

The Vienna RNA Package 2.0

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Overview

- extended nearest neighbor model (Turner '04)
- standardization of user interfaces
- standardization of implementations

Current state

- *testing*
- release in the next weeks

Review: Turner '04 nearest neighbor model

- tri-, hexa-loop parameters
- mismatch energies for exterior and multibranch loops
- 1xN-, 2x3-interior loops
- enthalpies for all energy contributions
- updated energy contributions

Changes for users

Command line options

Up to version 1.8.4

- POSIX standard (e.g. `-p`)
- X toolkit standard (e.g. `-noLP`)

Since version 2.0:

- GNU standard
 - '-' prefix for short options (e.g. `-p`)
 - '--' prefix for long options (e.g. `--noLP`)
- combination of command line options
`RNAsubopt -c -4 -D -e 5 equals`
`RNAsubopt -c4De 5`

more detailed help output (`-h` | `--help`) since `usage gengetopt`

Changes for users

New programs included

- RNA2Dfold - free energy landscape partitioning
- RNALfoldz - locally stable secondary structures + z-score
- RNALalifold - locally stable secondary structures for alignments
- RNAplex, RNAsnoop
- several updates on interfaced library functions
- RNAParconv - energy parameter file conversion tool
(version 1.x → 2.x)

Parameter sets

- Andronescu 07
- Mathews DNA
- Turner '99

Changes for developers

C/C++ API extensions

- unified design of functions and function wrappers
- several new or replacement functions in RNAlib (e.g. `findpath` direct path heuristic)
- several *deprecated* functions → obsolete/replacement
- tons of utility functions
- a **huge** amount of API code documentation

consult the reference manual and source code

API documentation with `doxygen`

- comments with detailed function description directly in sources (and there only)
- no need for 3+ way documentation (`code`, `man`, `TeX`)
- generate `man` pages, HTML and PDF reference manual

Be chatty while writing a function and lazy afterwards ;)

current reference manual available at

<http://www.tbi.univie.ac.at/~ronny/RNA>

some examples...

```
1 #ifndef _VIENNA_RNA_PACKAGE_LOOP_ENERGIES_H_
2 #define _VIENNA_RNA_PACKAGE_LOOP_ENERGIES_H_
3
4 #include <stdio.h>
5 #include <stdlib.h>
6 #include <math.h>
7 #include <ctype.h>
8 #include <string.h>
9 #include "params.h"
10 #include "fold_vars.h"
11 #include "energy_par.h"
12
13 #ifndef _GNUCC_
14 # define INLINE inline
15 #else
16 # define INLINE
17 #endif
18
19 INLINE PRIVATE int E_Mlstem(int type, int s1, int s1, paramT *P);
20
21 INLINE PRIVATE double exp_E_Mlstem(int type, int s1, int s1, pf-paramT *P);
22
23 INLINE PRIVATE int E_ExtLoop(int type, int s1, int s1, paramT *P);
24
25 INLINE PRIVATE double exp_E_ExtLoop(int type, int s1, int s1, pf-paramT *P);
26
27 INLINE PRIVATE int E_IntLoop(int u1,
28                               int u2,
29                               int type,
30                               int type2,
31                               int s1,
32                               int s1,
33                               int s1,
34                               int s1,
35                               paramT *P);
36
37 INLINE PRIVATE int E_Hairpin(int size, int type, int s1, int s1, const char *string, paramT *P);
38
39 INLINE PRIVATE int E_Stem(int type, int s1, int s1, int extLoop, paramT *P);
40
41 INLINE PRIVATE double exp_E_Stem(int type, int s1, int s1, int extLoop, pf-paramT *P);
42
43 INLINE PRIVATE double exp_E_Hairpin(int u, int type, short s1, short s1, const char *string, pf-paramT *P);
44
45 INLINE PRIVATE double exp_E_IntLoop(int u1,
46                                     int u2,
47                                     int type,
48                                     int type2,
49                                     short s1,
50                                     short s1,
51                                     short s1,
52                                     short s1,
53                                     paramT *P);
54
55 /*
56 #####
57 # SOME OTHER STUFF FOLLOWING #
58 #####
59 */
60 ...
61
62 // comment
63 /* another comment */
64 /* a doxygen comment */
65
66
67 #endif
```


