Nucleo-Miner

User Guide
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The Texinfo source for this manual may be obtained from `[MINER-URL]`

1 Introduction

The **Nucleo-Miner** package is a collection of programs for carrying out high-resolution mapping of nucleosomes using tiling arrays. The programs have been written from scratch in C, and are based on the Application Progam Interface (API) of the GDL library. The source code is distributed under the GNU General Public License.

1.1 Programs available in Nucleo-Miner Package

The **Nucleo-Miner** package has been designed to integrate a large variety of information required to finely map and characterize nucleosome occupancy and modifications at a genome-wide scale. To do so, **Nucleo-Miner** package contains a series of programs in order to efficiently store the data, to perform the analyses and to import/export data/results in various formats. Follows a list of the different command line programs included in the **Nucleo-Miner** package.

- **NMmpa** - Format Mummer output for tiling probes mapped on genome sequence.
- **NMcl2tab** - Extract and merge tiling array data
- **NMmprb** - Extract only the probes that share the same genomic and array coordinates between a reference and a query
- **NMtdb** - Create a tilling array database
- **NMt2feat** - Integrate tilling array values within custom annotations
- **NMt2featcis** - Look at the tilling array profile around custom annotations
- **NMhmmfit** - Fit a HMM to indentify nucleosomes
- **NMhmmvit** - Apply the Viterbi algorithm to call nucleosomes
- **NMalign** - Align nucleosome occupancy profiles between two genomes
- **NManova** - Fit an ANOVA nucleosome by nucleosome to detect SNEP
- **NManout** - Output results obtained with **NManova**
- **NManowin** - Summarizes results obtained with **NManova** using bin or sliding windows along the genome
- **NManofoc** - Summarizes results obtained with **NManova** by computing overlap score with custom annotations
- **NMt2feat2** - Fast integration of tilling array values within custom annotations
- **NMalign2** - Fast align nucleosome occupancy profiles between two genomes
- **NManova2** - Fast fit an ANOVA nucleosome by nucleosome to detect SNEP
- **NManout2** - Output results obtained with **NManova2**
- **NManofoc2** - Summarizes results obtained with **NManova2** by computing overlap score with custom annotations
- **NManowin2** - Summarizes results obtained with **NManova2** using bin or sliding windows along the genome

The use of these programs is described in this manual. Each chapter provides detailed definitions of the programs, followed by example.

1.2 The Nucleo-Miner Package is Free Software

The programs in the Nucleo-Miner package are "free software"; this means that everyone is free to use them, and to redistribute them in other free programs. The package is not in the public domain; it is copyrighted and there are conditions on its distribution. These conditions are designed to permit everything that a good cooperating citizen would want to do. What is not allowed is to try to prevent others from further sharing any version of the software that they might get from you.

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The precise conditions for the distribution of software related to the Nucleo-Miner are found in the GNU General Public License (see [GNU General Public License], page 16). Further information about this license is available from the GNU Project webpage *Frequently Asked Questions about the GNU GPL*,

`http://www.gnu.org/copyleft/gpl-faq.html`

The Free Software Foundation also operates a license consulting service for commercial users.

1.3 Obtaining the Nucleo-Miner Package

The source code for the package can be obtained in different ways, by copying it from a friend or downloading it from the internet.

`http://www.ens-lyon.fr/LBMC/gisv/snep/`

The preferred platform for the library and programs is a GNU system, which allows it to take advantage of additional features in the GNU C compiler and GNU C library. However, the library and the tools are fully portable and should compile on most systems. Precompiled versions of the library, tools and support contracts can be purchased from commercial redistributors listed on the website above.

1.4 No Warranty

The software described in this manual has no warranty, it is provided "as is". It is your responsibility to validate the behavior of the routines and their accuracy using the source code provided. Consult the GNU General Public license for further details (see [GNU General Public License], page 16).

1.5 Reporting Bugs

A list of known bugs can be found in the 'BUGS' file included in the Nucleo-Miner package distribution. Details of compilation problems can be found in the 'INSTALL' file.

If you find a bug which is not listed in these files, please report it to gael.yvert@ens-lyon.fr.

All bug reports should include:

- The version number of Nucleo-Miner package and the GDL library
- The hardware and operating system
- The compiler used, including version number and compilation options
- A description of the bug behavior
- A short program which exercises the bug

It is also useful if you can report whether the same problem occurs when the library is compiled without optimization. Thank you.

1.6 Further Information

Additional information, including online copies of this manual, links to related projects, and mailing list archives are available from the website mentioned above.

1.7 Conventions used in this manual

This manual contains many examples which can be typed at the keyboard. A command entered at the terminal is shown like this,

```
$ command
```

The first character on the line is the terminal prompt, and should not be typed. The dollar sign '$' is used as the standard prompt in this manual, although some systems may use a different character.

