

Class 11

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#PART 1

We need some packages for today's class. These include `bio3d` and `msa`

The `msa` package is from the BioConductor. These packages focus on the genomics type work and are managed by the `BiocManager` package.

Install `install.packages("BiocManager")` and then `BiocManager::install("msa")` all entered in the R "brain" console

```
library(bio3d)

aa <- get.seq("1ake_A")
```

Warning in `get.seq("1ake_A")`: Removing existing file: `seqs.fasta`

Fetching... Please wait. Done.

```
aa
```

```

      1      .      .      .      .      .      .      60
pdb|1AKE|A  MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLV
      1      .      .      .      .      .      .      60
      61      .      .      .      .      .      .      120
pdb|1AKE|A  DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMKEAGINVVDYVLEFDVPDELIVDRI
      61      .      .      .      .      .      .      120
      121      .      .      .      .      .      .      180
pdb|1AKE|A  VGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTAPLIG
      121      .      .      .      .      .      .      180
```

```

      181      .      .      .      214
pdb|1AKE|A  YYSKEAEAGNTKYAKVDGTPVAEVRADLEKILG
      181      .      .      .      214

```

Call:

```
read.fasta(file = outfile)
```

Class:

```
fasta
```

Alignment dimensions:

```
1 sequence rows; 214 position columns (214 non-gap, 0 gap)
```

```
+ attr: id, ali, call
```

Now I can search the PDB database for related sequences:

```
#b <- blast.pdb(aa)
```

```
#hits <- plot(b)
```

```
#attributes(b)
```

```
#head(b$hit.tbl)
```

These are the related structures in the PDB database that we found via a BLAST search...

```
hits <- NULL
```

```
hits$ pdb.id <- c('1AKE_A', '6S36_A', '6RZE_A', '3HPR_A', '1E4V_A', '5EJE_A', '1E4Y_A', '3X2S_A', ...)
```

Side-note: Lets annotate these structures (in other words find out what they are, what species they are from, stuff about the experiment they were solved in etc.)

For this we can use the `pdb.annotate()`

```
anno <- pdb.annotate(hits$ pdb.id)
```

```
attributes(anno)
```

```
$names
```

```

[1] "structureId"      "chainId"          "macromoleculeType"
[4] "chainLength"     "experimentalTechnique" "resolution"
[7] "scopDomain"      "pfam"             "ligandId"
[10] "ligandName"      "source"           "structureTitle"
[13] "citation"        "rObserved"        "rFree"
[16] "rWork"           "spaceGroup"

$class
[1] "data.frame"

$row.names
[1] "1AKE_A" "6S36_A" "6RZE_A" "3HPR_A" "1E4V_A" "5EJE_A" "1E4Y_A" "3X2S_A"
[9] "6HAP_A" "6HAM_A" "4K46_A" "3GMT_A" "4PZL_A"

```

```
head(anno)
```

	structureId	chainId	macromoleculeType	chainLength	experimentalTechnique
1AKE_A	1AKE	A	Protein	214	X-ray
6S36_A	6S36	A	Protein	214	X-ray
6RZE_A	6RZE	A	Protein	214	X-ray
3HPR_A	3HPR	A	Protein	214	X-ray
1E4V_A	1E4V	A	Protein	214	X-ray
5EJE_A	5EJE	A	Protein	214	X-ray
	resolution	scopDomain			pfam
1AKE_A	2.00	Adenylate kinase	Adenylate kinase, active site lid (ADK_lid)		
6S36_A	1.60	<NA>	Adenylate kinase, active site lid (ADK_lid)		
6RZE_A	1.69	<NA>	Adenylate kinase, active site lid (ADK_lid)		
3HPR_A	2.00	<NA>	Adenylate kinase, active site lid (ADK_lid)		
1E4V_A	1.85	Adenylate kinase	Adenylate kinase, active site lid (ADK_lid)		
5EJE_A	1.90	<NA>	Adenylate kinase, active site lid (ADK_lid)		
	ligandId		ligandName		
1AKE_A	AP5		BIS(ADENOSINE)-5'-PENTAPHOSPHATE		
6S36_A	CL (3),NA,MG (2)	CHLORIDE ION (3),SODIUM ION,MAGNESIUM ION (2)			
6RZE_A	NA (3),CL (2)		SODIUM ION (3),CHLORIDE ION (2)		
3HPR_A	AP5		BIS(ADENOSINE)-5'-PENTAPHOSPHATE		
1E4V_A	AP5		BIS(ADENOSINE)-5'-PENTAPHOSPHATE		
5EJE_A	AP5,CO	BIS(ADENOSINE)-5'-PENTAPHOSPHATE,COBALT (II) ION			
		source			
1AKE_A		Escherichia coli			
6S36_A		Escherichia coli			
6RZE_A		Escherichia coli			

```

3HPR_A          Escherichia coli K-12
1E4V_A          Escherichia coli
5EJE_A Escherichia coli O139:H28 str. E24377A

