

# The Workings of a Complex Molecular Machine

## RNA Polymerase: DNA → RNA

Combining Biology with Spectroscopy with Computation

Chem 121H - Fall 2011

Craig T. Martin

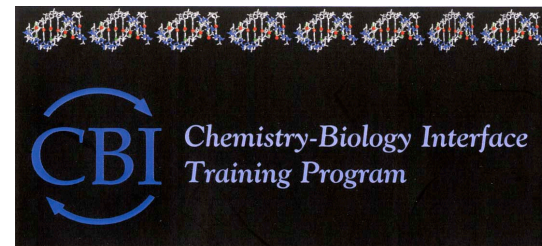
Department of Chemistry

Adjunct, Dept of Biochemistry & Molecular Biology

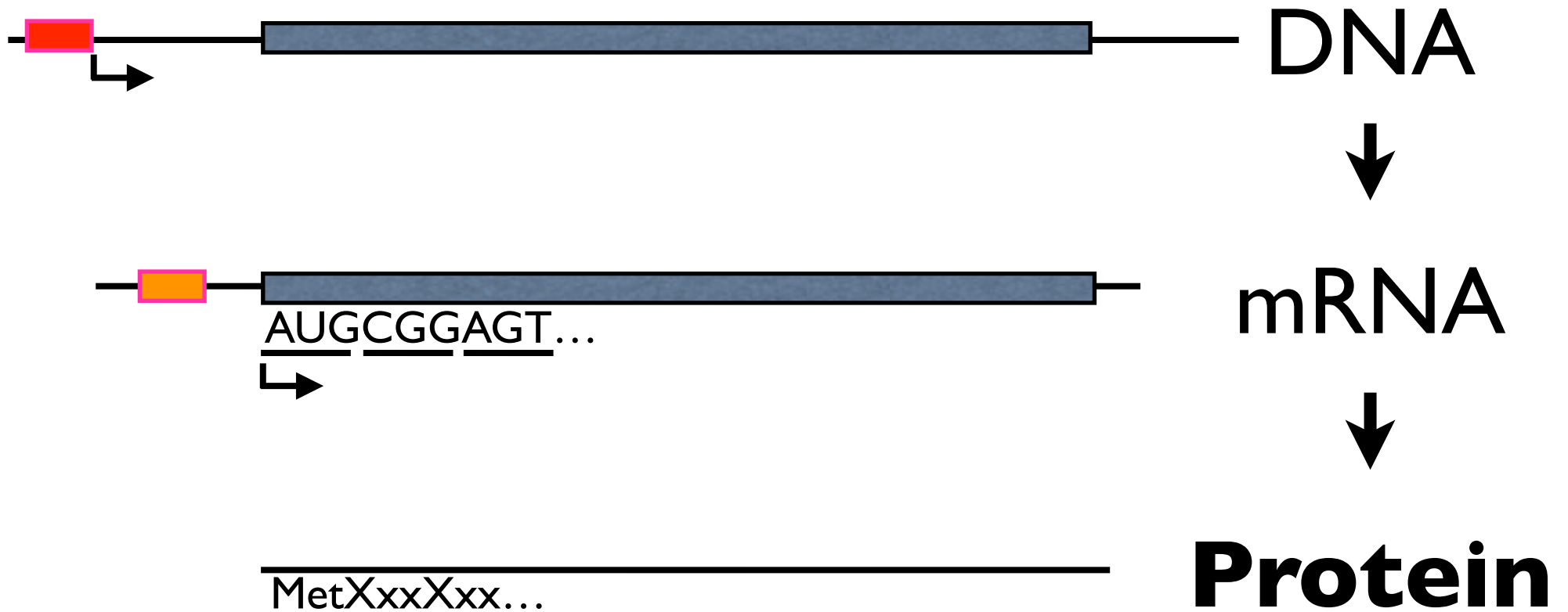
Member, Program in Molecular & Cellular Biology

