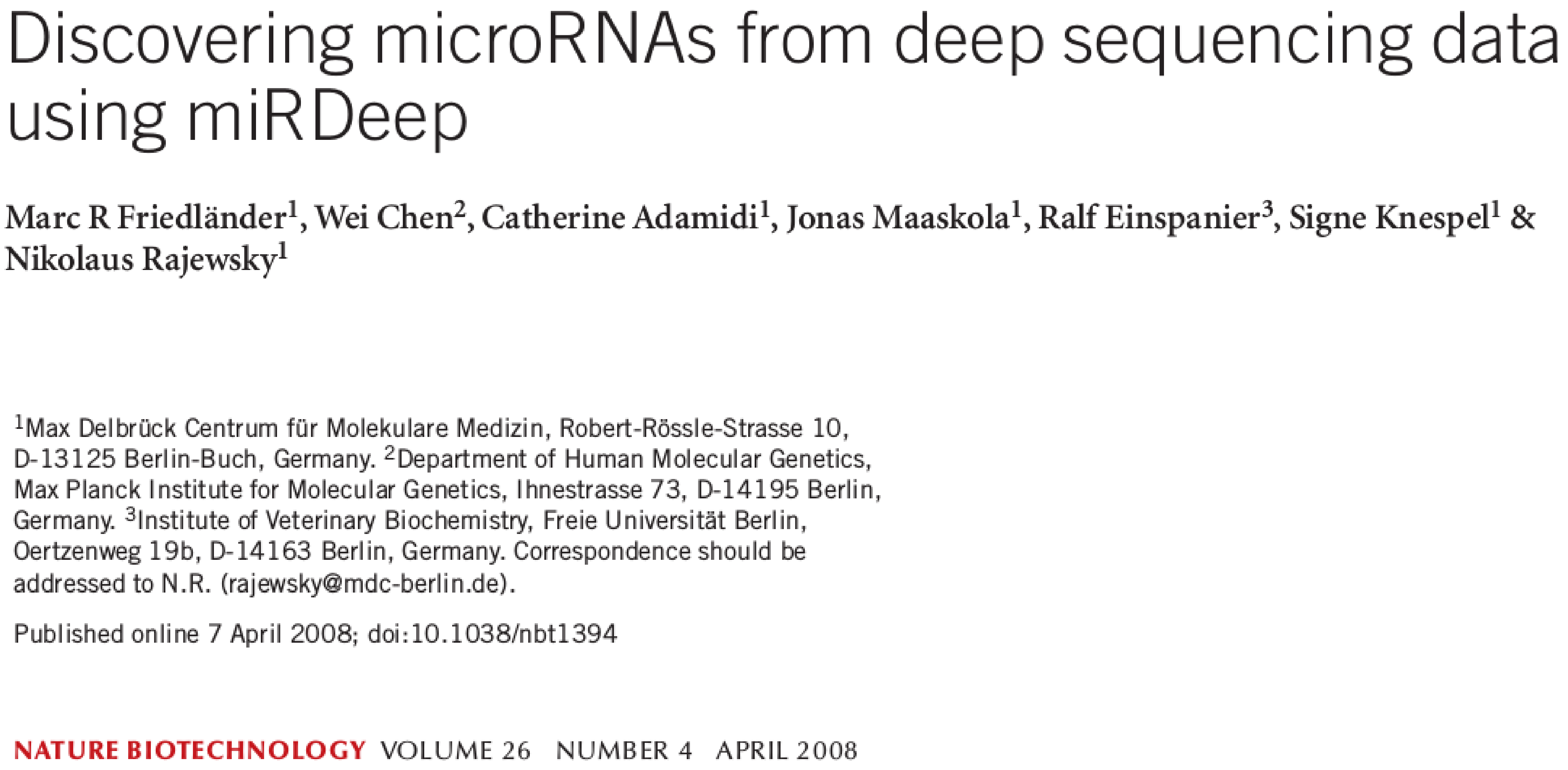

Discovering microRNAs from deep sequencing data using miRDeep

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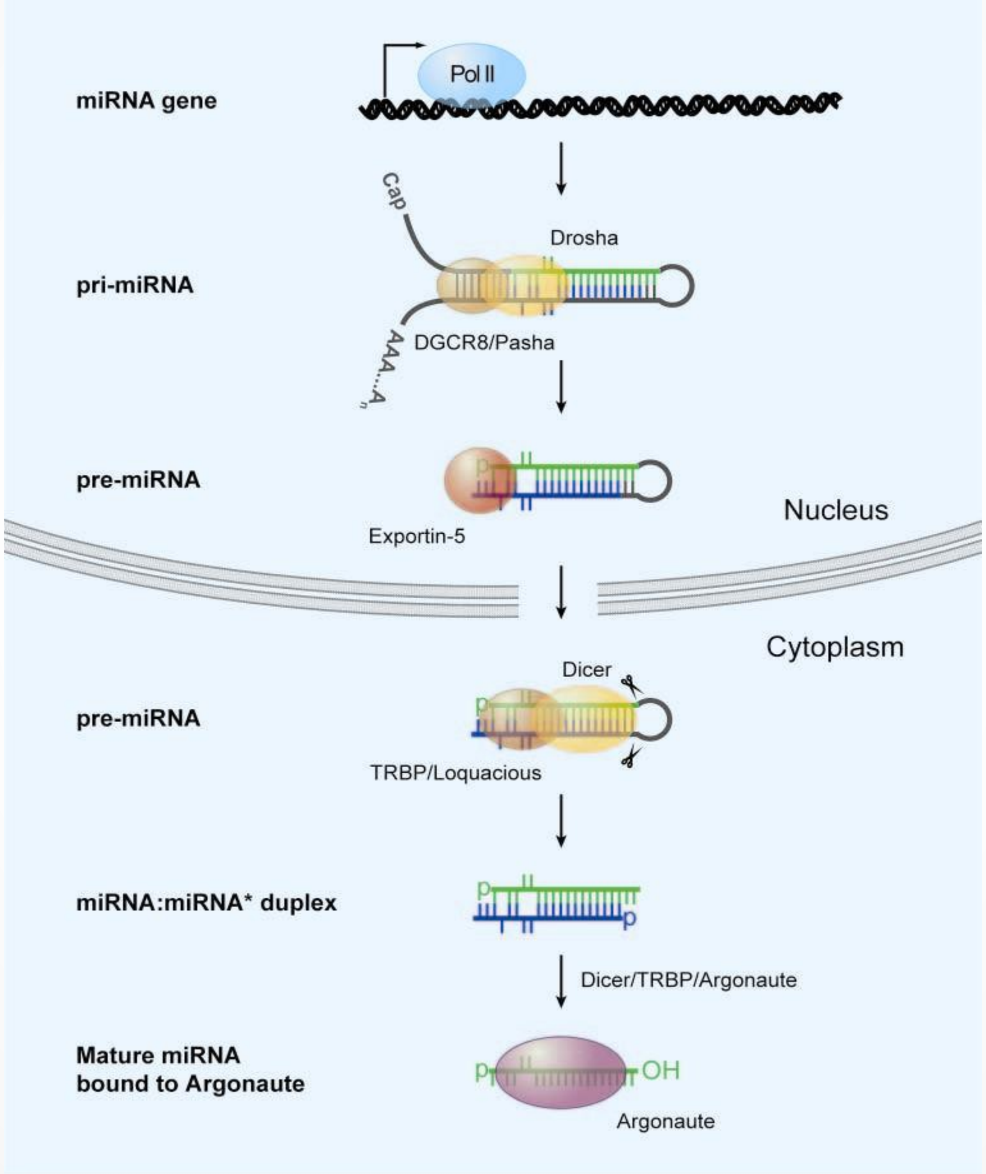
miRNA

