

Biophysics Seminar 3/5/18

"The action of Human DNA Primase"

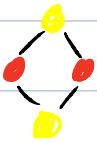
Walter Chazin - Vanderbilt

- Primase makes the first copies of the DNA during replication
 - ↳ only enzyme that can act upon single-strand DNA
- SAXS (small angle x-ray scattering)
 - ↳ population weighted average with parameters sensitive to dynamics
- Power analysis - tells something about the flexibility of the system (what is this?)
- Original crystal structure was inactive conformation
 - ↳ built the real structure out of bits of other info. and crystal structures.
 - ↳ made a movie to simulate the transformation from inactive to active conformation.
- including cofactors reduces the sampling space of the enzyme (2.9 \rightarrow 3.4). Not crystallizable, but close.
- closed configuration is sampled even by primase which is free of cofactor
- ★ - initiation is a rare event; fast, but rare
 - ↳ is this surprising? Most, if not all, enzymatic reactions are fast but rare events
 - ↳ is primase something special from other enzymes?
- linker region between the domains may be a mechanical

for counting the number of nucleotides that have been counted (the domain gets "caught" on the end of the end of the sequence.

- 4Fe-4S cluster in one of the domains

↳ not really known what it does, but it does have some functional relevance
↳ iron clusters are cool



- Look up: DNA can act as a wire (charge transfer)

- This primase reduces DNA, but doesn't oxidize back to original state.

↳ not destroying DNA, is reversible: oxidized protein has a higher affinity for the DNA than the reduced form.

(this is neat) ↗

↳ reversible once the primase diffuses away from the DNA.

- in the model, the primase sends charge down the copied DNA to oxidize the polymerase to cause handoff.