University of Massachusetts

Amherst, MA



# 20th Century Biology

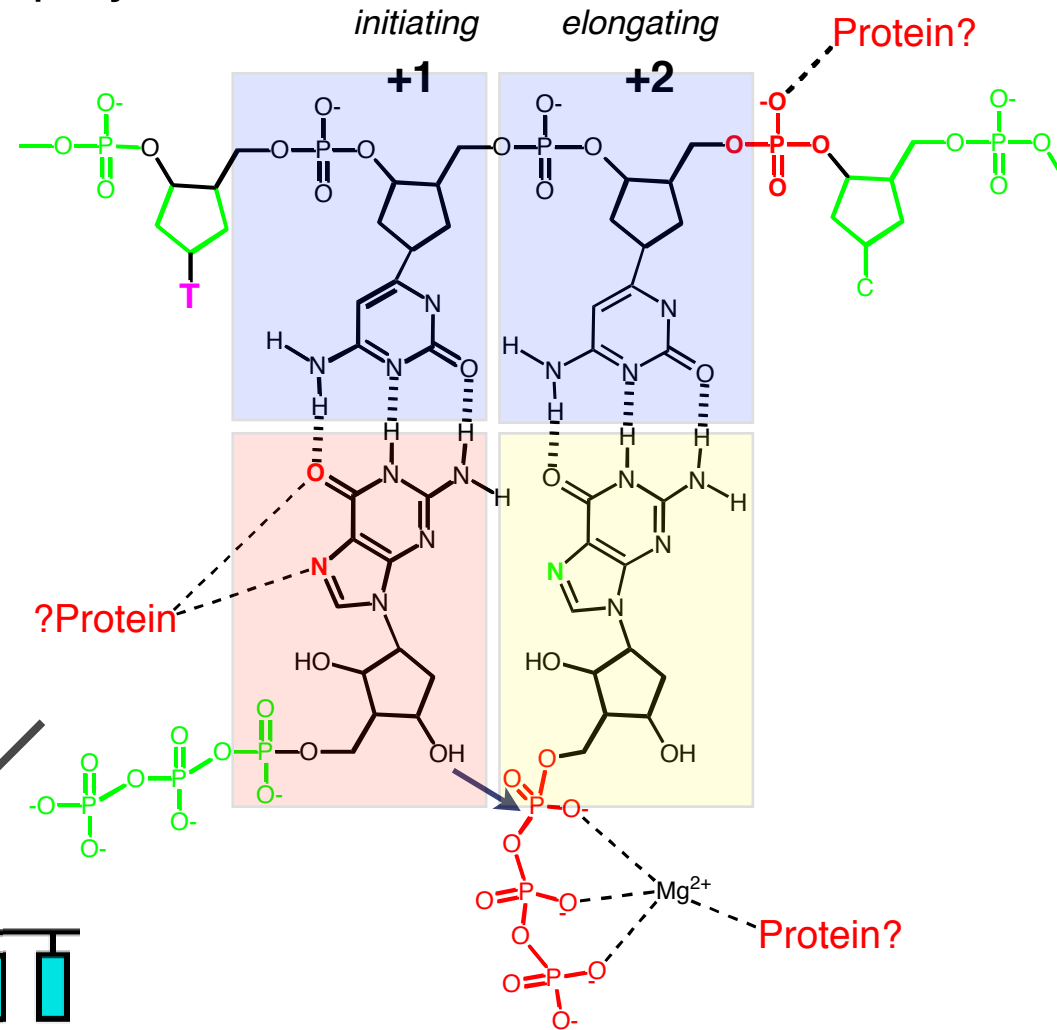
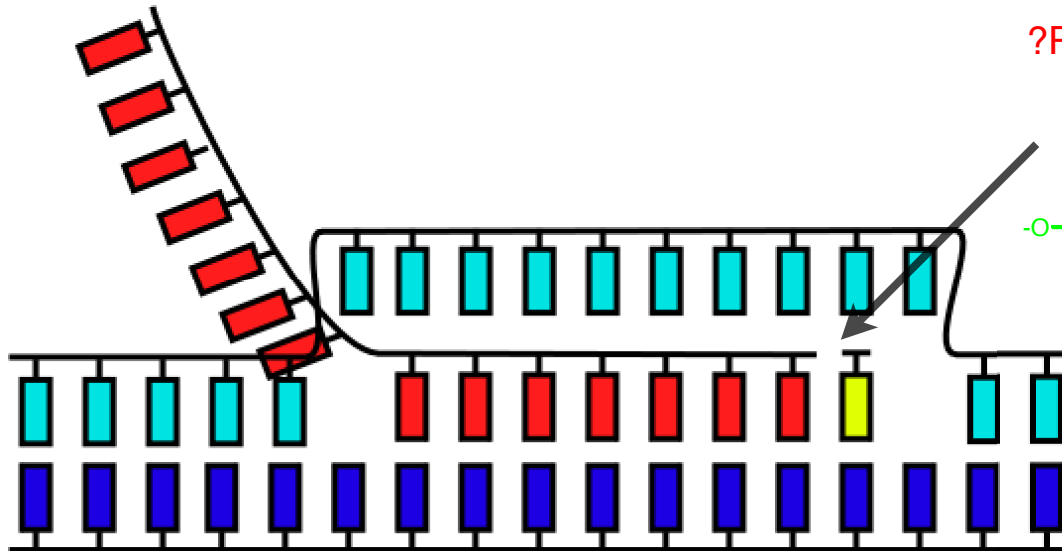