- small non coding RNA (18-24 bp)
- post transcriptional regulation
  - inhibition
  - destabilization
  - cleave

- miRBase (Release 21: June 2014)
  - 28645 hairpin precursor
    - 35828 miRNA in 223 species
    - 2813 miRNA in hg38

miRNA biogenesis



Bushati N, Cohen SM. 2007.
Annu. Rev. Cell Dev. Biol. 23:175–205

Problems

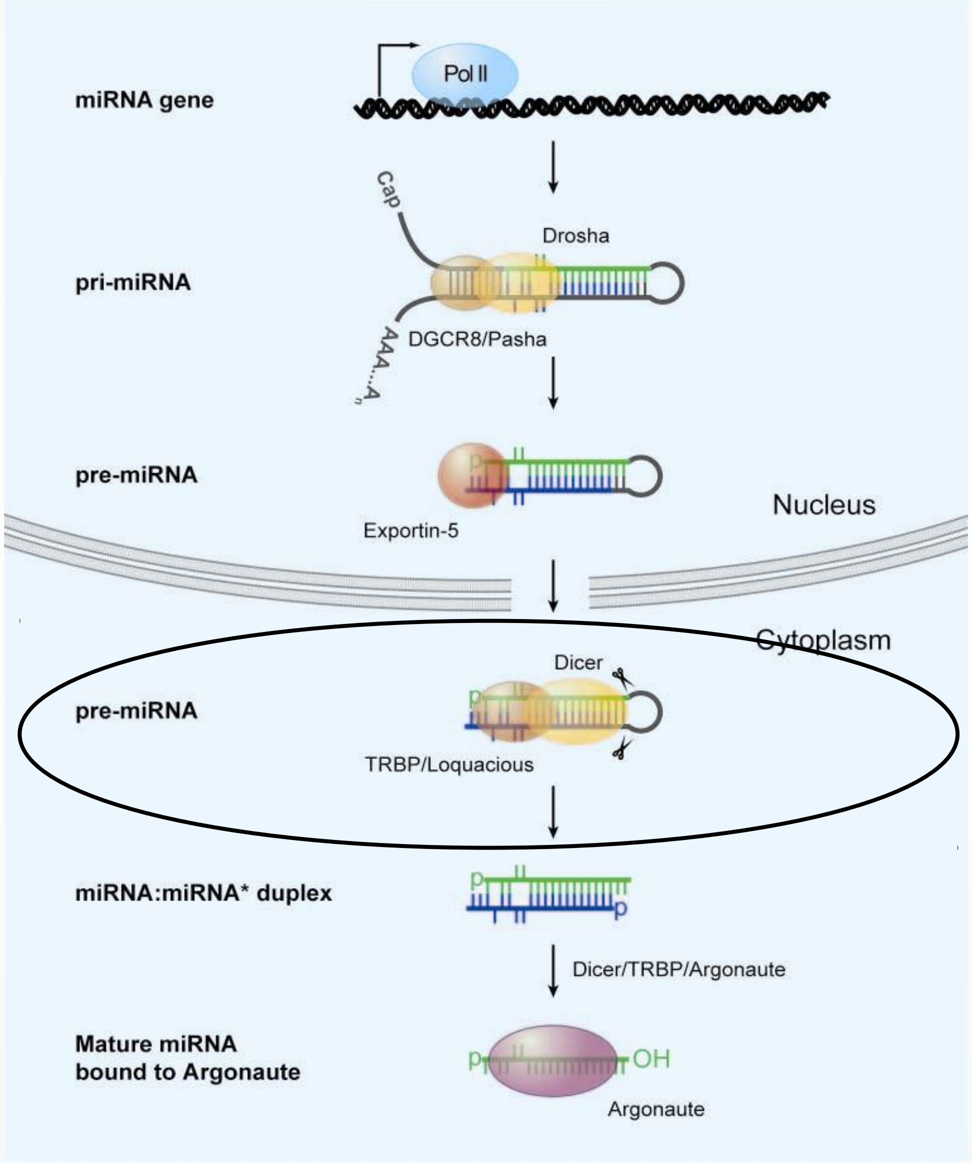
- traditional detection
  - Sanger
  - low expressed miRNA

