



RESEARCH_{NEWS}

Research Communications, 1125 Kinnear Road, Columbus, OH 43212-1153
Phone (614) 292-2711, Fax (614) 292-0154

Embargoed for release until 8:30 a.m. CST on Tuesday, March 4, 2003, to coincide with presentation at the American Physical Society meeting in Austin.

MATHEMATICAL MODELS REVEAL "MOLTEN" AND "GLASSY" STATES OF RNA

AUSTIN, Texas -- Mathematical models have given physicists a new look at DNA's chemical counterpart, RNA.

The models -- showing that RNA behaves differently depending on the temperature of its environment -- may help biologists better understand how life evolved on Earth.

The models suggest that high temperatures give twisted strands of RNA the flexibility to fold into many different shapes, while low temperatures cause it to collapse into a single shape.

Ralf Bundschuh, assistant professor of physics at Ohio State University, presented the results March 4 at the meeting of the American Physical Society in Austin, Texas.

RNA plays many different roles in a cell, such as the production of proteins that perform necessary functions, Bundschuh explained.

"People are probably more familiar with the genetic role of DNA, in which two strands of complementary base units bind to each other to create a double-helix structure. RNA behaves very much like a DNA molecule that has lost its complementary partner. In order for one strand of bases to form pairs, the strand must bend back onto itself -- it must fold," he said.

The structure of folded RNA resembles a severely twisted rubber band, with the shape of loops and branches determining its biological function.

RNA TURNS MOLTEN OR GLASSY -- 2

Exactly how RNA folds into any particular shape is a mystery. Other researchers have tried to tackle the problem with computer simulations, by calculating the possible formations that result from a certain number of base units coming together. But simulating very realistic RNA molecules -- that is, very long RNA strands with many base units -- is difficult.

Bundschuh and Terence Hwa of the University of California, San Diego, examined the problem differently. They have developed the first mathematical theory for the possible states of an RNA molecule.

In the past, scientists only knew for sure that RNA could fold into a given configuration, depending on its chemical makeup. Instead, these mathematical models show that high temperatures cause RNA to enter a flexible state in which it can take on a variety of configurations. The flexible state is known as the "molten" state. When temperatures fall too low, the RNA enters a tangled, or "glassy," state.

"We know at high temperatures RNA is molten, and low temperatures, it is glassy. Somewhere in between, something has to happen to change its state from one to the other. We don't know what that is, yet," Bundschuh said.

Whether RNA forms a functional structure depends on the alignment of four base units -- adenine, guanine, cytosine and uracil -- a sequence of which resembles a strand of beads. When molten, the strand folds and unfolds with ease, and each base unit can connect with many different mates to form many possible overall shapes. In the glassy state, the strand "freezes" in a random pattern.

The results hold implications for the study of the related "protein folding problem." Researchers are working to understand the issues nature has to overcome to design new RNA sequences, because someday researchers may be able to design sequences themselves, for drugs or other disease therapies.

"One does not want to end up with a sequence that gets stuck in some random structure, or cannot decide which structure to fold into," Bundschuh said.

The work also has broader relevance for evolutionary biology, where experts have speculated that early life might have relied exclusively upon RNA.

RNA TURNS MOLTEN OR GLASSY -- 3

"RNA could in fact be a stepping-stone to today's world of DNA. DNA cannot replicate without proteins, and proteins cannot be produced without RNA," Bundschuh said. "You could say we're characterizing what evolution is up against."

With five years' effort, Bundschuh and Hwa have only just begun to be able to model simple RNA activities that occur in less than a second, countless times every day.

"Now we can better appreciate what biology has to do to create a functional RNA molecule," he said.

Ohio State physics doctoral student Tsunglin Liu is working with Bundschuh to estimate how many base units would be required for computer simulations of more realistic RNA models, in order to observe the molten or glassy state. Liu has found that more than 8,000 units are necessary -- a computational task well beyond the reach of current studies, which are based on as few as 2,000 units.

#

Contact: Ralf Bundschuh, (614) 688-3978; Bundschuh.2@osu.edu

Written by Pam Frost Gorder, (614) 292-9475; Gorder.1@osu.edu

Editor's note: During the American Physical Society (APS) meeting, Bundschuh can be reached at the La Quinta Inn at (512) 476-1166. In addition, the APS is hosting a press conference for this and related RNA research in room ML2 of the Austin Convention center at 11:00 a.m. CST, Tuesday, March 4, 2003.