# RNA Polymerase

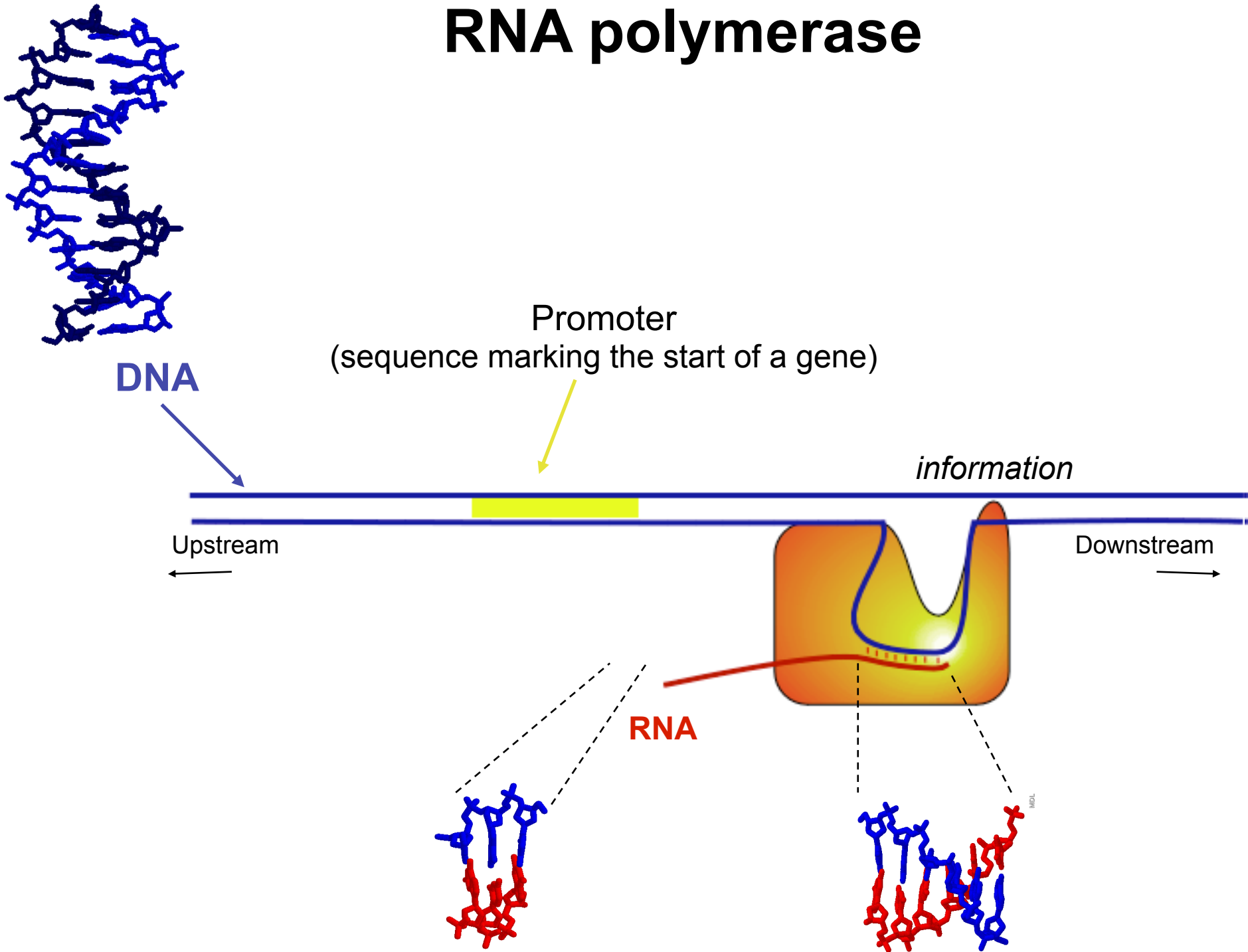
- Catalyzes the synthesis (polymerization) of RNA from a DNA template
- Synthesizes **very** complex, precise polymers
- Very high fidelity (few mistakes)