The examples assume the use of the GNU operating system. There may be minor differences in the output on other systems. The commands for setting environment variables use the Bourne shell syntax of the standard GNU shell (bash).

2 Programs

This chapter describes all the programs available in Nucleo-Miner

2.1 NMmpa - Program Arguments

This program formats the output of the mapping of the tilling array probes onto the genome sequences.

Short	Long	Description
	–rotate	Rotate the x,y coordinates of the array
-i	–input	The input file corresponding to the Mummer output
-o	–output	The output directory
-a	–array-size	The number of probe slots on the array (row/column)
-c	–chrom-file	A file which lists the chromosome sequence ids to focus on

2.2 NMmpa - Examples

```
$NMmpa -i mummer.out -o probe_annotation
```

2.3 NMcl2tab - Program Arguments

This program extract probe intensities from a batch of arrays and merge it into a single tabulated file. The program can also perform normalization of the arrays

Short	Long	Description
	–no-rotate	No rotation of the x,y coordinates of the array
	–CbyC	Export data chromosome by chromosome in the -o directory
-c	–cel	A file listing the name of the CEL files (in text format) to consider
-d	–cel-dir	The path to the directory containing the CEL files
-o	–output	The output file or directory
-p	–prb	The file which gives the genomic and x,y coordinates of the probes
-n	–qqnorm	Quantile-Quantile normalization. 'qq' = qqnorm, 'lqq' = log2 transformation followed by qqnorm, 'qql' = qqnorm followed by log2 transformation

2.4 NMcl2tab - Examples

```
$NMcl2tab
```

2.5 NMmprb - Program Arguments

The program selects only the probes that share the same genomic and array coordinates between a reference and a query genome.

Short	Long	Description
-r	–ref	The reference probes
-q	–qry	The query probes
-o	–output	The output file
-c	–ref2qry	The reference-query genomic alignment
-w	–window	The window around the reference probe position for accepting a query match

2.6 NMmprb - Examples

```
$NMmprb
```

2.7 NMtdb - Program Arguments

This program extract probe intensities from a batch of arrays and merge it into a single tabulated file. The program can also perform normalization of the arrays

Short	Long	Description
	–print	Print the dataset from the .db file (-i)
	–substract	Substract signal between two groups (2) - (1)
-i	–input	Input file: either the raw data file or the db file (–print)
-c	–config	Configuration file to create the db file from the raw data file
-o	–output	The output .db file
-t	–force-tiling	Force the tiling step to be a multiple of the given value
-l	–log-transform	Log-transform the intensities in the given base (default is no log transformation)

2.8 NMtdb - Examples

```
$NMtdb
```

2.9 NMt2feat - Program Arguments

Short	Long	Description
	–start	Look at the 5'end of the feature
	–end	Look at the 3'end of the feature
	–upstream	Look only at the upstream region of the feature boundary
	–matrix	Output the matrix of profiles
-i	–input	The input tiling dataset file (NMtdb)

-o	–output	The stem name of the output file(s)
-f	–feature	The feature file in gff format (version 3)
-l	–feature-id	The file listing the feature types to focus on and/or directly the name of a feature type
-w	–window	The window size (in bp) around the each feature boundary
-n	–nclass	The number of bins into which the upstream/downstream region will be split
-c	–non-zero-col	Remove features for which the corresponding column in the dataset indicates no signal (see –zero-value)
-z	–zero-value	The minimal value to consider the intensity as an actual signal to take into account

2.10 NMt2feat - Examples

```
$NMt2feat
```

2.11 NMt2feat2 - Program Arguments

Short	Long	Description
	–start	Look at the 5'end of the feature
	–end	Look at the 3'end of the feature
	–upstream	Look only at the upstream region of the feature boundary
-i	–input	The input tiling dataset file (NMtdb)
-o	–output	The stem name of the output file(s)
-f	–feature	The feature file in gff format (version 3)
-l	–feature-id	The file listing the feature types to focus on and/or directly the name of a feature type
-w	–window	The window size (in bp) around the each feature boundary
-c	–non-zero-col	Remove features for which the corresponding column in the dataset indicates no signal (see –zero-value)
-z	–zero-value	The minimal value to consider the intensity as an actual signal to take into account

2.12 NMt2feat2 - Examples

```
$NMt2feat2
```

2.13 NMt2featcis - Program Arguments

Short	Long	Description
	–no-overlap	Ignore overlapping cis-regions
	–square	Output also the (signal) sum of square
-i	–input	The input tiling dataset file (NMtdb)
-o	–output	The stem name of the output file(s)