- genomic DNA
  - sensitivity & FP

Idea

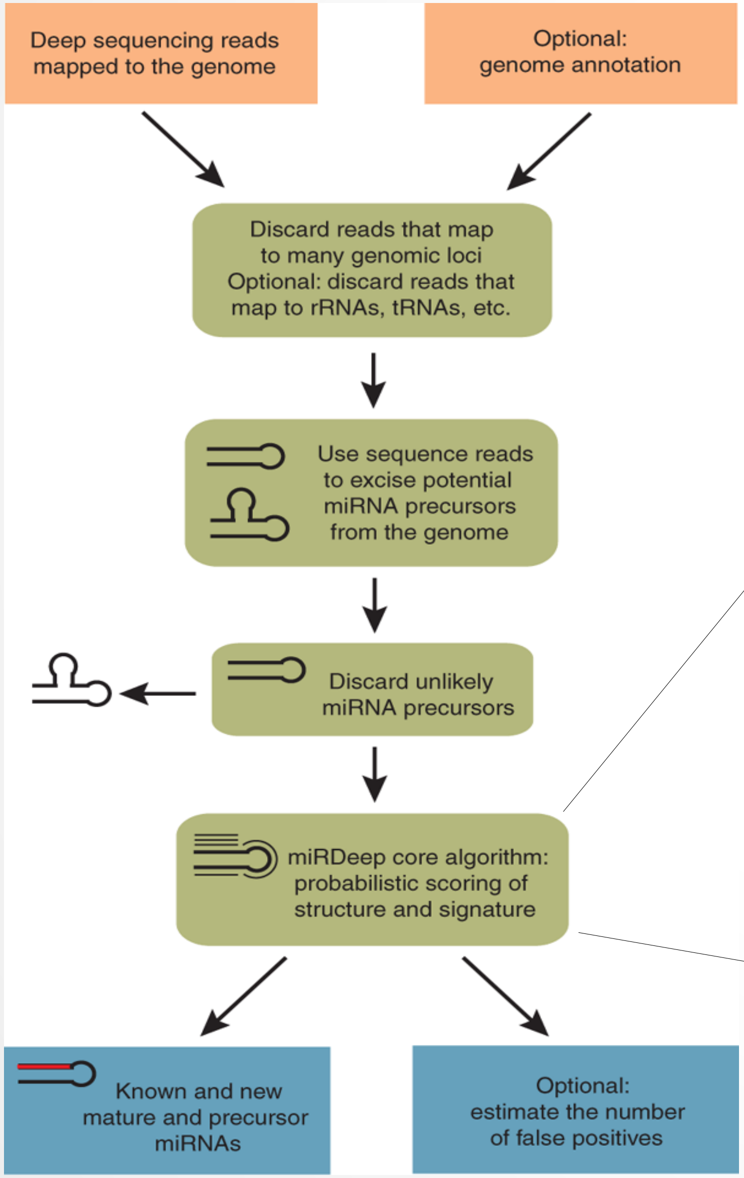
- NGS
- Compare sequenced miRNA with precursor processing

miRNA biogenesis



Bushati N, Cohen SM. 2007.
Annu. Rev. Cell Dev. Biol. 23:175–205

miRDeep



Deep sequencing reads mapped to the genome

Optional: genome annotation

Discard reads that map to many genomic loci
Optional: discard reads that map to rRNAs, tRNAs, etc.

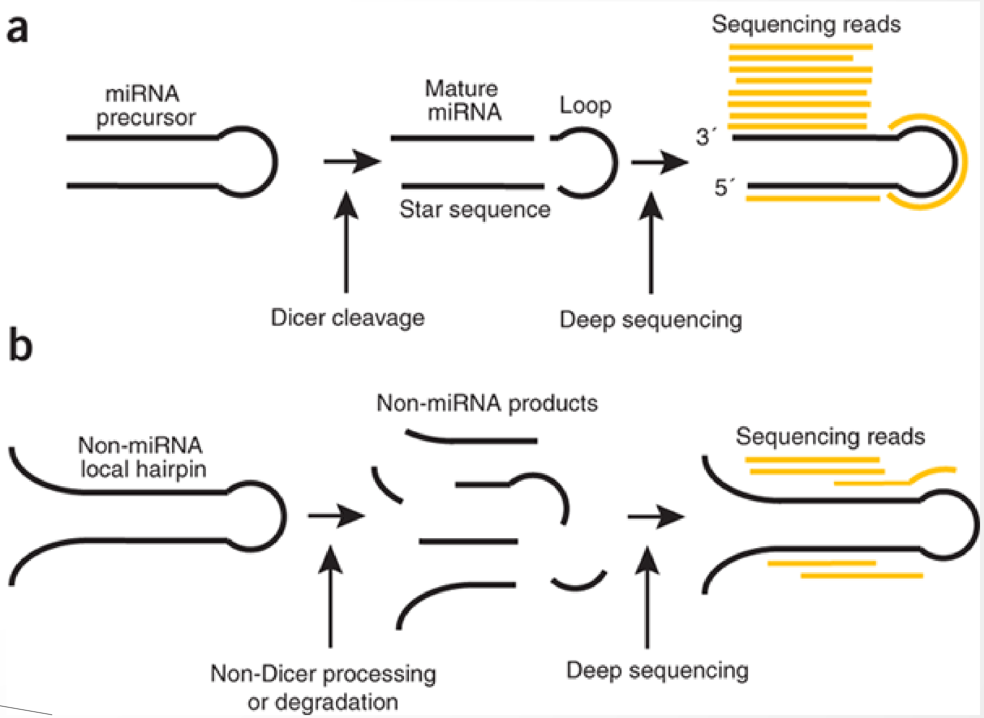
Use sequence reads to excise potential miRNA precursors from the genome

