Bio3D: Interactive Tools for Structural Bioinformatics

http://thegrantlab.org/bio3d/

What is Bio3D

A freely distributed and widely used R package for structural bioinformatics.

Provides a large number of integrated utilities for biomolecular sequence, structure and dynamics analysis.

Provides an unparalleled interactive environment for evolutionary and comparative dynamics analysis.*

What Bio3D is **NOT**

A performance optimized software library for incorporation into your own C/C++ etc. programs

A molecular graphics program with a slick GUI

Backed by a commercial guarantee or license agreement

Bio3D Features

Search, annotate and analyze using online sequence and structure databases.

Perform multivariate analysis of large structural and sequence datasets (PCA, MDS, DA, etc.).

High throughput ensemble normal mode analysis (NMA) of heterogenous structures.

Dynamic network analysis from NMA, molecular dynamics and experimental structure ensembles.

...

Bio3D Features

As well as foundational functionality for:
3D visualization, alignment, superposition, atom selection, rigid and dynamic domain analysis, sequence and conformational clustering, distance matrix analysis, sequence and structural conservation analysis, etc…

Features = **functions()**

```
> library(bio3d)
> lbio3d()
  [1] “aa.index"              "aa.table"
  [3] "aa123"                 "aa2index"
  [5] "aa2mass"               “aa321"
   …<cut>…
[307] "write.fasta"           “write.ncdf"
[309] "write.pdb"             "write.pir"
[311] "write.pqr"             "xyz2atom"
[313] "xyz2z.pca"             "z2xyz.pca"
```

Features = **functions()**

```
> help(package="bio3d")
```

```
aa.index          AAindex: Amino Acid Index Database
aa.table          Table of Relevant Amino Acids
aa123             Convert 1-letter and 3-letter Amino Acid Codes
aa2index          Convert Sequence to AAIndex Values
aa2mass           Amino Acid Residues to Mass Converter
…<cut>…
write.fasta       Write FASTA Formated Sequences
write.ncdf        Write AMBER Binary netCDF files
write.pdb         Write PDB Format Coordinate File
write.pir         Write PIR Formated Sequences
write.pqr         Write PQR Format Coordinate File
```

Features = **functions()**

```
> help(read.pdb)
read.pdb                  package:bio3d                  R Documentation

Description:
     Read a Protein Data Bank (PDB) coordinate file.

Usage:
     read.pdb(file, multi = FALSE, rm.insert = FALSE,
              rm.alt = TRUE, verbose = TRUE)

Arguments:
     file: the name of the PDB file to be read.

   multi: logical, if TRUE multiple ATOM records are read
          for all models in multi-model files.
  ...<cut>...
```

Modularity	Core bio3d functions are modular and work well with others
Interactivity	R/bio3d offers and Unparalleled exploratory data analysis environment
Infrastructure	Access to existing tools and cutting-edge statistical and graphical methods
Support	Extensive documentation and tutorials available online for both bio3d and R
R Philosophy	Encourages open standards and reproducibility

