

## How actinomycin binds to DNA and exerts its mechanism of action

In this remarkably simple and profound article — recently appearing in the March issue of the Journal of Structural and Functional Genomics — Henry M. Sobell describes his theory for the existence of “premeltons” in DNA — this providing a unifying explanation of much of DNA physical-chemistry and molecular-biology.

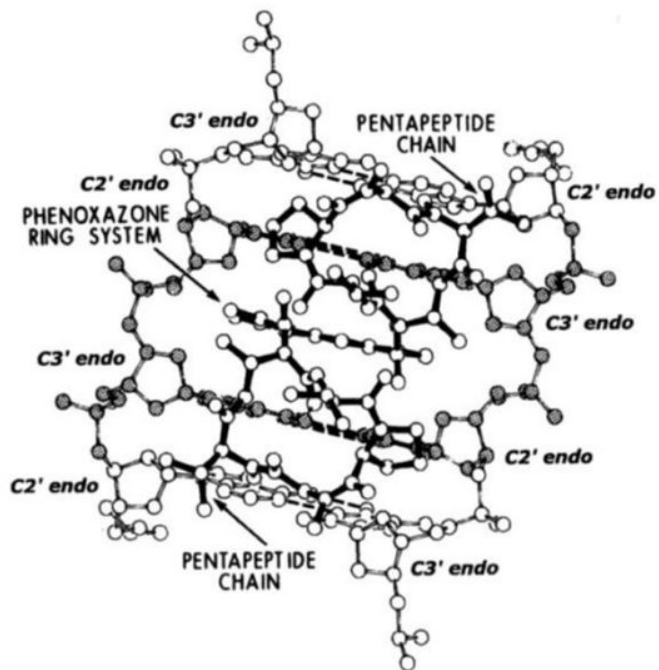
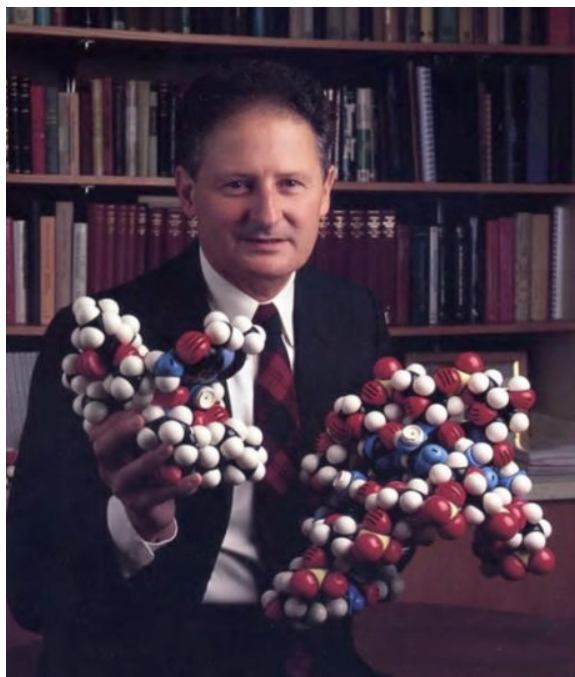


Fig. 1.

Key among these — is an understanding of how the anticancer agent actinomycin D binds to DNA and exerts its mechanism of action. His photo in Figure 1 — taken a number of years ago — shows Professor Sobell holding CPK space filling molecular models of actinomycin intercalating into (what he has called) the beta-DNA structural-form — this being a metastable and hyperflexible liquid-like phase that acts as a transition-state intermediate in DNA melting.

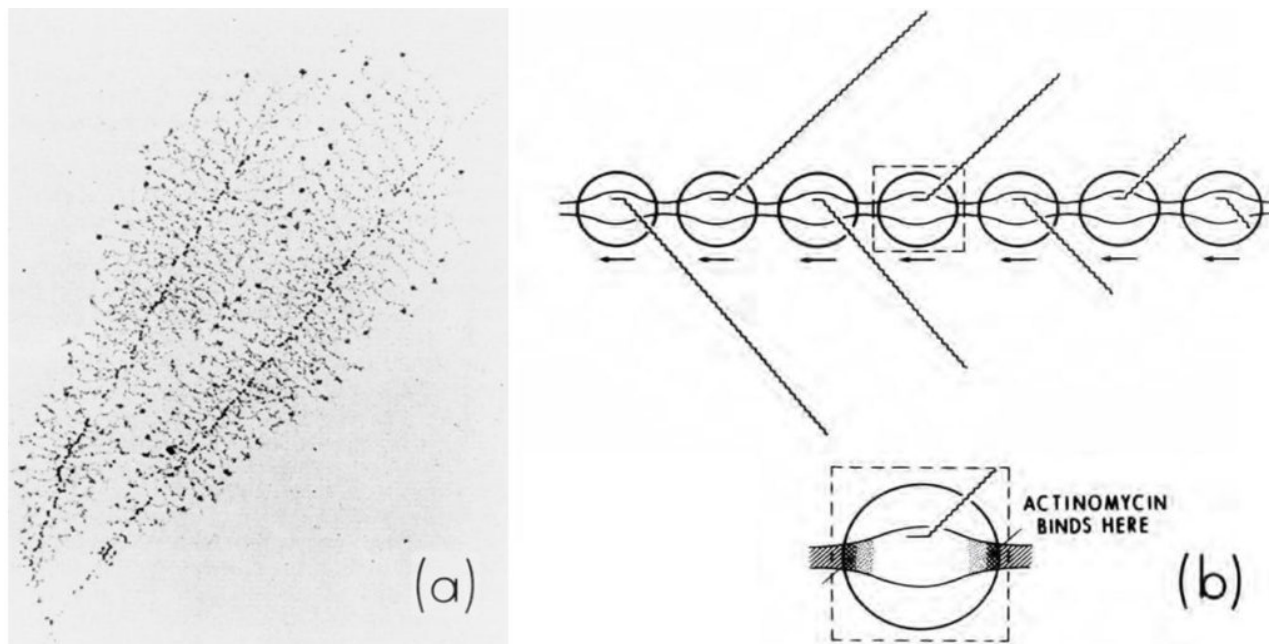


Fig. 2.

As can be seen in Figure 2, actinomycin binds to the highest-energy beta-DNA form found within the boundaries connecting double-stranded B-DNA with single-stranded DNA in the transcription complex. This immobilizes (i.e., “pins”) the complex, interfering with the elongation of growing RNA-chains. In nucleolar genes, where there be as many as 200 RNA polymerases moving down the DNA template while synthesizing growing ribosomal RNA-chains — positive and negative superhelical DNA regions between them annihilate one-another — causing adjacent transcription-complexes to bond-together to form “trains” of transcription-complexes, these now moving synchronously along DNA. If this were the case, then the binding by one actinomycin molecule is sufficient to stop the entire “transcription-train” from moving along DNA.

This insight is among many others that can be found in this fascinating article published by Professor Sobell.

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## Publication

[Premeltons in DNA.](#)

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