Discard unlikely miRNA precursors

miRDeep core algorithm: probabilistic scoring of structure and signature

Known and new mature and precursor miRNAs

Optional: estimate the number of false positives



Scoring

Scoring (log-odds) of candidate miRNA

miRNA precursor vs. background hairpin

$$score = \frac{P(pre|data)}{P(bgr|data)}$$

Scoring

$$P(pre|data)=\frac{\boxed{P(abs|pre)*P(rel|pre)*P(sig|pre)*P(star|pre)}*P(pre)}{P(data)}$$

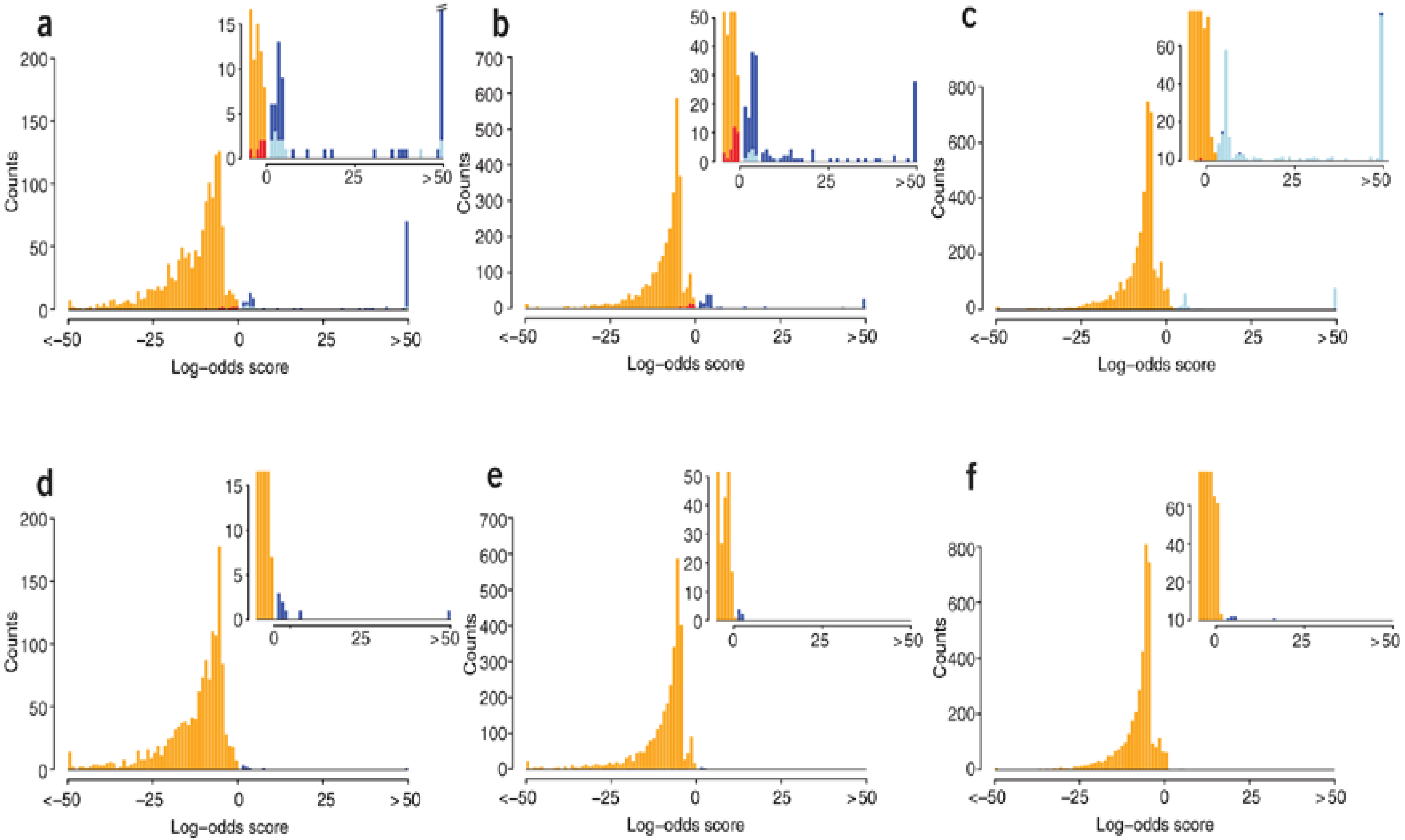
- abs = min. free energy
- rel = stable or unstable
- sig = mapped reads
- star = presence of star sequence

