

## **Evolutionary triplet models of structured RNA: Text S3**

Robert K. Bradley<sup>1</sup>, Ian Holmes<sup>1,2,\*</sup>

**1** Biophysics Graduate Group, University of California, Berkeley, CA, USA

**2** Department of Bioengineering, University of California, Berkeley, CA, USA

\* E-mail: [indiegram@postbox.biowiki.org](mailto:indiegram@postbox.biowiki.org)

## 1 Software

All tools are available from <http://biowiki.org/dart> as part of the DART software package for sequence analysis.

### 1.1 Automated grammar construction

We implemented our model construction algorithm on the three-taxon star phylogeny in a set of Perl scripts. Given a singlet transducer modeling ancestral sequences and structures and a branch transducer modeling structural evolution, the scripts generate C++ code to create the corresponding jointly-normalized SCFG. All possible models of structural evolution which can be represented by a Pair SCFG are permitted as input to the scripts, allowing for flexible and automated model design.

Given files describing the singlet and branch transducers, including weights of all transitions which may be functions of evolutionary distance, the package `ComposedTreeTransducer::FourWayComposedTT` can automatically generate the state graph and transition matrix of a multi-sequence model of three extant sequences. It removes the useless windback `Null` states described in the paper and introduces effective direct transitions caused by bifurcations with possibly-empty children. The package `ComposedTreeTransducer::TripletSCFG` transforms a multi-sequence model created by `ComposedTreeTransducer::FourWayComposedTT` into the corresponding jointly-normalized three-sequence SCFG and generates C++ code to build the model.

Example singlet and branch transducers files are provided for a simple Pair HMM model, a simple Pair SCFG model and the full TKF Structure Tree model.

### 1.2 Reconstruction of ancestral structures

The program INDIEGRAM can perform maximum-likelihood inference on the three-sequence SCFGs automatically generated by the `ComposedTreeTransducer::TripletSCFG` package. Complete or no structural information for the three extant sequences can be supplied as input.

### 1.3 Simulation of RNA family evolution

The program that we wrote to simulate RNA structural alignments from the TKFST model, `evolsayer.pl`, is available as part of the same software distribution as INDIEGRAM (the DART package). Another

script (`animate-evolsayer.pl`) can be used to make animations of the evolving RNA structures, in combination with the RNAPlot program in the ViennaRNA package [1].

## References

1. Hofacker IL, Fontana W, Stadler PF, Bonhoeffer S, Tacker M, et al. (1994) Fast folding and comparison of RNA secondary structures. *Monatshefte für Chemie* 125: 167-188.
2. Liberles DA, editor (2007) *Ancestral Sequence Reconstruction*. Oxford University Press.