Covalent Chemistry:

Phosphoryl Transfer

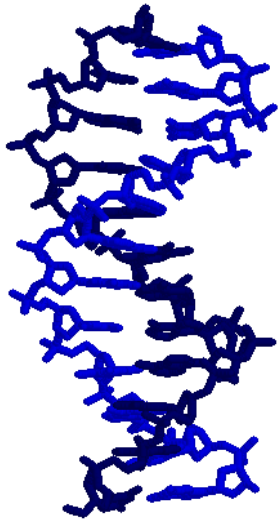


# RNA polymerase

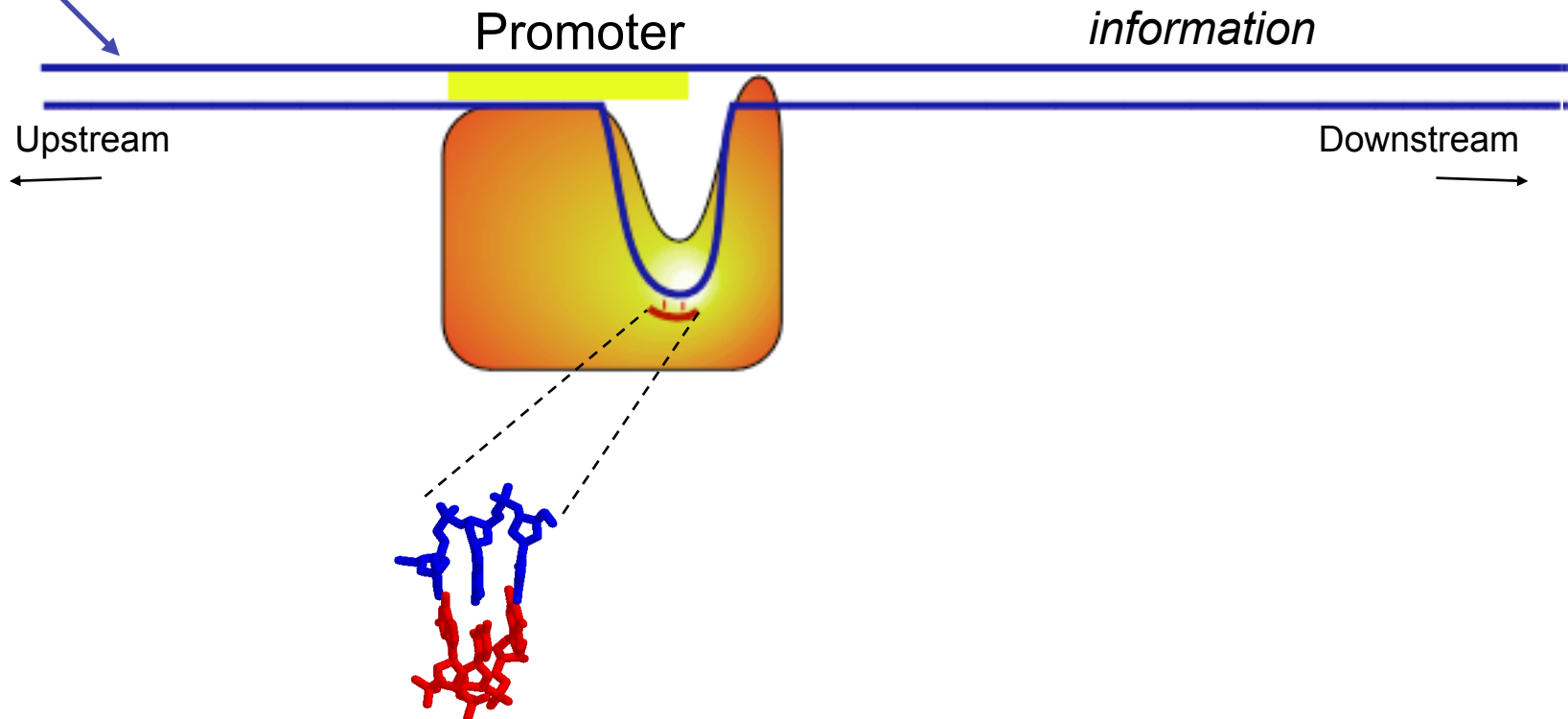


# Questions

- How does it know where to start?
- How does it melt the DNA at that site?
- How does it initiate synthesis *de novo*?