some statistics

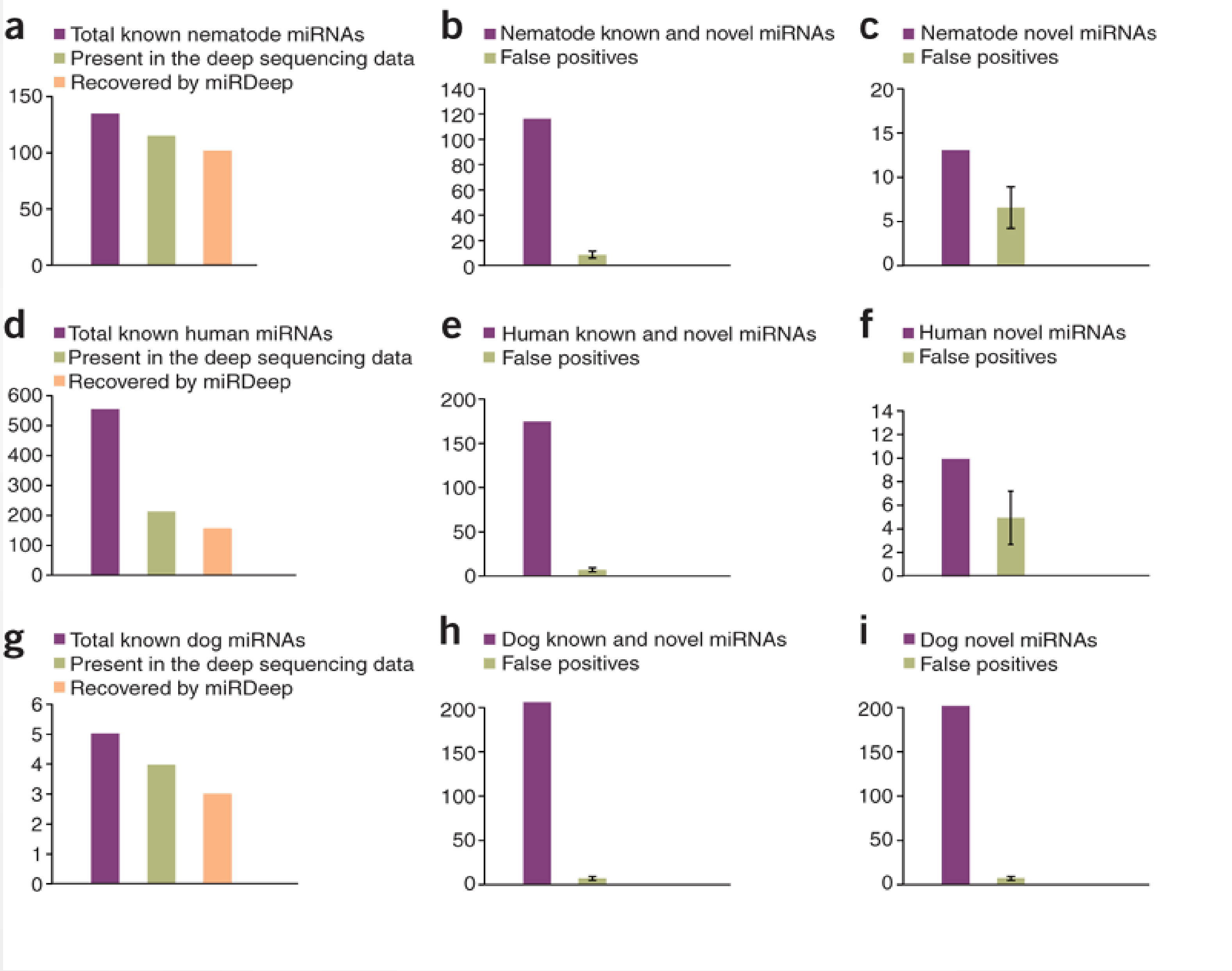
$$sensitivity = \frac{miRNA\ recovered}{reported\ miRNA\ \mathrm{in}\ dataset}$$

- FPR : permutation of structure & signature pairings

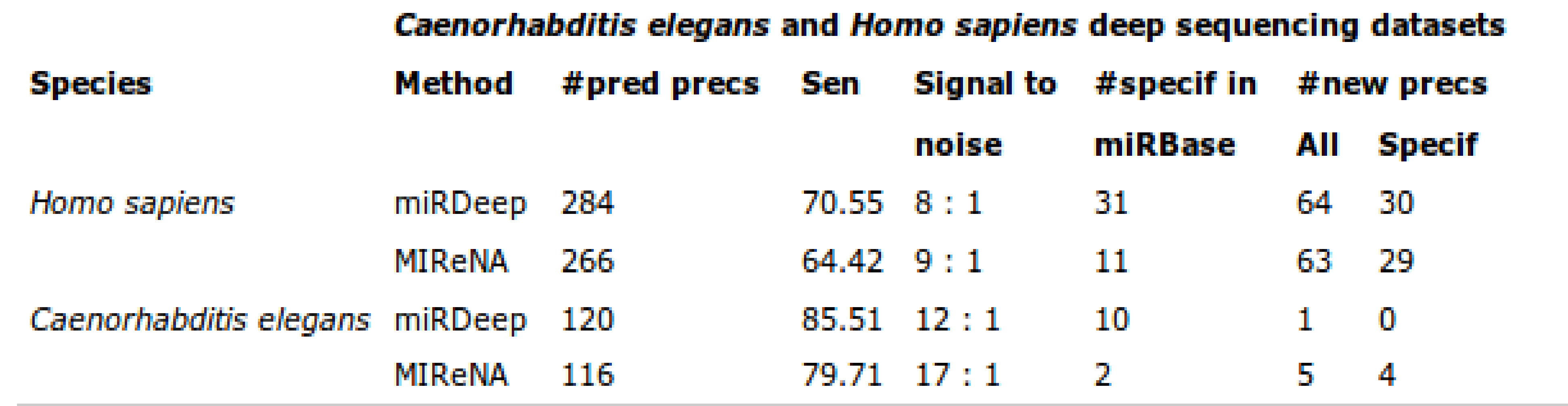
Results


a
Counts
200
150
100
50
0
<−50
−25
0
25
>50
Log−odds score
15
10
5
0
0
25
>50
b
Counts
700
600
500
400
300
200
100
0
<−50
−25
0
25
>50
Log−odds score
50
40
30
20
10
0
0
25
>50
c
Counts
800
600
400
200
0
<−50
−25
0
25
>50
Log−odds score
60
40
20
10
0
25
>50
d
Counts
200
150
100
50
0
<−50
−25
0
25
>50
Log−odds score
15
10
5
0
0
25
>50
e
Counts
700
600
500
400
300
200
100
0
<−50
−25
0
25
>50
Log−odds score
50
40
30
20
10
0
0
25
>50
f
Counts
800
600
400
200
0
<−50
−25
0
25
>50
Log−odds score
60
40
20
10
0
25
>50

Results


a
Total known nematode miRNAs
Present in the deep sequencing data
Recovered by miRDeep
150
100
50
0
b
Nematode known and novel miRNAs
False positives
140
120
100
80
60
40
20
0
c
Nematode novel miRNAs
False positives
20
15
10
5
0
d
Total known human miRNAs
Present in the deep sequencing data
Recovered by miRDeep
600
500
400
300
200
100
0
e
Human known and novel miRNAs
False positives
200
150
100
50
0
f
Human novel miRNAs
False positives
14
12
10
8
6
4
2
0
g
Total known dog miRNAs
Present in the deep sequencing data
Recovered by miRDeep
6
5
4
3
2
1
0
h
Dog known and novel miRNAs
False positives
200
150
100
50
0
i
Dog novel miRNAs
False positives
200
150
100
50
0

