

## NAME

**miranda** - Finds potential target sites for miRNAs in genomic sequence

## SYNOPSIS

Basic Usage:

**miranda** *file1 file2* [ *options ...* ]

Advanced:

**miranda** *file1 file2* [-sc *score*] [-en *energy*]  
[-scale *scale*] [-loose] [-go *X*] [-ge *Y*] [-out *fileout*]  
[-quiet] [-trim *T*] [-noenergy] [-shuffle] [-s *nshuff*]  
[-w *W*] [-uniform] [-z *zscore*]

## DESCRIPTION

**miRanda** is an algorithm for the detection of potential microRNA target sites in genomic sequences. **miRanda** reads RNA sequences (such as microRNAs) from **file1** and genomic DNA/RNA sequences from **file2**. Both of these files should be in FASTA format. This is an example of a FASTA formatted sequence:

```
>embl|AJ550546|DME550546 Drosophila melanogaster microRNA  
miR-bantam  
GTGAGAUCAUUUUGAAAGCUG
```

One or more miRNA sequences from **file1** are scanned against all sequences in **file2** and potential target sites are reported. Potential target sites are identified using a two-step strategy. First a dynamic programming local alignment is carried out between the query miRNA sequence and the reference sequence. This alignment procedure scores based on sequence complementarity and not on sequence identity. In other words we look for A:U and G:C

matches instead of A:A, G:G, etc. The G:U wobble pair is also permitted, but generally scores less than the more optimal matches. Here is an example alignment:

```
Query: 3' GTCGAAAGTTTTACTAGAGTG 5' (eg. miRNA)
      :||:||||| |||||
Ref:   5' TAGTTTTCAATGATCTCGG 3' (eg. 3'UTR)
```

The second phase of the algorithm takes high-scoring alignments (Those above a score threshold, defined by **-sc**) detected from phase 1 and estimates the thermodynamic stability of RNA duplexes based on these alignments. This second phase of the method utilizes folding routines from the **RNALib** library, which is part of the **ViennaRNA** package written by Ivo Hofacker. At this stage we generate a constrained fictional single-stranded RNA composed of the query sequence, a linker and the reference sequence (reversed). This structure then folded using **RNALib** and optionally some rudimentary **statistics** about each target site can be generated by performing a number of alignments using shuffled reference sequences (see **-shuffled** option). A distribution is built from these data and statistical parameters from this distribution are used to produce a Z-Score for a detected target site.

## OPTIONS

- help -h**  
Displays help, usage information and command-line options.
- version -v --license**  
Display version and license information.
- sc score**  
Set the score threshold to **score**. Only alignments with scores  $\geq$  **score** will be used for further analysis.
- en energy**  
Set the energy threshold to **energy**. Only alignments with energies  $\leq$  **energy** will be used for further analysis. This value should be negative.
- scale scale**  
Set the scaling parameter to **scale**. This scaling is applied to match / mismatch scores in the critical 10bp region of the 5' end of the microRNA. Many known examples of miRNA:Target duplexes are highly complementary in this region. This parameter can be thought of as a contrast function to more effectively detect alignments of this type.

- loose** Remove strict alignment heuristics. In normal mode heuristics are applied to predicted duplexes that count the number of complementary base-pairs in different regions of the alignment according to observations of known miRNA:target duplexes. Alignments that fail this test are not displayed. Turning this option off is less conservative but may result in more false-positive detections.
- go X** Set the gap-opening penalty to **X** for alignments. This value should be negative.
- ge Y** Set the gap-extend penalty to **Y** for alignments. This value should be negative.
- out** *fileout*  
Print results to an output file called **fileout**.
- quiet** Quiet mode, produces the minimum of output.
- trim T**  
Trim reference sequences to **T** nucleotides. Useful when using noisy predicted 3'UTRs as reference
- shuffle**  
For each analysis between a microRNA and a reference sequence, also do **nshuff** alignments between the microRNA and shuffled reference sequences. This is used to build a distribution of shuffled alignment scores that can be used to estimate the reliability of a given score. This analysis produces a **Z-Score** for each predicted target. It is possible to filter results using this score with the **-z** option. Shuffling statistics are optional and are not turned on by default. It should also be noted that this dramatically increase the number of alignments processed, and will slow the algorithm down considerably.
- s** *nshuff*  
Set the total number of random shuffle analyses to **nshuff**. Larger numbers of analyses produces a more reliable **Z-score**.
- w W** For window-based shuffling the window size can be changed by modifying the **W** parameter. Window based shuffling maintains nucleotide composition across the sequence, shuffling takes place in a small window that moves across the sequence.
- uniform**  
Disables windowed shuffling, and shuffles uniformly across the reference sequence.
- z zscore**  
Sets a **Z-Score** threshold for all targets based on sequence shuffling statistics. Only detected targets with **Z-Scores**  $\geq$  **zscore** will be displayed by

the algorithm.

## REFERENCES

If you use this program for your research then please include the following citation:

A.J. Enright, B. John, U. Gaul, T. Tuschl, C. Sander, D.S. Marks; (2003)  
MicroRNA targets in Drosophila; Genome Biology **5(1)**:R1.

RNAlib Citations:

I.L. Hofacker, W. Fontana, P.F. Stadler, S. Bonhoeffer, M. Tacker, P. Schuster (1994) Fast Folding and Comparison of RNA Secondary Structures. Monatshefte f. Chemie 125: 167-188

M. Zuker, P. Stiegler (1981) Optimal computer folding of large RNA sequences using thermodynamic and auxiliary information, Nucl Acid Res 9: 133-148

J.S. McCaskill (1990) The equilibrium partition function and base pair binding probabilities for RNA secondary

## BUGS

Comments and bug-reports should be sent to miranda@cbio.mskcc.org.

Anton Enright

1.0

miranda(1)

---

*Man(1) output converted with [man2html](#)*