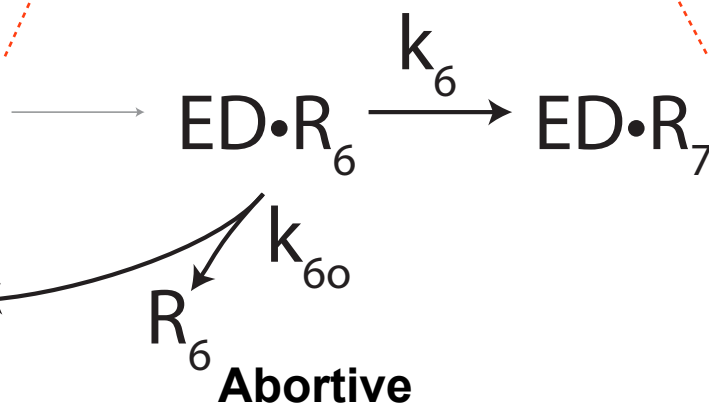
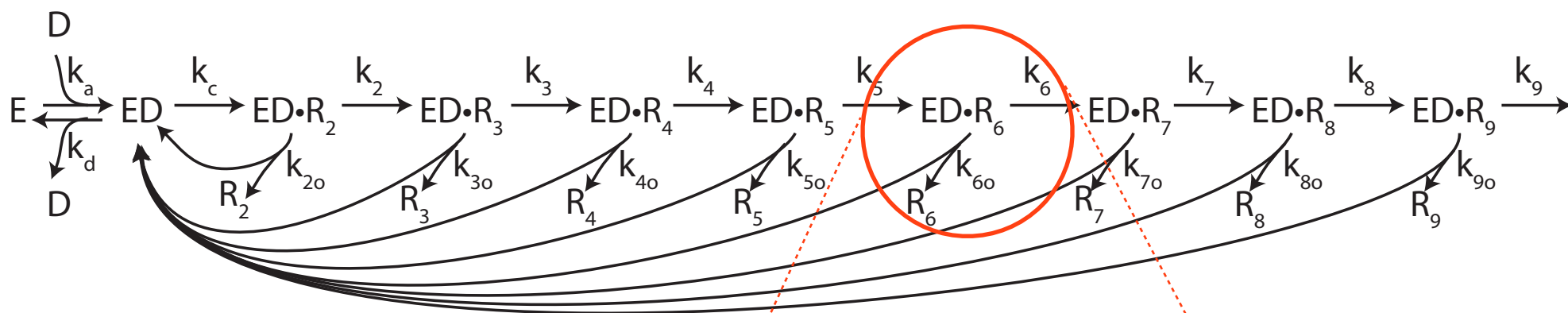
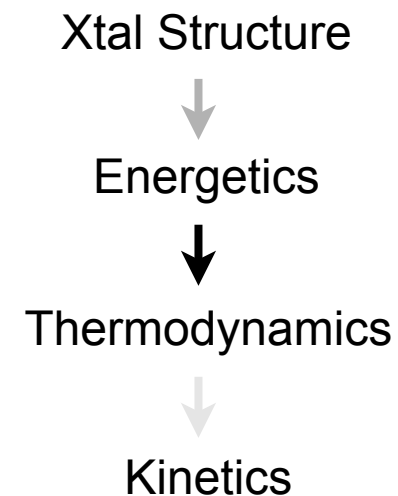
DNA



Nobel  
Prize in  
Chemistry  
2009!