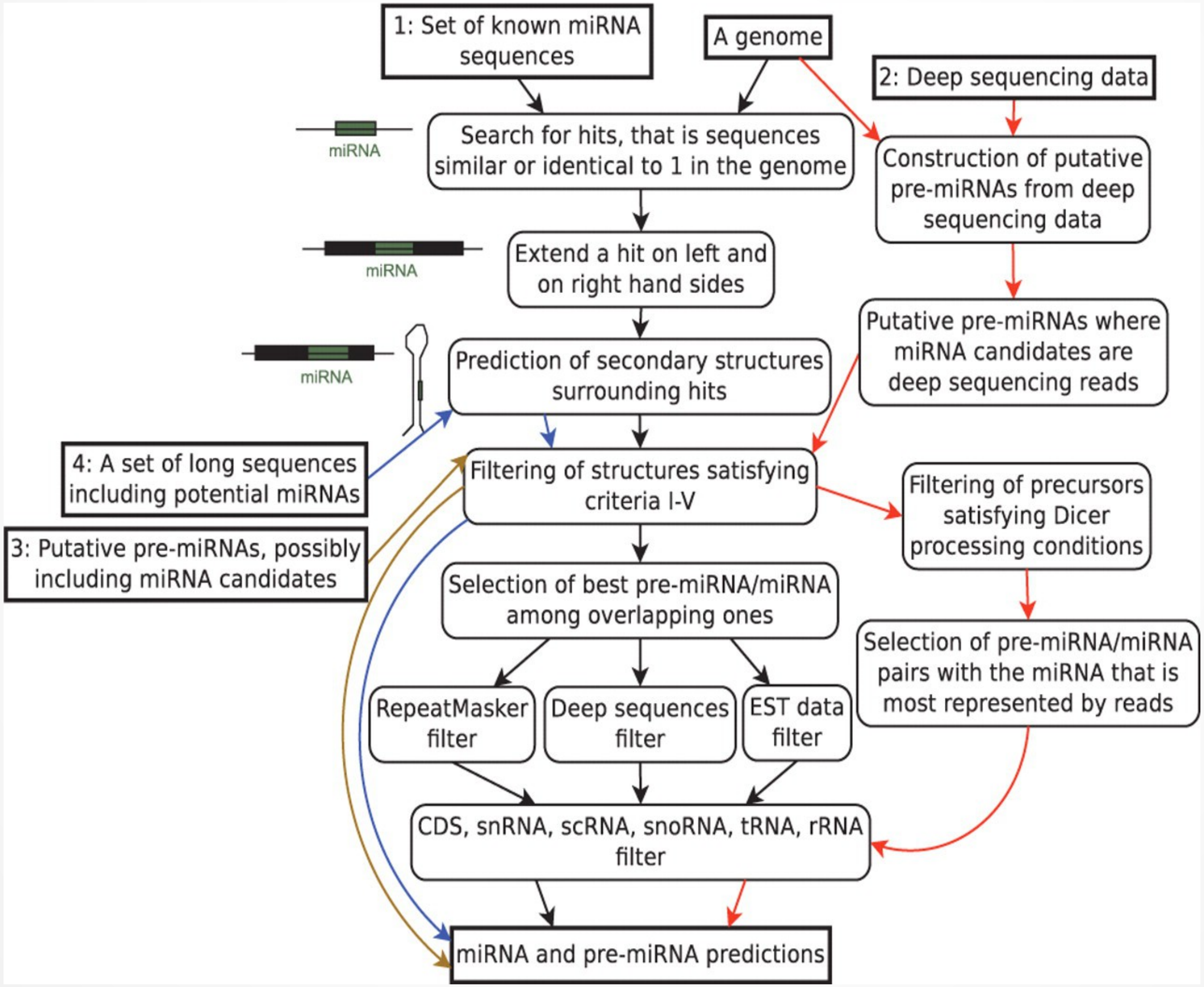
MIReNA



	***Caenorhabditis elegans* and *Homo sapiens* deep sequencing datasets**						
Species	**Method**	**#pred precs**	**Sen**	**Signal to noise**	**#specif in miRBase**	**#new precs**	
						All	**Specif**
Homo sapiens	miRDeep	284	70.55	8 : 1	31	64	30
	MIReNA	266	64.42	9 : 1	11	63	29
Caenorhabditis elegans	miRDeep	120	85.51	12 : 1	10	1	0
	MIReNA	116	79.71	17 : 1	2	5	4

- MIReNA: finding microRNAs with high accuracy and no learning at genome scale and from deep sequencing data
  - Anthonny Mathelier and Alessandra Carbone

