Responses to Reviewers’ Comments

We thank the referees for their many constructive recommendations. Below we delineate the changes that we made in response.

1. Reviewer I:

As requested, we now state specifically in section 2.2.2 how sampled structures were used to obtain gamma centroid estimates.

We modified the figure captions to explicitly state that performance of other methods shown in Fig 1 and 2 are as reported by Do *et al.* (2008), as requested.

We set the x and y axes to range from 0.3 to 1.0 and made a note of this fact in both figures 1 and 2 as requested.

We misstated the problem with the SRP family in the BRAliBASE II dataset. The real problem is that the server does not provide a reference secondary structure for the SRP family, which makes it impossible to fairly evaluate the performance of the algorithm. In an effort to address this, we emailed the author, Prof. Gardner, who compiled the data set for clarification. His e-mail reply is below.

" From memory there were problems with the SRP families that we failed to resolve in time for publication. I don't believe it was used for the final analysis. I certainly have no record of SRP in this dataset either."

Additionally, we e-mailed Do over 15 days ago to ask for the structure that he used but we have received no reply. Thus, we since cannot assure a fair comparison, we have excluded the SRP family.

We also added requested information about the speed of RNAG and other extant procedures as requested.

1. Reviewer III:

In response to the first review to more fully address the relationship of our work with CMfinder, we added CMfinder to comparisons with RNAG on all three data sets: MASTR, BRAliBASE II and Murlet.

1. We thank the referees for patiently pointing our minor changes and typos, which we corrected. These comments prompted us to review and revise our presentation. With the aid of colleagues who had not previously read the manuscript we made several changes to improve the clarity and focus of the submission. With one exception, none of these changes alter the substance. In this review we found that the section on riboswitches was tangential to the main focus of the paper and has therefore been removed. If you disagree, we will put the riboswitch section back in the submission.
2. Lauren Alpert has been helping us assure the reproducibility of our findings, and has made additional substantive contributions to the paper. Her work has become substantial enough to merit co-authorship, rather than acknowledgement. As such, we have added her as an author.
3. To aid others in the use of the three datasets used in this study, we have collected them, organized them in a readily accessible format, and posted them on our web server.

Yours Sincerely,

Donglai Wei, Lauren Alpert, Charles Lawrence

2011.6.3

Lauren\_Alpert@brown.edu