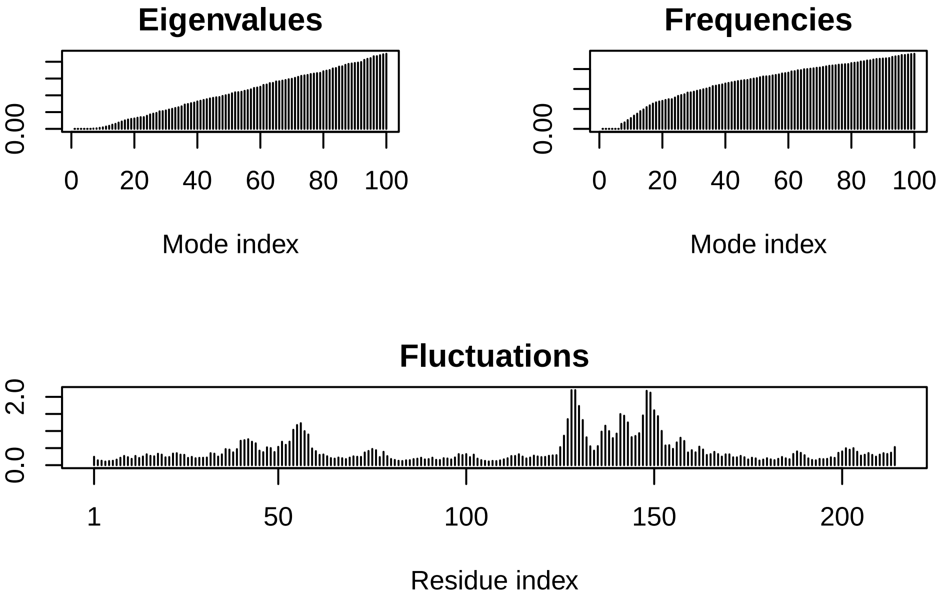
```r
adk
```

```

 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 0.01 seconds.
 Diagonalizing Hessian...   Done in 0.179 seconds.
```

```r
plot(m)
```



Write out a trajectory of the predicted molecular motion:

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