-f	–feature	The feature file in gff format (version 3)
-l	–feature-id	The file listing the feature types to focus on and/or directly the name of a feature type
-u	–up-window	The window size (in bp) of the upstream region
-d	–down-window	The window size (in bp) of the downstream region
-p	–up-nclass	The number of bins into the upstream region will be split
-w	–down-nclass	The number of bins into the downstream region will be split
-s	–inside	The number of bins used to split the feature region
-j	–col-from	The first column (from 0) from which threshold has to be computed
-k	–col-to	The last column (from 0) from which threshold has to be computed

2.14 NMt2featcis - Examples

```
$NMt2featcis
```

2.15 NMhmmfit - Program Arguments

This program fits a Hidden Markov Model (HMM) to identify nucleosome along the genome based on the intensities of the tiling array.

Short	Long	Description
	–full	Fit the HMM on the entire chromosome, without sliding window
-i	–input	The input db file representing the tiling array dataset(s) (see NMtdb)
-o	–output	The output directory
-x	–nmax	The maximum number of probes for a well-localized nucleosome
-n	–nmin	The minimum number of probes for a well-localized nucleosome
-w	–window	The size of the sliding window (number of equally spaced probes)
-t	–tiling	The size of the tiling step (default is 4bp)
-m	–iter-max	The maximum number of iterations for the EM
-e	–epsilon	The convergence threshold for the EM
-s	–wobs	The minimal fraction of observed probes within a sliding window
-c	–chrom	The name of the chromosome to focus on

2.16 NMhmmfit - Examples

```
$NMhmmfit
```

2.17 NMhmmvit - Program Arguments

This program performs the Viterbi algorithm on the results of **NMhmmfit** to call the nucleosomes.

Short	Long	Description
	–rm-outlier	Remove probes with obvious spurious estimates
	–print	Print in text format the output of NMhmmfit
-i	–input	The input db file representing the tiling array dataset(s) (see NMtdb)
-r	–result	The directory containing the files generated by NMhmmfit
-o	–output	The output directory
-x	–nmax	The maximum number of probes for a well-localized nucleosome
-n	–nmin	The minimum number of probes for a well-localized nucleosome
-t	–tiling	The size of the tiling step (default is 4bp)
-l	–chunk-min	The minimal size of probe chunks to be included
-m	–remove-min	
-c	–chrom	The name of the chromosome to focus on

2.18 NMhmmvit - Examples

```
$NMhmmvit
```

2.19 NMalign - Program Arguments

This program aligns the nucleosome occupancy profiles from a query genome onto a reference genome.

Short	Long	Description
	–print	Print in text format the alignments
-i	–input	The input directory containing alignment files (with –print)
-c	–config	The input configuration file
-o	–output	The output directory
-s	–chrom	The name of the chromosome to focus on
-t	–tiling	The size of the tiling step (default is 4bp)
-m	–nucmin	The minimal number of probes covering a nucleosome
-k	–prb-mapped	The minimal fraction of nucleosomal probes that can be mapped on both the ref and the qry (default is 1.0), otherwise nucleosome is discarded
-l	–prb-overlap	The minimal overlap between the reference and query nucleosomes to be considered as aligned (default is 0.85)

2.20 NMalign - Examples

```
$NMalign
```

2.21 NMalign2 - Program Arguments

This program aligns the nucleosome occupancy profiles from a query genome onto a reference genome. It is much more faster than **NMalign**.

Short	Long	Description
	–print	Print in text format the alignments
-i	–input	The input directory containing alignment files (with –print)
-c	–config	The input configuration file
-o	–output	The output directory
-s	–chrom	The name of the chromosome to focus on
-t	–tiling	The size of the tiling step (default is 4bp)
-m	–nucmin	The minimal number of probes covering a nucleosome
-v	–ovrmin	The minimal number of probes covering a nucleosome
-g	–coverage	The coverage fraction w.r.t to the average size of the nucleosome

2.22 NMalign2 - Examples

```
$NMalign2
```

2.23 NManova - Program Arguments

This program carries out an ANOVA nucleosome by nucleosome and report the p-values of the interaction term.

Short	Long	Description
	–filter	Filter the nucleosome alignment by removing regions with unexpected alignments
	–update	Update the binary files generated by NMalign
	–extract	Just extract the data used to perform the ANOVA
	–no-probe-effect	Do not include a probe effect into the model
-i	–input	The input directory containing alignment files
-c	–config	The input configuration fileT
-o	–output	The output directory
-d	–seqid	The name of the chromosome to focus on
-j	–prb-coverage	The minimal fraction of observed probes spanning the nucleosome (default is 0.5)
-k	–prb-anova	The minimal number of probes within the aligned nucleosome (default is 10)
-p	–permut	The number of permutations to do to compute the empirical p-value by permutations (default is 0)

-s	–start	The starting position on the chromosome (use with –extract)
-e	–end	The ending position on the chromosome (use with –extract)

2.24 NManova - Examples

```
$NManova
```

2.25 NManova2 - Program Arguments

This program carries out an ANOVA nucleosome by nucleosome and report the p-values of the interaction term. **NMalign2** must have been run before. It is much more faster than **NManova**.

