UM scientists demonstrate role of RNA polymerase in gene transcription

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In all organisms, RNA synthesis is carried out by proteins - known as RNA polymerases (RNAPs) - that transcribe the genetic information from DNA in a highly-regulated, multi-stage process. RNAP is the key enzyme involved in creating an equivalent RNA copy of a sequence of DNA. This transcription is the first step leading to gene expression. While the major steps in RNA synthesis have been known for several decades, scientists have only recently begun to decipher the detailed molecular steps of the complex transcription process.

In research published in the July 1, 2010 online Early Edition of the Proceedings of the National Academy of Sciences, University of Maryland biophysicists Devarajan (Dave) Thirumalai and Jie Chen, along with Rockefeller University collaborator Seth Darst, provide new insight into how the transcription process is initiated and the role that RNA polymerase plays in making this happen. Because the sequence, structure, and function of multi-subunit RNA polymerase are universally conserved in all organisms -- from bacteria to humans -- understanding the mechanisms of bacterial gene transcription is an important step in deciphering the role of genetics in disease.

"Previously, people didn't know the precise role of RNA polymerase in initiating transcription," explains Distinguished University Professor Dave Thirumalai (Department of Chemistry and Biochemistry and Institute for Physical Science and Technology), "but we showed that it plays an important role in forming the transcription bubble and in the process of bending the DNA to facilitate entry of DNA into the active

site. That is the process we described computationally."

Their simulation of the initiation phase of transcription in bacterial RNA polymerase showed a three-step process. It begins when the RNA polymerase binds with transcription promoting regions of DNA. Through interactions with the RNA polymerase, the DNA helix then unwinds, forming an open "bubble" that allows the polymerase access to the exposed DNA sequence to begin transcription. The DNA molecule then bends to relieve stress produced by the opening.

Dr. Jie Chen, who conducted this research while a graduate student in the Chemical Physics program, simulated the transcription bubble formation using a Brownian dynamics-based computer model developed by Dr. Thirumalai's laboratory. "By creating this molecular movie, we can look at the dynamics of RNAP and simulate how it shifts from one structure to another structure," explains Chen. "Our simulation confirms experimental observations, and goes further to establish a clear and active role for RNA polymerase."

Dr. Thirumalai's research group is continuing to study RNA polymerase by looking at the second phase of the transcription process in bacteria and also through models of human transcription.

More information: The paper "Promoter melting triggered by bacterial RNA polymerase occurs in three steps" was written by Jie Chen, Seth A. Darst, and D. Thirumalai.

Provided by University of Maryland

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