```

```

1AKE_A STRUCTURE OF THE COMPLEX BETWEEN ADENYLATE KINASE FROM ESCHERICHIA COLI AND THE INHIBIT
6S36_A
6RZE_A
3HPR_A
1E4V_A
5EJE_A

```

Cryst

		citation	rObserved	rFree
1AKE_A	Muller, C.W., et al. J Mol Biol (1992)	0.1960	NA	
6S36_A	Rogne, P., et al. Biochemistry (2019)	0.1632	0.2356	
6RZE_A	Rogne, P., et al. Biochemistry (2019)	0.1865	0.2350	
3HPR_A	Schrank, T.P., et al. Proc Natl Acad Sci U S A (2009)	0.2100	0.2432	
1E4V_A	Muller, C.W., et al. Proteins (1993)	0.1960	NA	
5EJE_A	Kovermann, M., et al. Proc Natl Acad Sci U S A (2017)	0.1889	0.2358	

	rWork	spaceGroup
1AKE_A	0.1960	P 21 2 21
6S36_A	0.1594	C 1 2 1
6RZE_A	0.1819	C 1 2 1
3HPR_A	0.2062	P 21 21 2
1E4V_A	0.1960	P 21 2 21
5EJE_A	0.1863	P 21 2 21

Now we can download all these structures for further analysis with the `get.pdb()` function

```

# Download releated PDB files
files <- get.pdb(hits$pdb.id, path="pdbs", split=TRUE, gzip=TRUE)

```

```

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1AKE.pdb.gz exists. Skipping download

```

```

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6S36.pdb.gz exists. Skipping download

```

```

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6RZE.pdb.gz exists. Skipping download

```

```

Warning in get.pdb(hits$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3HPR.pdb.gz exists. Skipping download

```

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1E4V.pdb.gz exists. Skipping download

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/5EJE.pdb.gz exists. Skipping download

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/1E4Y.pdb.gz exists. Skipping download

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3X2S.pdb.gz exists. Skipping download

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6HAP.pdb.gz exists. Skipping download

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/6HAM.pdb.gz exists. Skipping download

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/4K46.pdb.gz exists. Skipping download

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/3GMT.pdb.gz exists. Skipping download

Warning in get.pdb(hits\$pdb.id, path = "pdbs", split = TRUE, gzip = TRUE):
pdbs/4PZL.pdb.gz exists. Skipping download

	0%
=====	8%
=====	15%
=====	23%
=====	31%
=====	38%

	=====	46%
	=====	54%
	=====	62%
	=====	69%
	=====	77%
	=====	85%
	=====	92%
	=====	100%

Now we have all these related structures we can align and Superpose...

```
# Align related PDBs
pdbbs <- pdbaln(files, fit = TRUE, exefile="msa")
```

Reading PDB files:

```
pdbbs/split_chain/1AKE_A.pdb
pdbbs/split_chain/6S36_A.pdb
pdbbs/split_chain/6RZE_A.pdb
pdbbs/split_chain/3HPR_A.pdb
pdbbs/split_chain/1E4V_A.pdb
pdbbs/split_chain/5EJE_A.pdb
pdbbs/split_chain/1E4Y_A.pdb
pdbbs/split_chain/3X2S_A.pdb
pdbbs/split_chain/6HAP_A.pdb
pdbbs/split_chain/6HAM_A.pdb
pdbbs/split_chain/4K46_A.pdb
pdbbs/split_chain/3GMT_A.pdb
pdbbs/split_chain/4PZL_A.pdb
  PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
.   PDB has ALT records, taking A only, rm.alt=TRUE
..  PDB has ALT records, taking A only, rm.alt=TRUE
.... PDB has ALT records, taking A only, rm.alt=TRUE
```

```
.   PDB has ALT records, taking A only, rm.alt=TRUE
...
```