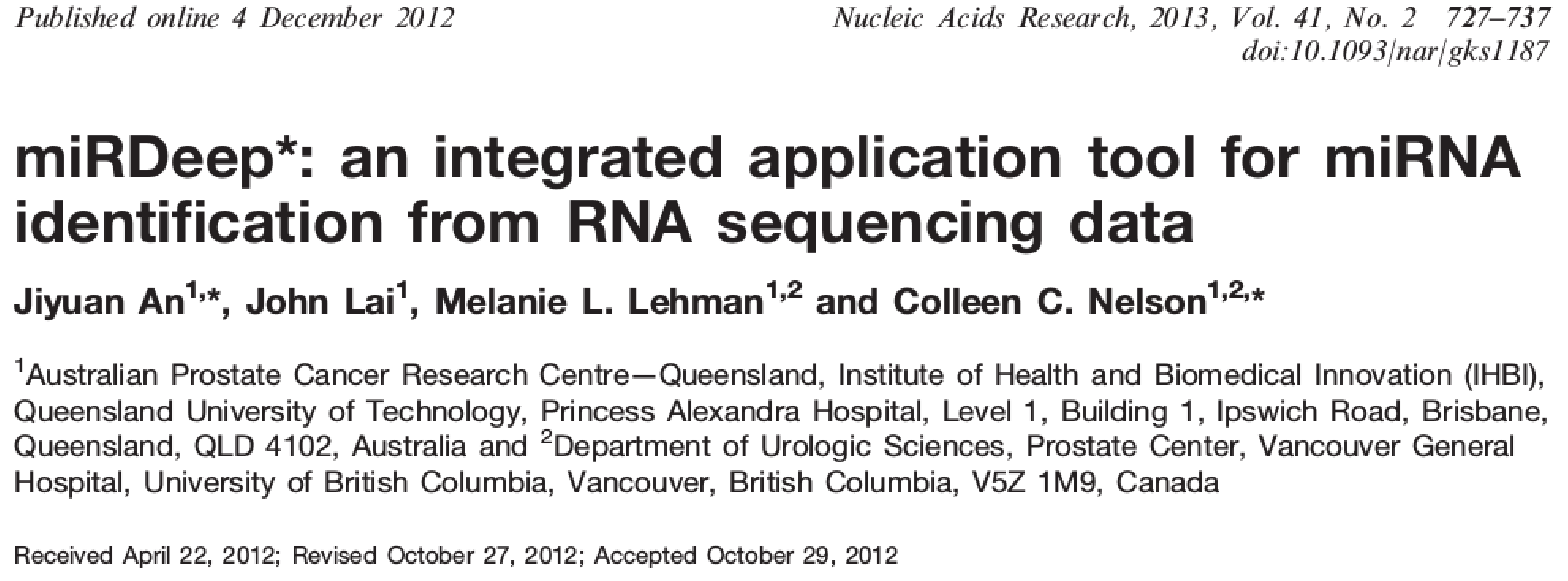
alternative to miRDeep



miRDeep vs. MIReNA

- miRDeep favours read abundant candidates
- MIReNA favours Criteria I-V candidates
- probabilistic model versus combinatorial rules

miRDeep*



Nucleic Acids Research, 2013, Vol. 41, No. 2 ***727–737***
doi:10.1093/nar/gks1187

miRDeep*: an integrated application tool for miRNA identification from RNA sequencing data

Jiyuan An[1,*], John Lai[1], Melanie L. Lehman[1,2] and Colleen C. Nelson[1,2,*]

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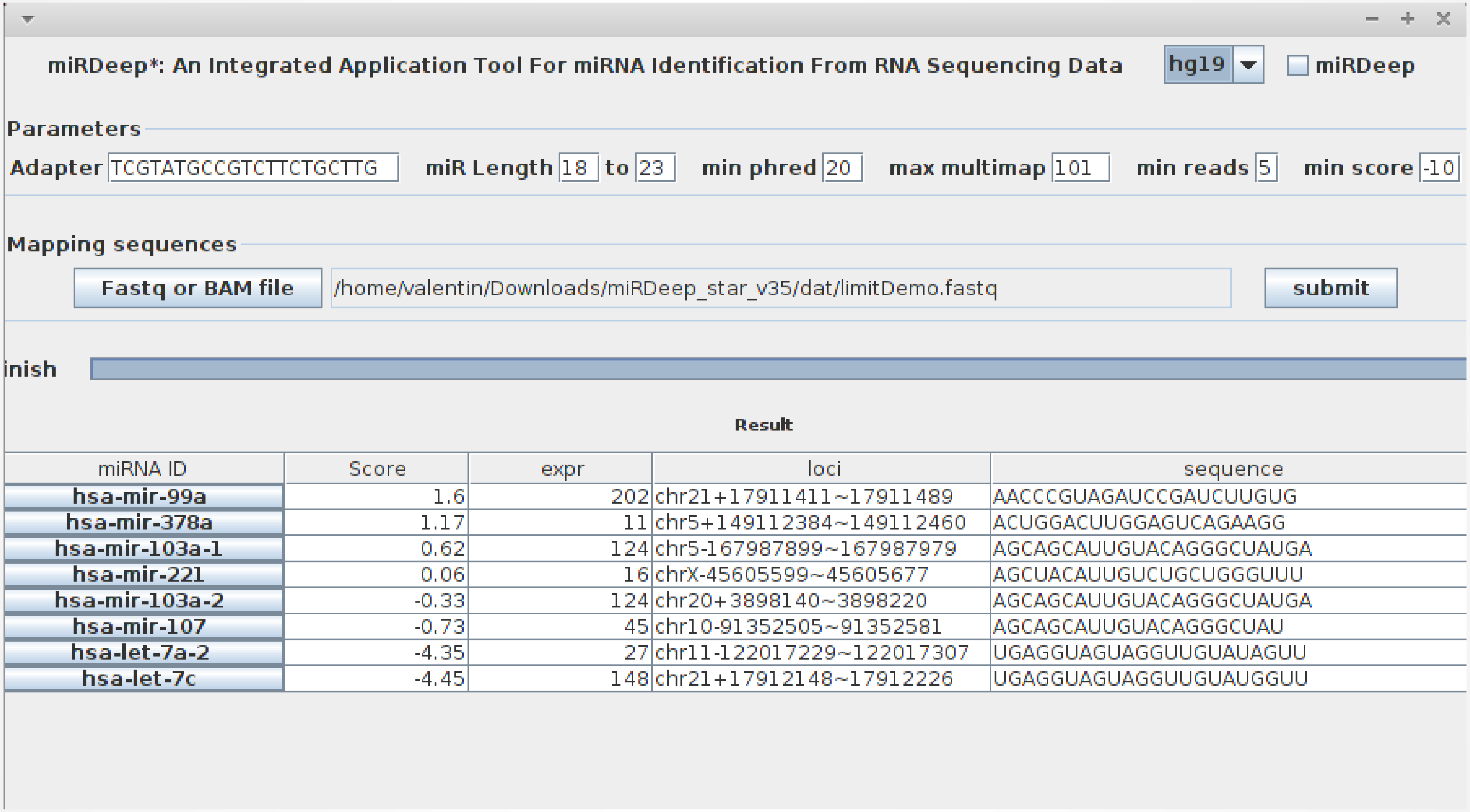
miRDeep*



miRDeep*: An Integrated Application Tool For miRNA Identification From RNA Sequencing Data hg19 ☐ miRDeep

