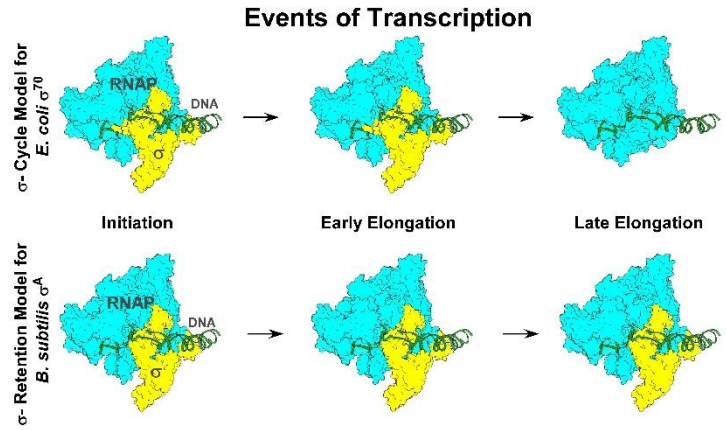
Study by Bose Institute scientist Challenges Longstanding Dogma of Bacterial Gene Regulation

Researchers from Bose Institute, in collaboration with Rutgers University, show the "σ cycle" is not universal across bacteria

A new study published in the *Proceedings of the National Academy of Sciences (PNAS)* overturns a central textbook model of bacterial gene regulation. Researchers from the Bose Institute and Rutgers University report that, contrary to decades of scientific belief, the principal transcription initiation factor in *Bacillus subtilis*—σA—and a modified version of the *Escherichia coli* σ70 factor remain bound to RNA polymerase throughout transcription, rather than being released after initiation.

For nearly 50 years, the so-called "σ cycle" model has proposed that σ factors bind RNA polymerase to initiate transcription and then dissociate to allow elongation. This concept was built largely on observations of *E. coli* σ70. However, the new findings reveal that the cycle is not a universal phenomenon.



Prof. Jayanta Mukhopadhyay from the Bose Institute, whose lab works on understanding the fundamental mechanism of transcription and gene regulation in bacteria, is the lead author of this study, doi:10.1073/pnas. 2503801122.

The central dogma of molecular biology depicts the unidirectional flow of genetic information from DNA to RNA to protein. In this essential process for life, the information encoded in the DNA (gene) is transcribed into RNA as the messenger carrying instructions, which is finally translated into proteins that carry out the cellular tasks. This flow occurs through DNA replication (DNA to DNA), transcription (DNA to RNA), and translation (RNA to protein).

RNA polymerase, the enzyme responsible for transcription, orchestrates gene expression by various sigma (σ) factors and transcriptional regulators. Bacteria in general contain several σ factors. During normal growth conditions, bacteria use a principal σ factor, whereas under different environmental stimuli, the other σ factors are used. The "σ cycle" has been considered an essential step for σ-exchange, involving all principal σ factors from various bacteria. However, the study from Jayanta Mukhopadhyay's lab shows that the "σ cycle" may not exist across all bacteria. Their *in vitro* and *in vivo* assays confirm that, in contrast to *E. coli* σ70, the *B. subtilis* principal σ factor, σA and a mutant of σ70 without region 1.1 are not released and are stably associated with RNAP core throughout transcription elongation. Notably, σ contains four conserved regions: 1.1, 2, 3 and 4. Comparison of the conserved regions between σ70 and σA indicates that while regions 2, 3, and 4 exhibit a higher degree of sequence similarity between these two proteins, region 1.1 has less sequence similarity. Thus, the structural organisation of σ and its interactions with RNAP would dictate whether σ would be retained or released during transcription elongation.

The discovery has broad implications for microbiology, potentially influencing how researchers approach bacterial physiology, stress response, and the development of antibiotics targeting transcription.

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