Extracting sequences

```
pdb/seq: 1   name: pdbs/split_chain/1AKE_A.pdb
           PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 2   name: pdbs/split_chain/6S36_A.pdb
           PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 3   name: pdbs/split_chain/6RZE_A.pdb
           PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 4   name: pdbs/split_chain/3HPR_A.pdb
           PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 5   name: pdbs/split_chain/1E4V_A.pdb
pdb/seq: 6   name: pdbs/split_chain/5EJE_A.pdb
           PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 7   name: pdbs/split_chain/1E4Y_A.pdb
pdb/seq: 8   name: pdbs/split_chain/3X2S_A.pdb
pdb/seq: 9   name: pdbs/split_chain/6HAP_A.pdb
pdb/seq: 10  name: pdbs/split_chain/6HAM_A.pdb
           PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 11  name: pdbs/split_chain/4K46_A.pdb
           PDB has ALT records, taking A only, rm.alt=TRUE
pdb/seq: 12  name: pdbs/split_chain/3GMT_A.pdb
pdb/seq: 13  name: pdbs/split_chain/4PZL_A.pdb
```

pdbs

	1	.	.	.	40
[Truncated_Name:1] 1AKE_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:2] 6S36_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:3] 6RZE_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:4] 3HPR_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:5] 1E4V_A.pdb	-----	MRIILLGAPVAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:6] 5EJE_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:7] 1E4Y_A.pdb	-----	MRIILLGALVAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:8] 3X2S_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:9] 6HAP_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:10] 6HAM_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMEKYGIPQIS			
[Truncated_Name:11] 4K46_A.pdb	-----	MRIILLGAPGAGKGTQAQFIMAKFGIPQIS			
[Truncated_Name:12] 3GMT_A.pdb	-----	MRLILLGAPGAGKGTQANFIKEKFGIPQIS			

[Truncated_Name:13] 4PZL_A.pdb	TENLYFQSNAMRIILLGAPGACKGTQAKIIEQKYNIAHIS	
	~*** ***** * *~* **	
	1 	40
	41 	80
[Truncated_Name:1] 1AKE_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDAGKLVTDDELVIALVKE	
[Truncated_Name:2] 6S36_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDAGKLVTDDELVIALVKE	
[Truncated_Name:3] 6RZE_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDAGKLVTDDELVIALVKE	
[Truncated_Name:4] 3HPR_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDAGKLVTDDELVIALVKE	
[Truncated_Name:5] 1E4V_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDAGKLVTDDELVIALVKE	
[Truncated_Name:6] 5EJE_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDACKLVTDDELVIALVKE	
[Truncated_Name:7] 1E4Y_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDAGKLVTDDELVIALVKE	
[Truncated_Name:8] 3X2S_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDCGKLVTDDELVIALVKE	
[Truncated_Name:9] 6HAP_A.pdb	TGDMRLRAAVKSGSELGKQAKDIMDAGKLVTDDELVIALVRE	
[Truncated_Name:10] 6HAM_A.pdb	TGDMRLRAAIKSGSELGKQAKDIMDAGKLVTDDEIIIALVKE	
[Truncated_Name:11] 4K46_A.pdb	TGDMRLRAAIKAGTELGKQAKSVIDAGQLVSDDIILGLVKE	
[Truncated_Name:12] 3GMT_A.pdb	TGDMRLRAAVKAGTPLGVEAKTYMDEGKLVPSLIIGLVKE	
[Truncated_Name:13] 4PZL_A.pdb	TGDMIRETIKSGSALGQELKKVLDAGELVSDEFIIKIVKD	
	****~* ~* *~ ** * ~* ** * ^^ ~*^^	
	41 	80
	81 	120
[Truncated_Name:1] 1AKE_A.pdb	RIAQEDCRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:2] 6S36_A.pdb	RIAQEDCRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:3] 6RZE_A.pdb	RIAQEDCRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:4] 3HPR_A.pdb	RIAQEDCRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:5] 1E4V_A.pdb	RIAQEDCRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:6] 5EJE_A.pdb	RIAQEDCRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:7] 1E4Y_A.pdb	RIAQEDCRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:8] 3X2S_A.pdb	RIAQEDSRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:9] 6HAP_A.pdb	RICQEDSRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:10] 6HAM_A.pdb	RICQEDSRNGFLLDGFPR TIPQADAMKEAGINVDYVLEFD	
[Truncated_Name:11] 4K46_A.pdb	RIAQDDCAKGFLDGFPR TIPQADGLKEVGVVVDYVIEFD	
[Truncated_Name:12] 3GMT_A.pdb	RLKEADCANGYLFDFPR TIPQADAMKEAGVAIDYVLEID	
[Truncated_Name:13] 4PZL_A.pdb	RISKNDCCNNGFLLDGVPR TIPQAQELDKLGVNIDYIVEVD	
	*~ * *~* ** ***** ** ~ *~ ~**~*~* *	
	81 	120
	121 	160
[Truncated_Name:1] 1AKE_A.pdb	VPDELIVDRIVGRRVHAPSGRVYHV KFNPPKVEGKDDVTG	
[Truncated_Name:2] 6S36_A.pdb	VPDELIVDKIVGRRVHAPSGRVYHV KFNPPKVEGKDDVTG	
[Truncated_Name:3] 6RZE_A.pdb	VPDELIVDAIVGRRVHAPSGRVYHV KFNPPKVEGKDDVTG	
[Truncated_Name:4] 3HPR_A.pdb	VPDELIVDRIVGRRVHAPSGRVYHV KFNPPKVEGKDDGTG	

