BY KATHARINE MILLER

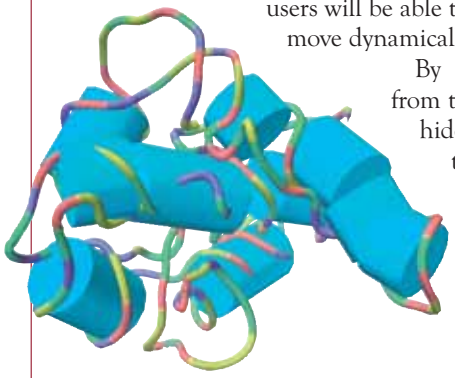
Now Available: User-Friendly RNA Dynamics Applications

Now, with just a few mouse clicks, anyone with a computer and an Internet connection can create graphic images of RNA molecules (using ToRNADo) or generate the ion environments that surround these highly charged molecules (using ISIM). This user-friendliness is a striking trait shared by Simtk.org's new tools for visualizing and simulating RNA, and it's a sign of things to come.

"With ToRNADo and ISIM, we've created a paradigm for what constitutes an easy-to-use application," says **Jeanette Schmidt, PhD**, Executive Director of Simbios at Stanford University.

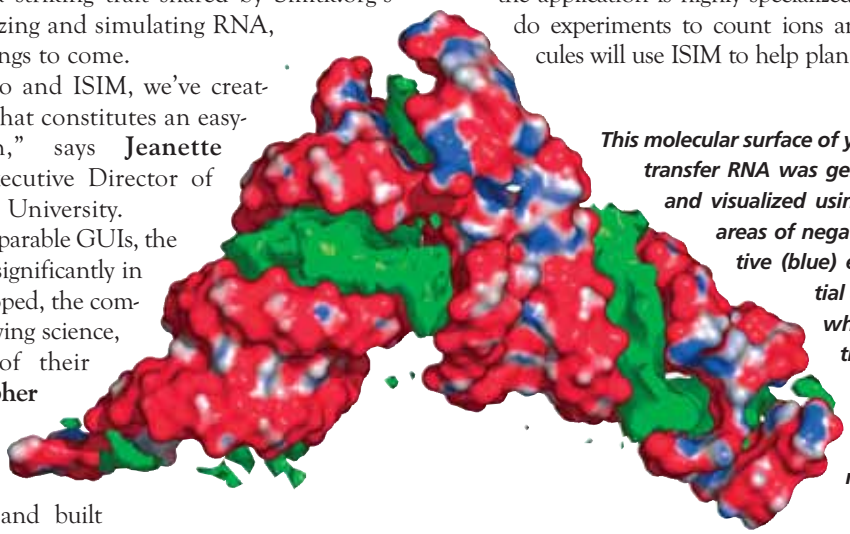
Despite their comparable GUIs, the two programs differ significantly in how they were developed, the complexity of the underlying science, and the breadth of their appeal, says **Christopher Bruns, PhD**, the Simbios computational biologist who created ToRNADo and built the user-interface for ISIM.

ToRNADo is a relatively straightforward RNA visualization tool that can create atomic-level or coarse-grained pictures of known RNA structures. It has broad applicability (it already has hundreds of users) and was built from the user-interface down. Eventually it will meet up with the Simbody multibody dynamics engine in the SimTK tool kit. "When that happens we'll have a tool that can be used not only for visualization but also for simulation," Bruns says. Ultimately, with the same simple interface, users will be able to make the RNA structure move dynamically.



SimTK's ToRNADo software produced this image showing the structure of the Tetrahymena ribozyme (Protein Data Bank ID 1GRZ). Blue cylinders represent double helical RNA duplexes, while ropes show the RNA backbone, colored according to the nucleotide sequence.

By contrast, ISIM was built from the bottom up. Its interface hides complex computations that formed the basis of several publications by **J. Andrew McCammon, PhD**, and his colleagues at the University of California, San Diego as well as a 2006 dissertation by then–Stanford student **Mark Engelhardt, PhD**. For Bruns, the challenge was to take that complexity and put an easy-to-use wrapper around it. And easy it is, with four buttons to click: choose your molecule, choose the ion conditions, simulate the ions, and view the results. But, unlike ToRNADo, the application is highly specialized. Biology labs that do experiments to count ions around RNA molecules will use ISIM to help plan experimentation.



This molecular surface of yeast phenylalanine transfer RNA was generated using ISIM and visualized using Pymol. It shows areas of negative (red) and positive (blue) electrostatic potential as well as locations where high concentrations of magnesium ions appear in the ion atmosphere around the molecule (green).

Of course, ToRNADo and ISIM are exciting not only because they have helped Simtk.org develop user-friendly GUIs. They are valuable research tools for basic science. "ToRNADo can provide some nifty coarse-grained representations," says Bruns, "We have a special interest in coarse-grained views because that makes larger problems become more tractable." And ISIM advances efforts to simulate the molecular dynamics of RNA, Bruns says. "Simulating the ion environment more accurately will improve our understanding of how these important biological molecules fold and function."

Together, the new tools provide the building blocks for numerous future applications, Bruns says. The ISIM wrapper will help Simbios create user-friendly applications from complex computation, while ToRNADo provides a model for enhancing simple applications by bridging to underlying computational tools. "This is an important step for building best-of-breed tools for simulating molecules," says Bruns. □

Simbios is a National Center for Biomedical Computing located at Stanford University.