# Initial Transcription

Lots of Structural Data  
Very Little Mechanistic Data

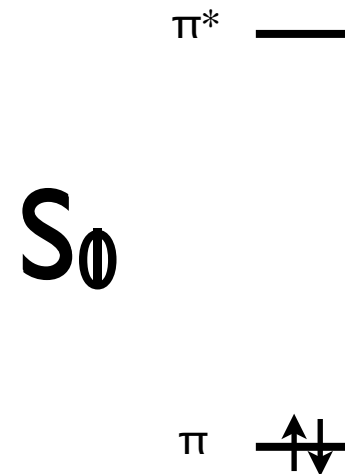
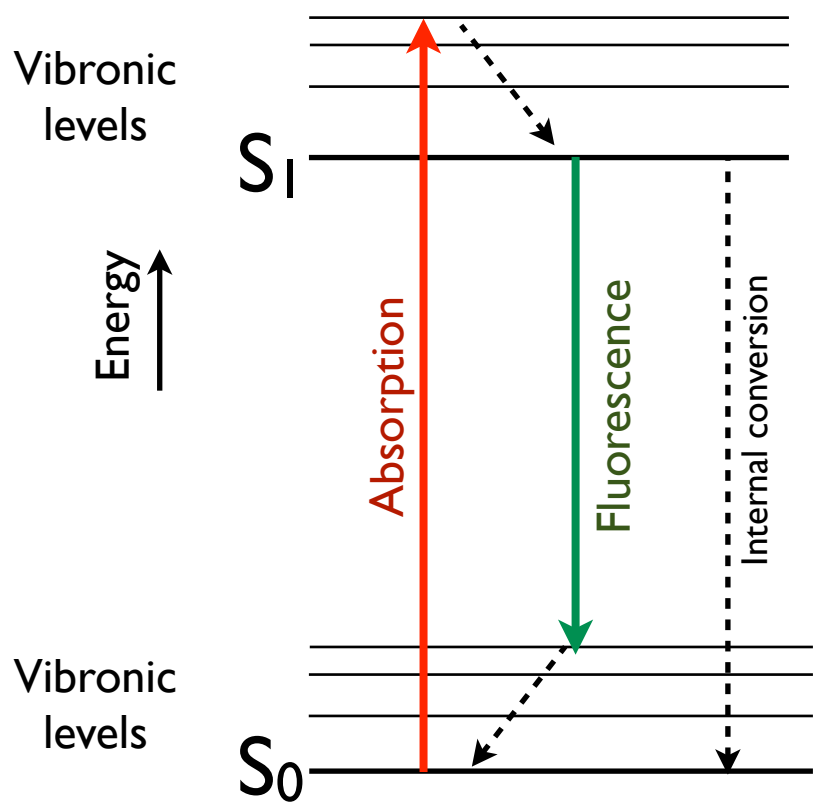