[Truncated_Name:5] 1E4V_A.pdb	VPDELIVDRIVGRRVHAPSGRVYHVKFNP	PKVEGKDDVTG
[Truncated_Name:6] 5EJE_A.pdb	VPDELIVDRIVGRRVHAPSGRVYHVKFNP	PKVEGKDDVTG
[Truncated_Name:7] 1E4Y_A.pdb	VPDELIVDRIVGRRVHAPSGRVYHVKFNP	PKVEGKDDVTG
[Truncated_Name:8] 3X2S_A.pdb	VPDELIVDRIVGRRVHAPSGRVYHVKFNP	PKVEGKDDVTG
[Truncated_Name:9] 6HAP_A.pdb	VPDELIVDRIVGRRVHAPSGRVYHVKFNP	PKVEGKDDVTG
[Truncated_Name:10] 6HAM_A.pdb	VPDELIVDRIVGRRVHAPSGRVYHVKFNP	PKVEGKDDVTG
[Truncated_Name:11] 4K46_A.pdb	VADSVIVERMAGRRAHLASGRTYHN	VYNPPKVEGKDDVTG
[Truncated_Name:12] 3GMT_A.pdb	VPFSEIIERMGRRTHPASGRTYHV	KFNPPKVEGKDDVTG
[Truncated_Name:13] 4PZL_A.pdb	VADNLLIERITGRRIH	PASGRTYHTKFNP
	KVDKDDVTG	
	* ^^^ ^ *** * *** ** ^***** *** **	
	121 . . .	160
	161 . . .	200
[Truncated_Name:1] 1AKE_A.pdb	EELTTRKDDQEETVRKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:2] 6S36_A.pdb	EELTTRKDDQEETVRKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:3] 6RZE_A.pdb	EELTTRKDDQEETVRKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:4] 3HPR_A.pdb	EELTTRKDDQEETVRKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:5] 1E4V_A.pdb	EELTTRKDDQEETVRKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:6] 5EJE_A.pdb	EELTTRKDDQEECVKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:7] 1E4Y_A.pdb	EELTTRKDDQEETVRKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:8] 3X2S_A.pdb	EELTTRKDDQEETVRKRLCEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:9] 6HAP_A.pdb	EELTTRKDDQEETVRKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:10] 6HAM_A.pdb	EELTTRKDDQEETVRKRLVEYHQMTAP	LIGYYSKEAEAGN
[Truncated_Name:11] 4K46_A.pdb	EDLVIREDDKEETVLARLGVYHNQTAP	LIAYYGKEAEAGN
[Truncated_Name:12] 3GMT_A.pdb	EPLVQRDDDKKEETVKKRLDVYEAQTK	PLITYYGDWARRGA
[Truncated_Name:13] 4PZL_A.pdb	EPLITRTDDNEDTVKQRLSVYHAQTA	KLIDFYRNFSSNT
	* * * * * ^ * * * * ^ *	
	161 . . .	200
	201 . . .	227
[Truncated_Name:1] 1AKE_A.pdb	T--KYAKVDG	TKPVAEVRADLEKILG-
[Truncated_Name:2] 6S36_A.pdb	T--KYAKVDG	TKPVAEVRADLEKILG-
[Truncated_Name:3] 6RZE_A.pdb	T--KYAKVDG	TKPVAEVRADLEKILG-
[Truncated_Name:4] 3HPR_A.pdb	T--KYAKVDG	TKPVAEVRADLEKILG-
[Truncated_Name:5] 1E4V_A.pdb	T--KYAKVDG	TKPVAEVRADLEKILG-
[Truncated_Name:6] 5EJE_A.pdb	T--KYAKVDG	TKPVAEVRADLEKILG-
[Truncated_Name:7] 1E4Y_A.pdb	T--KYAKVDG	TKPVAEVRADLEKILG-
[Truncated_Name:8] 3X2S_A.pdb	T--KYAKVDG	TKPVAEVRADLEKILG-
[Truncated_Name:9] 6HAP_A.pdb	T--KYAKVDG	TKPVCEVRADLEKILG-
[Truncated_Name:10] 6HAM_A.pdb	T--KYAKVDG	TKPVCEVRADLEKILG-
[Truncated_Name:11] 4K46_A.pdb	T--QYLKFDG	TKAVAEVSAELEKALA-
[Truncated_Name:12] 3GMT_A.pdb	E-----NGLKAPA----	YRKISG-
[Truncated_Name:13] 4PZL_A.pdb	KIPKYIKINGDQAVEKVSQDIFDQLNK	

```

                *
            201  .      .      227