Short	Long	Description
-i	–input	The input directory containing alignment files
-a	–align	The alignment directory (as generated by NMalign2)
-o	–output	The output directory
-p	–prb-min	The minimum number of probes within a nucleosome

2.26 NManova2 - Examples

```
$NManova2
```

2.27 NManout - Program Arguments

This program outputs the SNEPs together with additional information from results obtained by **NManova**.

Short	Long	Description
	–main-feature-only	When –feature is used, output only parent features
	–summary	Output a single file with only the aligned nucleosomes and their statistics
-i	–input	The input directory
-c	–config	The input configuration fileT
-o	–output	The output directory
-s	–seqid	The name of the chromosome to focus on
-f	–feature	A GFF (version 3) file providing the genomic annotations
-w	–window	The window (bp) around SNEP to look at
-p	–pv-cutoff	The p-value cut-off for calling SNEP
-m	–prob-min	The probability threshold above which aligned nuleosomes will be considered
-b	–neighbour	The number of nucleosomes to look at around each SNEP

2.28 NManout - Examples

```
$NManout
```

2.29 NManout2 - Program Arguments

This program outputs the SNEPs together with additional information from results obtained by **NManova2**.

Short	Long	Description
	–main-feature-only	When –feature is used, output only parent features
	–summary	Output a single file with only the aligned nucleosomes and their statistics
-i	–input	The input directory
-o	–output	The output directory
-s	–seqid	The name of the chromosome to focus on
-f	–feature	A GFF (version 3) file providing the genomic annotations
-w	–window	The window (bp) around SNEP to look at
-p	–pv-cutoff	The p-value cut-off for calling SNEP
-m	–prob-min	The probability threshold above which aligned nuleosomes will be considered
-b	–neighbour	The number of nucleosomes to look at around each SNEP

2.30 NManout2 - Examples

```
$NManout2
```

2.31 NManowin - Program Arguments

This program

Short	Long	Description
	–sliding	Use a sliding window instead of contiguous bins
-i	–input	The input directory
-c	–config	The input configuration file
-o	–output	The output file
-s	–seqid	The name of the chromosome to focus on
-f	–feature	A GFF (version 3) file providing the genomic annotations
-w	–window	The window (bp) around SNEP to look at
-p	–pv-cutoff	The p-value cut-off for calling SNEP
-l	–feature-id	A file listing the features to consider

2.32 NManowin - Examples

```
$NManowin
```

2.33 NManowin2 - Program Arguments

This program

Short	Long	Description
	–sliding	Use a sliding window instead of contiguous bins
-i	–input	The input directory
-d	–data	The data file
-o	–output	The output file
-s	–seqid	The name of the chromosome to focus on
-f	–feature	A GFF (version 3) file providing the genomic annotations
-w	–window	The window (bp) around SNEP to look at
-p	–pv-cutoff	The p-value cut-off for calling SNEP
-l	–feature-id	A file listing the features to consider

2.34 NManowin2 - Examples

```
$NManowin2
```

2.35 NManofoc - Program Arguments

This program reports the fraction of genomic annotation that overlap with each nucleosome interrogated with NManova.

Short	Long	Description
-i	–input	The input directory
-c	–config	The input configuration file
-o	–output	The output file
-s	–seqid	The name of the chromosome to focus on
-f	–feature	A GFF (version 3) file providing the genomic annotations
-l	–feature-id	A file listing the features to consider

2.36 NManofoc - Examples

```
$NManofoc
```

2.37 NManofoc2 - Program Arguments

This program reports the fraction of genomic annotation that overlap with each nucleosome interrogated with **NManova2**.

Short	Long	Description
-i	–input	The input directory
-d	–data	The data
-o	–output	The output file
-s	–seqid	The name of the chromosome to focus on

-f	–feature	A GFF (version 3) file providing the genomic annotations
-l	–feature-id	A file listing the features to consider

2.38 NManofoc2 - Examples

```
$NManofoc2
```

Free Software Needs Free Documentation

The following article was written by Richard Stallman, founder of the GNU Project.

The biggest deficiency in the free software community today is not in the software—it is the lack of good free documentation that we can include with the free software. Many of our most important programs do not come with free reference manuals and free introductory texts. Documentation is an essential part of any software package; when an important free software package does not come with a free manual and a free tutorial, that is a major gap. We have many such gaps today.

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