Text S1

SHAPE-directed RNA structure modeling. Inclusion of SHAPE information provides an experimental adjustment to the well-established nearest neighbor model for RNA folding [1]. For secondary structure prediction, SHAPE data are incorporated as a pseudo-free energy change term, $\Delta G_{\mathrm{SHAPE}}$, implemented in *RNAstructure* [2]:

$$\Delta G_{\mathrm{SHAPE}} = m\ ln[\mathrm{SHAPE} + 1] + b \qquad (1)$$

The slope, m, corresponds to a penalty for base pairing that increases with the experimental SHAPE reactivity, and the intercept, b, reflects a favorable pseudo-free energy change term for base pairing at nucleotides with low SHAPE reactivities. These two parameters must be determined empirically. When Watts *et al.* analyzed the HIV-$1_{\mathrm{NL4\text{-}3}}$ genome, m = 3.0 and b = -0.6 were the optimal parameters [3]; in general, these parameters still perform well. The recently updated parameters are m = 1.9 and b = -0.7 give the highest sensitivities in a bootstrapping statistical analysis of multiple RNAs [4]. Changing the slope and intercept parameters from m = 3.0, b = -0.6 to m = 1.9, b = -0.7 results in a reduction of 34% in the number of base pairs that were predicted in the HIV-$1_{\mathrm{NL4\text{-}3}}$ genome, most were in weakly structured regions.

References

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