Imogene

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This manual is for Imogene (version 1.0-258, 30 April 2013).

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1 Installation

1.1 Download

1.1.1 Stable version

The last stable version can be found on *github* at the address:

    https://github.com/hrouault/Imogene/tarballs.

1.1.2 Development version

This project's git repository can be checked out through the following clone instruction:

      `git clone http://github.com/hrouault/Imogene.git`

1.2 Requirements

C++ and make

- GNU Scientific Library
- Python (version >= 2.5 and < 3.0) :
- corebio :
- weblogo :
- python module argparse (for python version <2.7)

If you use a development version, you will need some additional tools:

- GNU Automake: http://www.gnu.org/software/autoconf
- GNU Autoconf: http://www.gnu.org/software/automake
- GNU Libtool: http://www.gnu.org/software/libtool
- GNU Gengetopt: http://www.gnu.org/software/gengetopt
- Cython: http://www.cython.org

Many standard Unix systems include packages for these tools.

In fact many files included in the distribution version have been generated automatically and are thus not included in the development version.

1.3 Installation

1.3.1 Quick procedure for distribution versions

These instructions apply to the distribution versions only. More detailed instructions can be found in the file `INSTALL` available in the tarball file imogene-version.tar.gz.

Start by unzipping the tarball:

      `tar xvzf imogene-version.tar.gz`
      `cd imogene-version`

Invoke then the usual commands to install a package:

```
mkdir build
cd build
../configure --prefix="install/full/path"
make
make install
```

Imogene provides description files for the *Mobyle* interface. You can install it by appending `--enable-mobyle` to the configure command:

```
../configure --prefix="install/full/path" --enable-mobyle
```

Imogene is now installed but cannot be used yet. You will need to download the genomic alignment files and background sequences (see next sections).

Finally, you can generate the documentation corresponding to your version by running `make dvi`, `make ps`, `make pdf` and `make html` depending on the format you want, and install them on you system by running `make install-dvi`, `make install-ps`, `make install-pdf` and `make install-html` respectively.

1.3.2 Development version

Note that if you use the development version from *github*, you have to first automatically generate files that are normally provided within the tarball:

```
git clone http://github.com/hrouault/Imogene.git
cd Imogene
./autogen.sh
```

The instructions are then identical to the distribution version:

```
mkdir build
cd build
../configure --prefix="install/full/path"
make
make install
```

1.4 Alignment files download

Imogene provides a helper script to download the necessary genomic alignment files. This script is present in `$PREFIX/bin/getalign`.

To download the genomes, you have to execute the proper python script: `$PREFIX/bin/getalign --species {droso,eutherian}` (see `$PREFIX/bin/getalign --help`).

1.5 Background sequences generation

In order to compare the statistics of the sequences taken into account for motif generation, some background sequences need to be selected. Two options are offered to you:

1. generate a new set of coordinates
2. use the set of coordinates provided in the data folder (easier and necessary to reproduce the examples provided).

1.5.1 Generate a new set of coordinates (optional)

This step generates coordinates for background sequences. Note that background coordinates are already provided by the package so that this step is optional.

You have to execute the command `python $PREFIX/bin/extract-bgrnd-coord > your-background-coords.bed`.

1.5.2 Download the alignements corresponding to the background coordinates

You have to execute the command `imogene extract -i coordinate_file -s species --background`. If you want for instance to download the alignment for the drosophila background with the coordinates provided with the package, you should type `imogene extract -i $PREFIX/share/imogene/background-droso-coords.dat -s droso --background`.

2 Extract an alignment from a coordinate file

This is the output of `imogene extract --help`:

```
Imogene 1.0-257

Alignment extraction.

Usage: imogene [OPTIONS]...

  -h, --help         Print help and exit
  -V, --version      Print version and exit
  -i, --input=str    Coordinate file
  -s, --species=str  Species selected  (possible values="droso",
                       "eutherian")
  -b, --background   When this flag is on, the alignments are moved to the
                       folder dedicated to background sequences
```

You mainly need to provide a coordinate file in the BED4 format:

```
chr2L 2345  3456 enhancer1
chr2R 4567  5678 enhancer2
```

The coordinates should use the release 5 (or dm3) system for *Drosophila Melanogaster* and the mm9 system for *Mus Musculus*. You can find example files in the folder `example` of the tarball. You can then try:

```
imogene extract --input example/enhancer-coords.dat
```