```

Call:

```
pdbaln(files = files, fit = TRUE, exefile = "msa")
```

Class:

```
pdb, fasta
```

Alignment dimensions:

```
13 sequence rows; 227 position columns (204 non-gap, 23 gap)
```

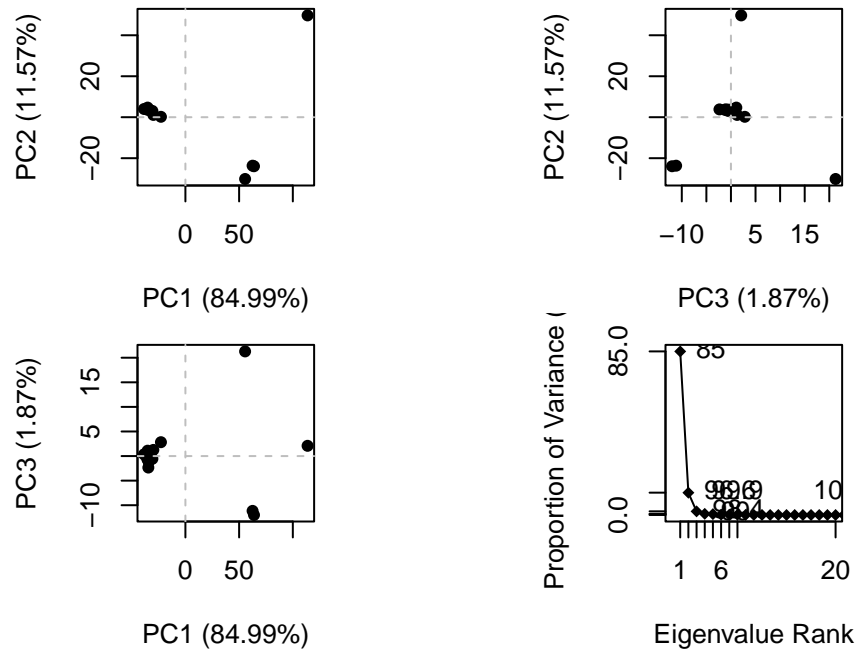
```
+ attr: xyz, resno, b, chain, id, ali, resid, sse, call
```

```
# Vector containing PDB codes for figure axis
ids <- basename.pdb(pdb$id)
```

```
# Draw schematic alignment
#plot(pdb, labels=ids)
```

##Principal Component Analysis

```
# Perform PCA
pc.xray <- pca(pdb)
plot(pc.xray)
```



```
# Visualize first principal component
pc1 <- mktrj(pc.xray, pc=1, file="pc_1.pdb")
```

And a nicer PC plot

```
# Calculate RMSD
rd <- rmsd(pdbbs)
```

Warning in rmsd(pdbbs): No indices provided, using the 204 non NA positions

```
# Structure-based clustering
hc.rd <- hclust(dist(rd))
grps.rd <- cutree(hc.rd, k=3)

plot(pc.xray, 1:2, col="grey50", bg=grps.rd, pch=21, cex=1)
```