some examples...

```
1  /*
2  *** <HD>Compute the Energy of a Hairpin-loop</HD>
3  *** To evaluate the free energy of a hairpin-loop, several parameters have to be known.
4  *** A general hairpin-loop has this structure:<BR>
5  *** <PRE>
6  ***
7  ***      a3 a4
8  ***      a2 a5
9  ***      a1 a6
10 ***      | |
11 ***      5' 3'
12 ***
13 *** where X-Y marks the closing pair [e.g. a<B>(G,C)</B> pair]. The length of this loop
14 *** is 6 as there are six unpaired nucleotides (a1-a6) enclosed by (X,Y). The 5' mismatching
15 *** nucleotide is a1 while the 3' mismatching nucleotide is a6. The nucleotide sequence of this loop is
16 *** \seq:a1.a2..a3.a4..a5.a6\seq;<BR>
17 *** \note The parameter sequence should contain the sequence of the loop in capital letters
18 *** of the nucleic acid alphabet if the loop size is below 7. This is useful for manually
19 *** stable tri-, tetra- and hexa-loops which are treated differently (based on experimental
20 *** data) if they are tabulated.
21 *** \see scale-parameters()
22 *** \see paramT
23 *** \warning Not (really) thread safe! A threadsafe implementation will replace this function
24 *** in a future release!\n
25 *** Energy evaluation may change due to updates in global variable "tetra-loop"
26 ***
27 *** \param size The size of the loop (number of unpaired nucleotides)
28 *** \param type The pair type of the base pair closing the hairpin
29 *** \param a1 The 5'-mismatching nucleotide
30 *** \param a2 The 3'-mismatching nucleotide
31 *** \param string The sequence of the loop
32 *** \param P The datastructure containing scaled energy parameters