3 Distance between PWMs

3.1 Description of the distance

copy paste from the paper

3.2 Invoking the command line tool

This is the output of `imogene distinfo --help`:

```
Imogene 1.0-257

Distance between PWMs.

Usage: imogene [OPTIONS]... [<motifs>]...

  -h, --help               Print help and exit
  -V, --version            Print version and exit
  -w, --width=int          Width of the motifs  (default='10')
  -t, --threshold=double   Threshold used for motif scanning
  -s, --species=str        Species used for motifs generation.
  -m, --motifs=str         file containing a list of motif definitons
  -d, --displaydist        Display the distance in the standard output
```

You mainly need to provide two PWMs in the format produced with the genmot mode:

```
AATGGAAATT -47.211 299.182 14 12 0.00168 9.16e-05\
0.388,-0.302,-3.55,-3.66,-3.66,1.15,1.19,1.19,-0.528,-3.59,\
0.0655,-0.037,-3.55,-3.66,-3.66,-3.66,-3.66,-3.66,-1.15,-1.32,\
-3.49,-3.56,0.624,1.59,1.59,-1.53,-3.66,-3.66,-3.53,-1.32,\
0.119,0.659,0.714,-3.66,-3.66,-3.66,-3.66,-3.66,0.921,1.08,\
8485,1251,217,41,6,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
TTTGGTTTTG -45.567 6391.4 14 13 0.00182 0.000143\
-3.86,-3.82,-2.5,-0.505,-2.33,-3.87,-3.86,-1.68,-3.74,-3.72,\
-3.86,-3.82,-3.74,-3.63,-3.74,-2.32,-3.86,-2.14,0.965,1.1,\
-3.86,-2.15,1.02,1.36,1.54,-3.87,-3.86,-2.04,-3.74,-0.282,\
1.19,1.17,0.333,-2.18,-2.23,1.17,1.19,1.09,0.434,-0.215,\
7831,1633,415,91,21,5,3,1,0,0,0,0,0,0,0,0,0,0,0,0
```

You can find example files in the folder **examples/pwms** of the tarball. You can then try:

```
imogene distinfo --motifs=pwms.dat --species=droso --displaydist
```

4 Generating motifs de novo

4.1 Invoking the command line tool

This is the output of `imogene genmot --help`:

```
Imogene 1.0-257

Genome analysis for the inference of gene cis-regulatory modules.

Usage: imogene [OPTIONS]... [<motifs>]...

  -h, --help                    Print help and exit
  -V, --version                 Print version and exit
  -w, --width=int               Width of the motifs  (default='10')
  -t, --threshold=double        Threshold used for motif scanning
                                  (default='9')
  -x, --neighbext=int           Extent of the motif search within an alignment
                                  (default='20')
  -a, --align=str               Folder containing the fasta formatted (.fa)
                                  files of enhancer alignments.
  -b, --background=str          Folder containing the fasta formatted (.fa)
                                  files of background enhancers alignments. Per
                                  default, uses 10,000 intergenic sequences of
                                  2kb.
  -e, --evolutionary-model=int  Evolutionary model used for motif generation
                                  (1=felsen, 2=halpern)  (default='1')
  -s, --species=str             Species selected  (possible values="droso",
                                  "eutherian")
      --progress                Show progression while running
      --method=str              Method used for PWM optimization  (possible
                                  values="max", "mean", "inde"
                                  default='max')
```

5 Scan the genome for the predicted motifs

5.1 Invoking the command line tool

This is the output of `imogene scangen --help`:

```
Imogene 1.0-257

Genome-wide prediction of cis-regulatory modules.

Usage: imogene [OPTIONS]... [<motifs>]...

  -h, --help                 Print help and exit
      --detailed-help        Print help, including all details and hidden
                               options, and exit
  -V, --version              Print version and exit
  -t, --threshold=double     Threshold used for motif scanning  (default='9')
  -x, --neighbext=int        Extent of the motif search within an alignment
                               (default='20')
  -m, --motifs=str           file containing a list of motif definitons
  -n, --nbmots=int           Number of motifs to consider at maximum
                               (default='5')
  -s, --species=str          Species selected  (possible values="droso",
                               "eutherian")
      --scanwidth=int        Width of selected enhancers  (default='1000')
      --wocons               Do NOT use conservation

 Group: discarding
  The way enhancers are grouped for the definitive sorting
      --discard-on-gene-names
      --discard-on-position
  -p, --phenotype=str        file containing a list of genes annotated with a
                               relevant phenotype (used for histograms
                               construction)
      --print-histo-sets     Print histograms for different gene sets
      --score=str            Computes score on a set of sequences (for a
                               given number of motifs)
      --progress             Show progression while running
```