Parameters

Adapter TCGTATGCCGTCTTCTGCTTG **miR Length** 18 **to** 23 **min phred** 20 **max multimap** 101 **min reads** 5 **min score** -10

Mapping sequences

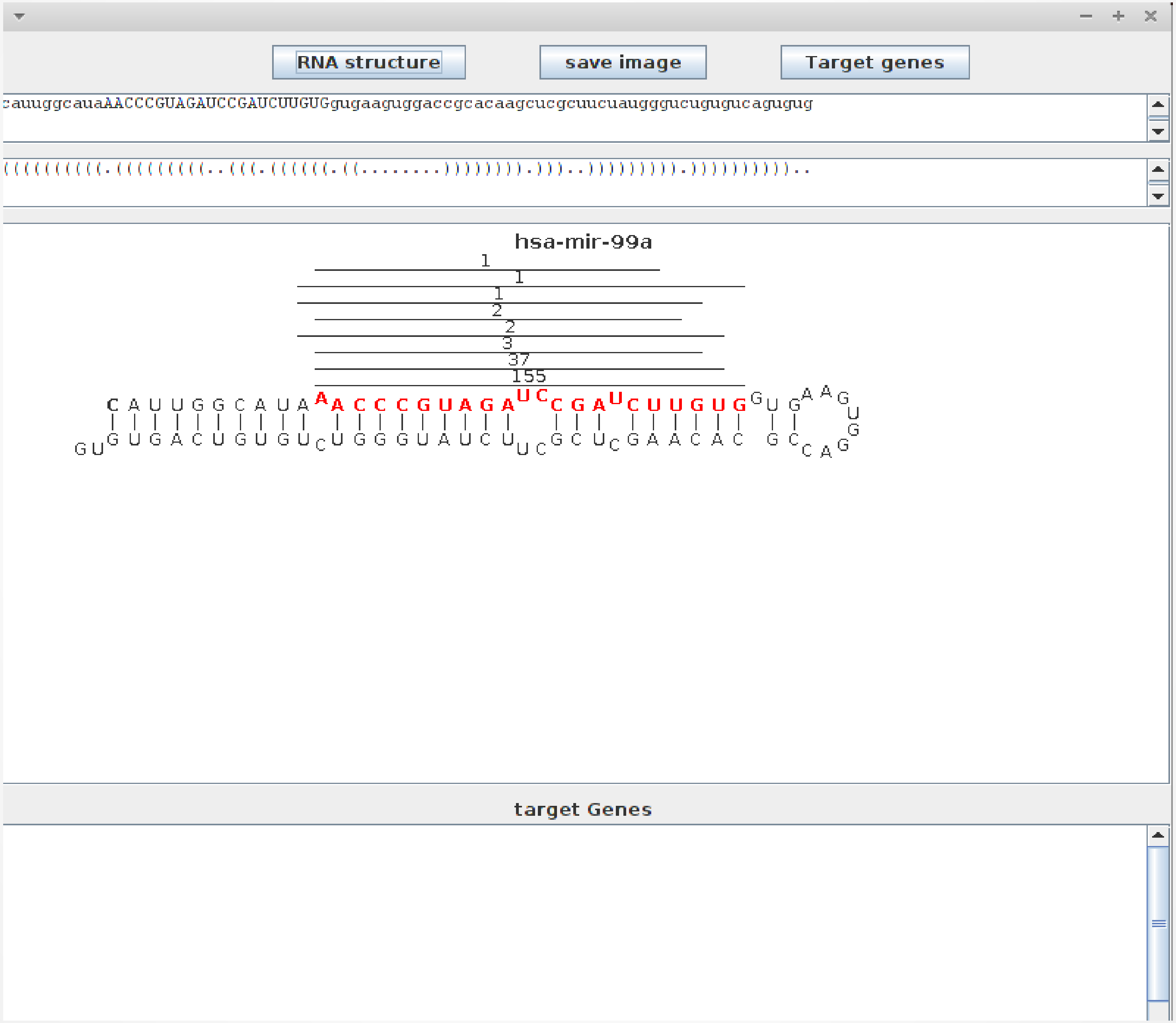
/home/valentin/Downloads/miRDeep_star_v35/dat/limitDemo.fastq

inish

Result

miRNA ID	Score	expr	loci	sequence
hsa-mir-99a	1.6	202	chr21+17911411~17911489	AACCCGUAGAUCCGAUCUUGUG
hsa-mir-378a	1.17	11	chr5+149112384~149112460	ACUGGACUUGGAGUCAGAAGG
hsa-mir-103a-1	0.62	124	chr5-167987899~167987979	AGCAGCAUUGUACAGGGCUAUGA
hsa-mir-221	0.06	16	chrX-45605599~45605677	AGCUACAUUGUCUGCUGGGUUU
hsa-mir-103a-2	-0.33	124	chr20+3898140~3898220	AGCAGCAUUGUACAGGGCUAUGA
hsa-mir-107	-0.73	45	chr10-91352505~91352581	AGCAGCAUUGUACAGGGCUAU
hsa-let-7a-2	-4.35	27	chr11-122017229~122017307	UGAGGUAGUAGGUUGUAUAGUU
hsa-let-7c	-4.45	148	chr21+17912148~17912226	UGAGGUAGUAGGUUGUAUGGUU

miRDeep*



```
cauuggcauaAACCCGUAGAUCCGAUCUUGUGgugaaguggaccgcacaagcucgcuucuaugggucugugucagugug
```

```
((((((((((.(((((((((..(((.((((((.((........)))))))).)))..))))))))).))))))))))..
```

Discussion

- simple model for miRNA detection
- basis for new tools
- more sensitive than genomic based algorithms

- hard to run
- not sensitive for SNPs

➔ use MIReNA/miRDeep*

Thank you for the attention!