

Biomedical Computation Review

Simbios AN NIH NATIONAL CENTER FOR BIOMEDICAL COMPUTING

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seeing science

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Building RNA 3-D Structure

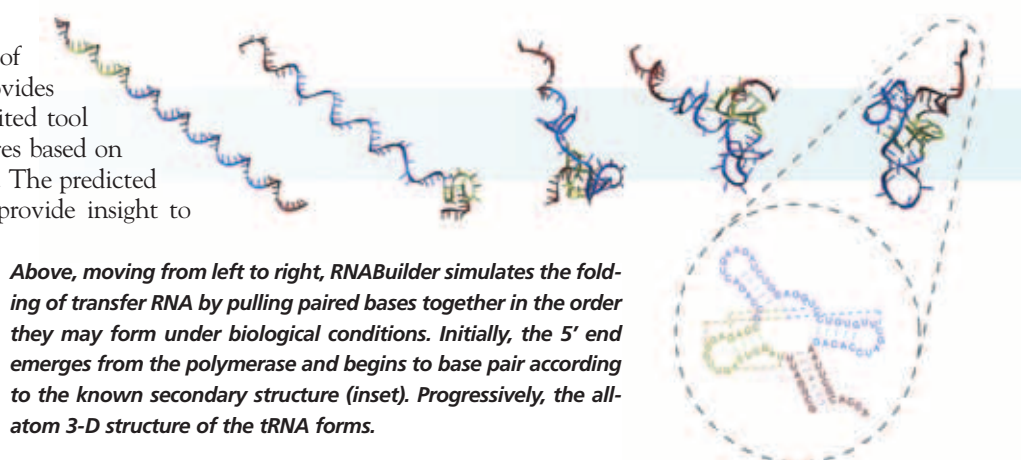
The structure of RNA is an important key to its function—including its role in disease. However, the structure of most RNAs is unknown because their extreme flexibility and high charge make them difficult to crystallize. In addition, prediction of RNA structure based only on its nucleotide sequence remains elusive for all but the smallest molecules.

Aiming to bridge the gap between successful sequence-based structure prediction codes that predict the structure of small RNAs and unsuccessful attempts to predict larger ones, Samuel Flores, PhD, a postdoc in bioengineering at Stanford University, and his colleagues have developed a rigid body dynamics software program called RNABuilder. Because the software relies only on readily available information such as base-pairing contacts (which are often known even when the full 3-D structure of the molecule is unknown), it provides experimentalists with a long-awaited tool to quickly model possible structures based on limited experimental information. The predicted structures and folding pathways provide insight to guide further experiments.

RNABuilder mimics how RNA is made in nature—enforcing base-pairing starting at the 5' end and finishing with the 3' end. It uses Simbody, SimTK's Multibody Dynamics

code library. Simbody's Contact subsystem is used to economically account for steric and Coulomb repulsion. Selected bonds are rigidified to reduce the number of bodies for greater economy. For tRNA and the P4/P6 domain of the *Tetrahymena* ribozyme, the program has been shown to recover the correct topology, base-pairing contacts, and overall structure using only the base-pairing information that was available before the three-dimensional structure was known. □

DETAILS: RNABuilder is an RNA modeling program based on Simbios' Simbody code for multi-body mechanics, which is freely available as part of the SimTK toolkit (<http://simtk.org/home/simtkcore>). A workshop on using RNABuilder and NAST (see Simbios News column in this issue) will be held at Stanford University on June 19, 2009. For more information, contact Blanca Pineda, bpineda@stanford.edu.



Above, moving from left to right, RNABuilder simulates the folding of transfer RNA by pulling paired bases together in the order they may form under biological conditions. Initially, the 5' end emerges from the polymerase and begins to base pair according to the known secondary structure (inset). Progressively, the all-atom 3-D structure of the tRNA forms.