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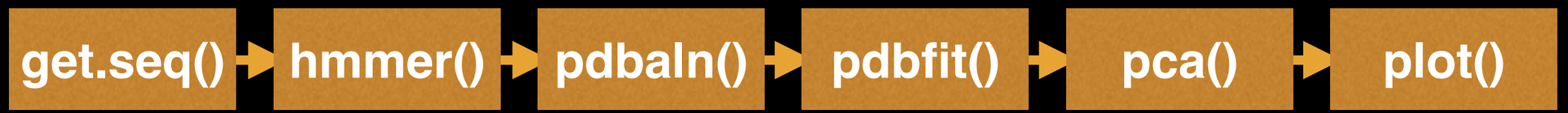
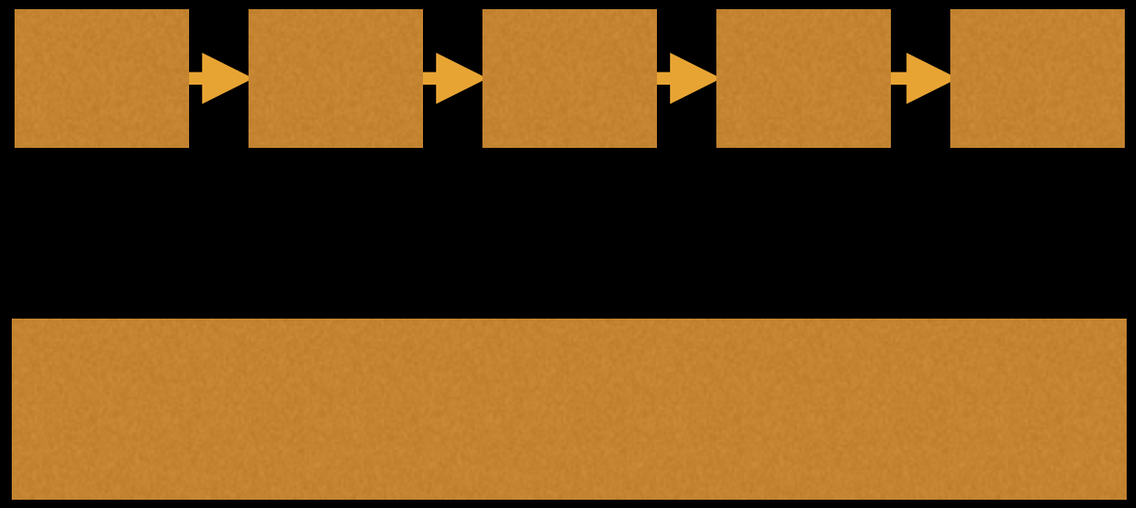
Modularity

Bio3D was designed to allow users to interactively build complex workflows by interfacing smaller '**modular' functions** together.



An alternative approach is to write a **single complex program** that takes raw data as input, and after hours of data processing, outputs publication figures and a final table of results.

Which would you prefer and why?



Modular

vs

Custom

Advantages/Disadvantages

The ‘monster approach’ is customized to a particular project but results in massive, fragile and difficult to modify (therefore inflexible, untransferable, and error prone) code.

With **modular workflows**, it’s easier to:

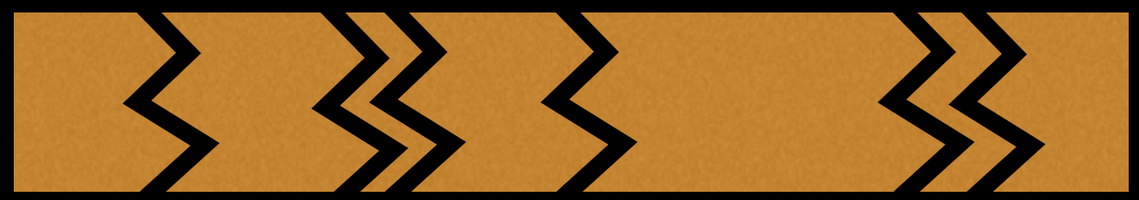
- Spot errors and figure out where they’re occurring by inspecting intermediate results.
- Experiment with alternative methods by swapping out components.
- Tackle novel problems by remixing existing modular tools.

‘Scripting’ approach

Another common approach to bioinformatics data analysis is to write individual scripts in Perl/ Python/Awk/C etc. to carry out each subsequent step of an analysis

1. 

2. 

3. 

This can offer many advantages but can be challenging to make robustly modular and interactive.

Interactivity & exploratory data analysis

Learning R/Bio3D will give you the freedom to explore and experiment with your biomolecular data.

"*Data analysis, like experimentation, must be considered as a highly interactive, iterative process, whose actual steps are selected segments of a stubbily branching, tree-like pattern of possible actions*". [**J. W. Tukey**]

