JOURNAL OF RNA and Genomics ISSN: 2591-7781

ISSN: 2591-7781 J RNA Genomics, 2021, Vol 17, 657-658

SHORT COMMENTARY

A Shot Note on Thermodynamics of RNA

Shaheed Shettipally*

Department of Biology, University of Delhi, New Delhi, India

*Correspondence to: Shaheed Shettipally, E-mail: shaheedshettipally1122@gmail.com,

Received: 02 Mar 2021; Accepted: 16 Mar 2021; Published: 31 Mar 2021

ABSTRACT

Reliable prediction of RNA–RNA binding energies is crucial, e.g. for the understanding on RNAi, microRNA–mRNA binding and antisense interactions. The thermodynamics of such RNA–RNA interactions can be understood as the sum of two energy contributions: (1) the energy necessary to 'open' the binding site and (2) the energy gained from hybridization.

KEYWORDS: microRNA; RNAi; RNA

INTRODUCTION

Secondary structure prediction for a single RNA molecule is a classical problem of computational biology, which has received increasing attention in recent years owing to mounting evidence that emphasizes the importance of RNA structure in a wide variety of biological processes Despite its limitations, free energy minimizations at present the most accurate and most generally applicable approach of RNA structure prediction, at least in the absence of a large set of homologous sequences. It is based upon a large number of measurements performed on small RNAs and the assumption that stacking base pairs and loop entropies contribute additively to the free energy of an RNA secondary structure (Andronescu & Condon 2005) In this framework, a secondary structure is interpreted as the collection of all the three-dimensional structures that share a common pattern of base pairs, hence we speak of a free energy of an individual secondary structure. Under the assumption that RNA secondary structures are pseudo-knot free, i.e. that base pairs do not cross, there are efficient exact dynamic programming algorithms that solve not only the folding problem but also provide access to the full thermodynamics of the model via its partition function.

More recently, the secondary structure approach has been applied to the problem of interacting RNA molecules. In the simplest approaches secondary structures within both monomers are omitted for the sake of computational speed, so that only intermolecular base pairs are taken into account (Zhang & Anderson 2006). This is implemented in the program A biophysically more plausible model is the 'co-folding' of two RNAs. Algorithmically, this is very similar to folding a single RNA molecule. The idea is to concatenate the two sequences and to use different energy parameters for the loop that contains the cut-point between the two sequences.

A corresponding RNA co fold program for calculation of the minimum free energy structure is described in the restriction of the folding algorithm to pseudo-knot-free structures, however, excludes a large set of structures that should not be excluded when studying the hybridization of a short oligonucleotide to a large mRNA. In particular, binding of the olio is in practice not restricted to the exterior loop of the target RNA, as is implicitly assumed in the RNA cofold approach. On the other hand, there is no biophysically plausible reason to exclude elaborate secondary structures in the target molecule Here we extend previous RNA/RNA cofold algorithms by taking into account that the oligo can bind also to unpaired sequences in hairpin, interior, or multi-branch loops. These cases could in principle be handled using a generic approach to pseudo-knotted RNA structures at the expense of much more costly computations. Instead we conceptually decompose RNA/RNA binding into two stages: We calculate the partition function for secondary structures of the target RNAs subject to the constraint that a certain sequence interval (the binding site) remains unpaired. We then compute the interaction energies given that the binding site is unpaired in the target The total interaction probability at a possible binding site is then obtained as the sum over all possible types of binding. The predicted binding energies correlate well with expression data, showing that the effect of RNAi depends quantitatively on siRNA/mRNA binding. In addition to assessing the interactions at known binding sites, our approach also provides an effective way of identifying alternative binding sites, since the computational effort for scanning target mRNA is small compared with the initial partition function calculation (Bohula, et al. 2003). RNA up is therefore ideally suited to study RNA–RNA interactions in detail, in particular

When the interaction partners are known or when a candidate set has already been obtained by faster, less accurate methods.

In context of RNA silencing it should be noted that efficiency is not only a function of thermodynamics of RNA–RNA interaction but will also depend on protein factors. As long as the binding energies of the protein component(s) are independent of the RNA sequences our approach is still useful since it correctly reproduces at least the relative order of RNA–RNA binding energies. (Dimitrov & Zuker, 2004). A further concern is whether the underlying assumption of thermodynamically controlled binding is correct; it is possible that in particular when RNA binding is associated with large structural changes, kinetic effects of structure formation might be important. Nevertheless, one would expect that even a kinetically controlled structure will energetically be close to the ground state, in which case RNA up at least provides a meaningful approximation to the energetics of the interaction.

REFERENCES

Andronescu, M., & Condon, A. (2005). Secondary structure prediction of interacting RNA molecules. Journal of molecular biology, 345(5), 987-1001.

Bohula, E. A., et al. (2003). The efficacy of small interfering RNAs targeted to the type 1 insulin-like growth factor receptor (IGF1R) is influenced by secondary structure in the IGF1R transcript. Journal of Biological chemistry, 278(18), 15991-15997.

Dimitrov, R. A., & Zuker, M. (2004). Prediction of hybridization and melting for double-stranded nucleic acids. Biophysical Journal, 87(1), 215-226.

Zhang B, & Anderson T A., (2006). Computational identification of microRNAs and their targets. Computational biology and chemistry. 30(6):395-407.

.