6 Displays motifs on sequences

6.1 Invoking the command line tool

This is the output of `imogene display --help`:

```
Imogene 1.0-257

Display the different output of imogene

Usage: imogene [OPTIONS]...

  -h, --help              Print help and exit
  -V, --version           Print version and exit

Display the output of imogene genmot:

 Mode: genmot
  -m, --motifs=str        file containing a list of motif definitions
  -t, --threshold=double  Threshold used for motif scanning  (default='12')
  -s, --species=str       Species used for motifs generation.
  -n, --nbmots=int        Number of motifs to display (max=10)  (default='5')
  -a, --align=str         Folder containing the fasta formatted (.fa) files of
                            enhancer alignments.
      --tex-ref           Output is tex formatted. Display only reference
                            species sequence.
      --html-ref          Output is html formatted. Display only reference
                            species sequence.
      --tex-align         Output is tex formatted. Display the entire
                            alignment.
      --svg               Training set multiple alignment with instances, svg
                            formatted.
      --jaspar            Motif matrix for searching the jaspar database
      --logos             Motif logos.
      --pdf               Motif logo in pdf format.
      --png               Motif logo in png format (default)
      --score             Display motifs poissonian scores on aligned sequences
                            in a txt file.

    Display the output of imogene scangen:

 Mode: scangen
   -e, --enhancers=str     file containing a list of enhancer definitions
```

You need to provide a motif file as generated by the genmot mode, and the path to the folder containing the fasta (.fa) formatted alignments you wish to scan. These alignments can be automatically generated from a coordinate file using the extract mode. Depending on the chosen mode, the output will be the tex formatted sequences (`tex-ref` and `tex-align`), or a svg formatted graphical representation of motifs instances on the sequences (`svg`). You can find example files in the folder `example` of the tarball. You can then try:

```
imogene display -s eutherian -m motifs.txt -a align --tex-ref
imogene display -s eutherian -m motifs.txt -a align --tex-align
imogene display -s eutherian -m motifs.txt -a align --svg
```

6.2 Generating motif logo

This mode uses the `python` modules corebio and weblogo. You can install them with:

```
> pip install corebio
> pip install weblogo
```

You can obtain the logos by running:

```
imogene display -s eutherian -m motifs.txt -a align --logos
```

(the folder align do not need to exist in that case).

7 Running test files

7.1 Extraction

For drosophila, there is a file `examples/extract/coords-droso.dat` that can be used as an input for `imogene extract`:

```
imogene extract -s droso --input examples/extract/coords-droso.dat
```

It creates a folder `align` containing the extracted fasta formatted alignments.

7.2 Running genmot on the extracted sequences

You now have to run genmot on the extracted alignments

```
imogene genmot -s droso -a align
```

8 Mobyle interface

You can run imogene from the Mobyle interface:

* Execution mode **?**   [genmot: Generate motifs from a training set   ⬍]

General options

* Family of species to consider **?**   [Eutherians   ⬍]

* Width of the motifs **?**   [10   ]

* Allowed shift of a binding site position in orthologous species **?**

[20   ]

Genmot options

* Evolutionary model used for motif generation **?**   [Felsenstein model   ⬍]

* Threshold used for motif generation **?**   [11.0   ]

* Threshold used to scan training set sequences for display **?**   [8.0   ]

* Training set sequences coordinates **?**

| **paste** | **upload** | EDIT   CLEAR

Enter your data below:

```
chr8   91462919 91464123 CYLD-SALL1
chr4   99040833 99042291 APG4C-FOXD3
chr14 118834760    118836087    SOX21-ABCC4
chr18 69658816 69660452 TCF4(intragenic)
chr6   138199417    138201368    MGST1-LMO3
chr12 51291542 51292872 FOXG1B-PRKD1
```

Scangen options

* Threshold used to scan the genome **?**   [8.0   ]

* Width of selected enhancers **?**   [1000   ]

* Number of motifs to consider at maximum **?**   [5   ]

* File containing a list of motif definitions **?**

| **paste** | **upload** | EDIT   CLEAR

Enter your data below:

[   ]

The interface can be installed locally on your computer but more simply, we made it available for the community at: `http://mobyle.pasteur.fr/cgi-bin/portal.py\#forms::imogene`.

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Version 1.3, 3 November 2008

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