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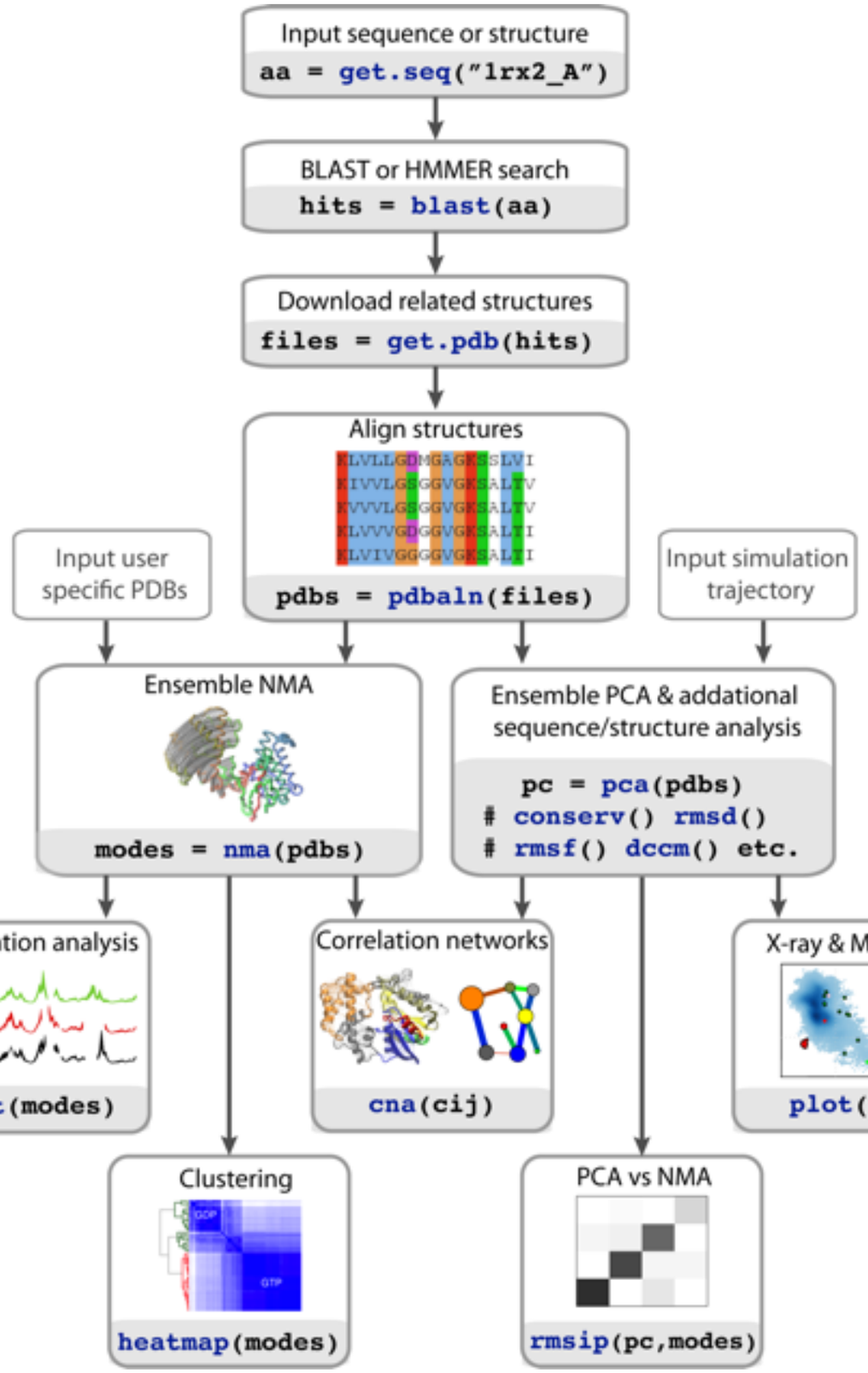
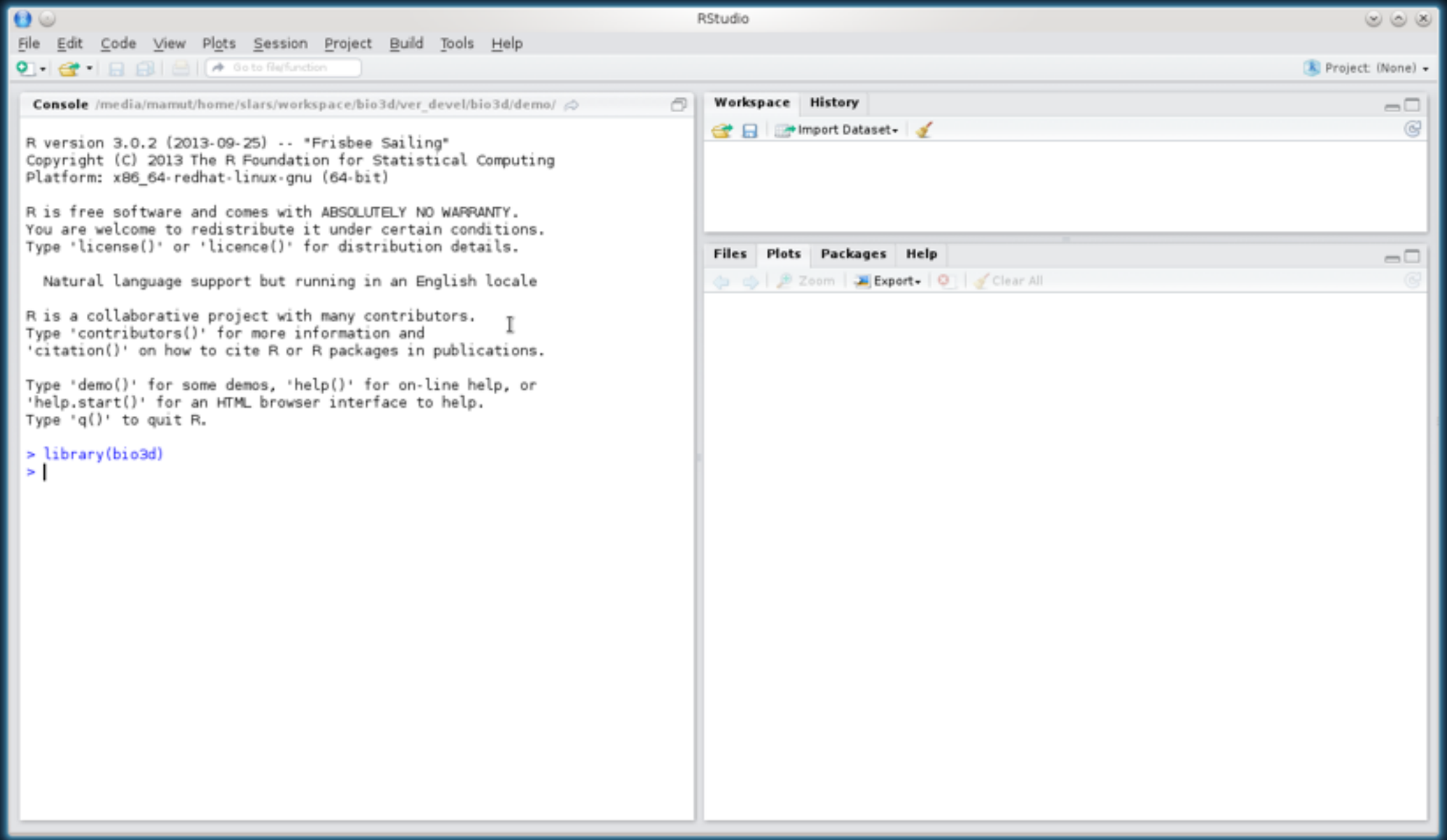
Structural bioinformatics data is intrinsically **high dimensional** and frequently 'messy' requiring **exploratory data analysis** to find patterns - both those that indicate interesting biological signals or suggest potential problems.


Input sequence or structure
aa = get.seq("1rx2_A")
BLAST or HMMER search
hits = blast(aa)
Download related structures
files = get.pdb(hits)
Align structures
pdbs = pdbaln(files)
Input user specific PDBs
Input simulation trajectory
Ensemble NMA
modes = nma(pdbs)
Ensemble PCA & addational sequence/structure analysis
pc = pca(pdbs)
# conserv() rmsd()
# rmsf() dccm() etc.
Fluctuation analysis
plot(modes)
Correlation networks
cna(cij)
X-ray & MD PCA
plot(pc)
Clustering
heatmap(modes)
PCA vs NMA
rmsip(pc,modes)

Lets get started...

Do it Yourself!



Do it Yourself!

Demo 1

https://github.com/bioboot/demo2-github

Furthering your R/Bio3D knowledge…

Bio3D's: **Tutorials and vignettes** http://thegrantlab.org/bio3d/

Hadley Wickham's: **Advanced R** http://adv-r.had.co.nz

Joseph Adler's: **R in a Nutshell** http://tinyurl.com/rbionutshell

StackOverflow, Coursera, R-Bloggers