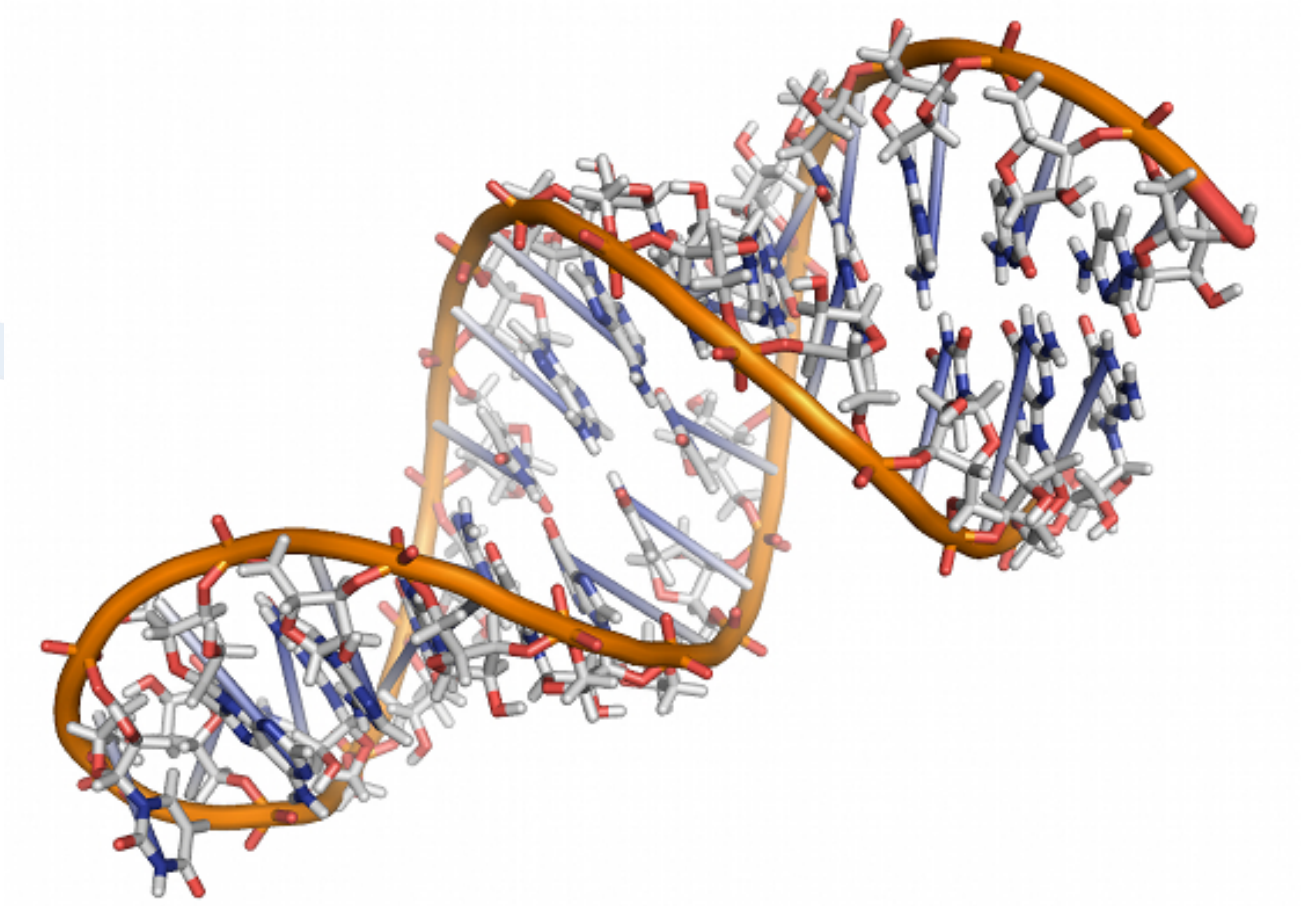
Choosing Correct Models



Physical Models of RNA in Molecular Dynamics under scrutiny

September 28,2016

A group from the International School for Advanced Studies (SISSA) in Trieste has developed a faster and simpler methodology requiring modest resources for validating physical models ("descriptions" of molecule operation) of RNA used in molecular dynamics. These models are essential for research on RNA, one of the most important macromolecules of life, with computer simulations. The method also helps define areas of improvement for increasing accuracy of the models. The study was published in the *Journal of Physical Chemistry Letters.*

Imagine having to rent a car by choosing from a catalog with nothing but photos: no make or model, no data sheet. You have specific requirements, however. You need a sturdy car suitable for rough terrain and steep inclines (this year you have opted for an adventurous vacation "in the

wild"). To better understand which car would be most suitable for your needs, you would create a hypothetical model of the vehicle in your mind based on its appearance and your prior knowledge of cars. The hypothesized model would tell you if the image you see corresponds to a small city car, a sports car or an SUV, and this would be the basis of your choice. It would then be the experience of placing your hands on the wheel that would tell you if your assumptions were right or wrong.

Scientists like SISSA Professor Giovanni Bussi are doing something similar in their study of RNA in molecular dynamics. "We study RNA through computer simulations. We start from the structure of the molecule, which is described in a precise way by experimental measurements, kind of like the car photos in the example," says Bussi. "The structure, being the result of experimental observation, is accurate within a good approximation. The real issue is with the physical models."

It is like holding a three-dimensional model of a molecule. In order to experiment, even virtually, (through simulation), you must know how the different parts that make up the molecule move together, how they interact, how the structure can deform. This information makes up the so-called "physical" model. "The problem is that the assumptions the model is based on are not always verified or easily verifiable," says Bussi. "There is a risk that the model will eventually prove wrong, that it does not correctly describe the behavior of the molecule, which means results based on these simulations may be unreliable."

Smart Strategies

Molecular Dynamics is used for other types of molecules besides RNA. "For example, David Shaw, founder of the high-tech firm, D.E. Shaw & Co, and his group have done a tremendous job of validating physical models of proteins, which has allowed us to do some serious clean-up in the field."

Works like this require a lot of time and powerful computer equipment, however, as it means painstakingly examining each individual model, before developing it and testing it in its complete form. This can mean several months of computing time. "Unfortunately, no data exists for RNA at present," notes Bussi. For this reason, he and his team sought a viable solution by developing a "smart" methodology for validating RNA templates.

"We do not do extensive analysis like Shaw did for proteins, but we adopted strategies to reduce complexity and calculation time, while preserving accuracy in our results." How well do the current RNA physical models measure up in these analyses? "Not well, unfortunately. The model we tested, which was supposed to be one of the best in the literature according to tests made by others, does not allow us to make correct predictions on the structure of an RNA molecule." Back to the drawing board? "I would not be so drastic. There is no need to destroy all that has been done so far. The important thing is to work on improving the current models. The value of our

method is that it indicates where and how the model is wrong in order to provide solutions on how to improve it. "

USEFUL LINKS:

- **Link to the original paper on *Journal of Physical Chemistry Letters:***
  http://dx.doi.org/10.1021/acs.jpclett.6b01905

IMAGE:

- **Credits: Luuva (Wikimedia Commons: https://goo.gl/PKR2LO)**

Contatti:

Ufficio stampa:
pressoffice@sissa.it
Tel: (+39) 040 3787644 | (+39) 366-3677586

via Bonomea, 265
34136 Trieste

Maggiori informazioni sulla SISSA: www.sissa.it