33 *** \return The Free energy of the Hairpin-loop in kcal/mol
34 **/
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```

Concurrent computations capability

All folding algorithms are OpenMP threadsave¹

changes in energy model might result in unexpected behavior!

Simple to use

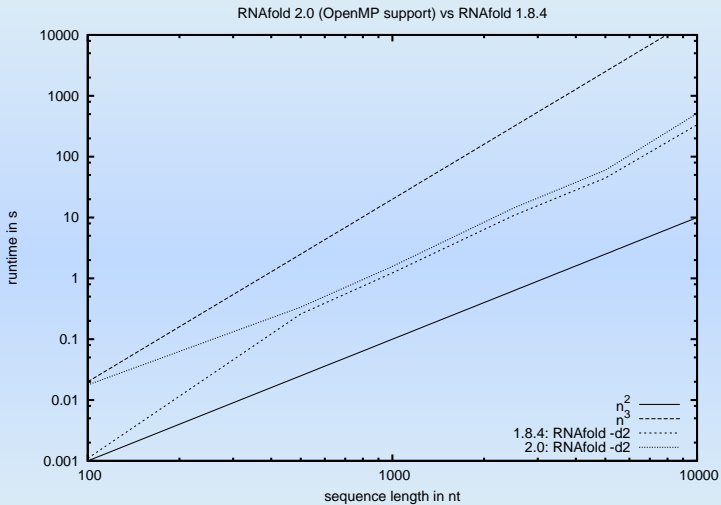
```
1 #pragma omp parallel for private(i, structure, en)
2 for(i=0; i<n; i++){
3     en[i] = fold(sequence[i], structure[i]);
4     free_arrays();
5 }
```

8 sequences, 8 threads, Intel(R) Xeon(R) X5550

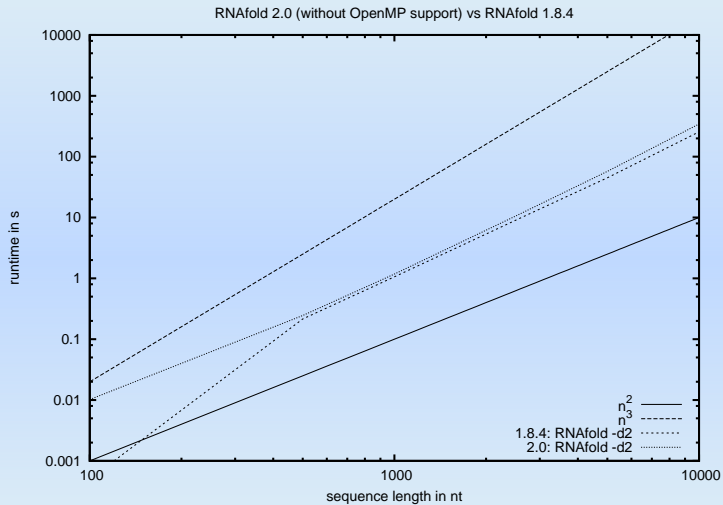
- **1000nt**: speedup 7.26, overhead 1.08
- **2500nt**: speedup 6.02, overhead 1.33
- **5000nt**: speedup 4.94, overhead 1.6
- **10000nt**: speedup 4.16, overhead 1.91

¹at least w/o model change

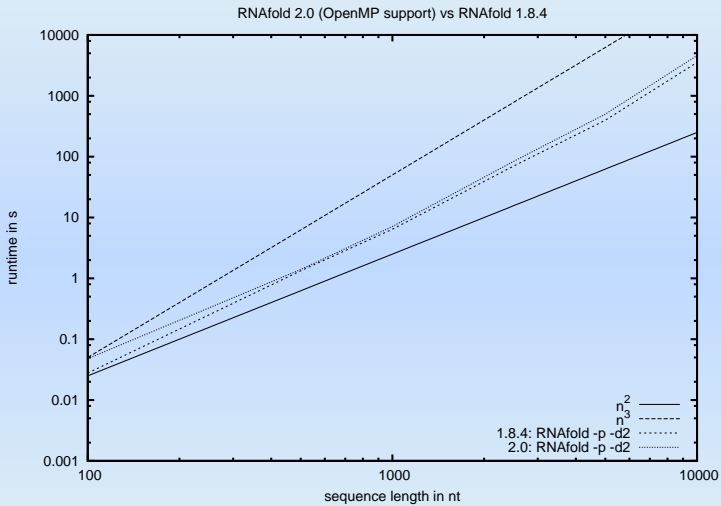
Runtime comparison 2.0 vs 1.8.4



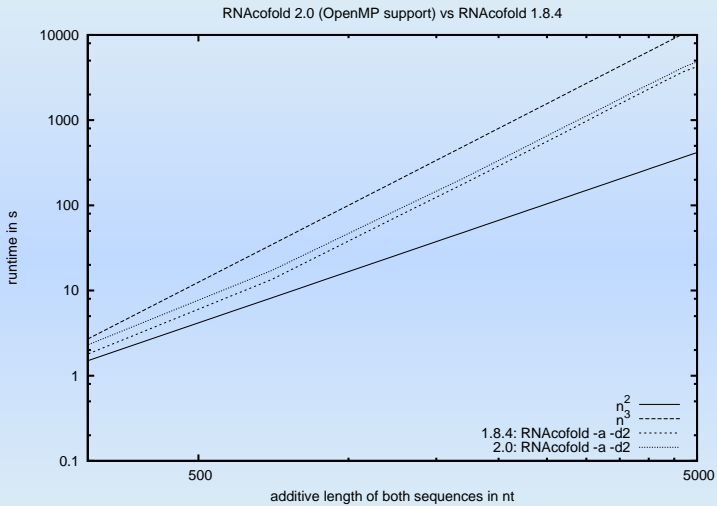
Runtime comparison 2.0 vs 1.8.4



Runtime comparison 2.0 vs 1.8.4



Runtime comparison 2.0 vs 1.8.4



Prediction accuracy

will be done next week

Summary

- soon to be released!
- improved energy model
- more energy parameter sets:
Turner '99, Mathews DNA & Andronescu '07
- standardized user interface
- improved API:
one structure → one function
- much more documentation for developers
- re-use existing code from RNAlib!
(instead of re-inventing the wheel)

latest snapshots available

<http://www.tbi.univie.ac.at/~ronny/RNA>

Thanks to

Stephan Bernhard

Christoph Flamm

Andreas Gruber

Ivo Hofacker

Christian Höner zu Siederdisen

rest of TBI team

You for listening