Kinetic Competition

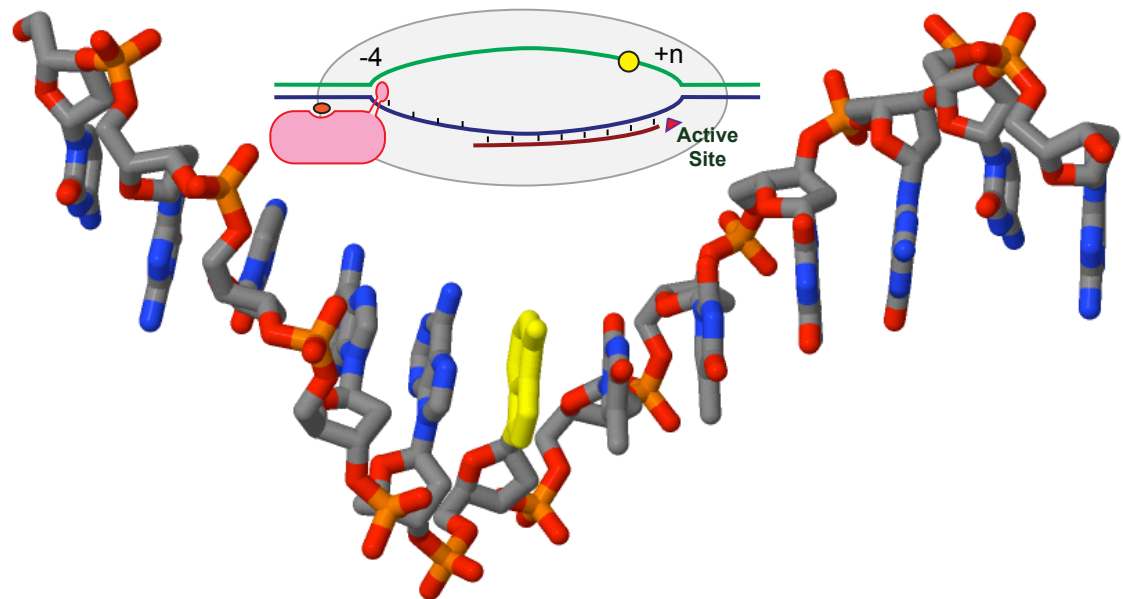
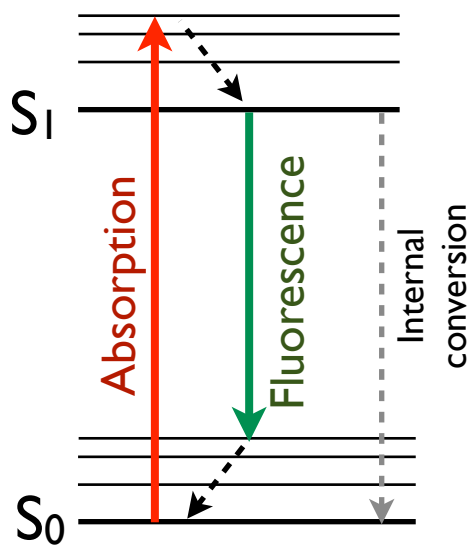
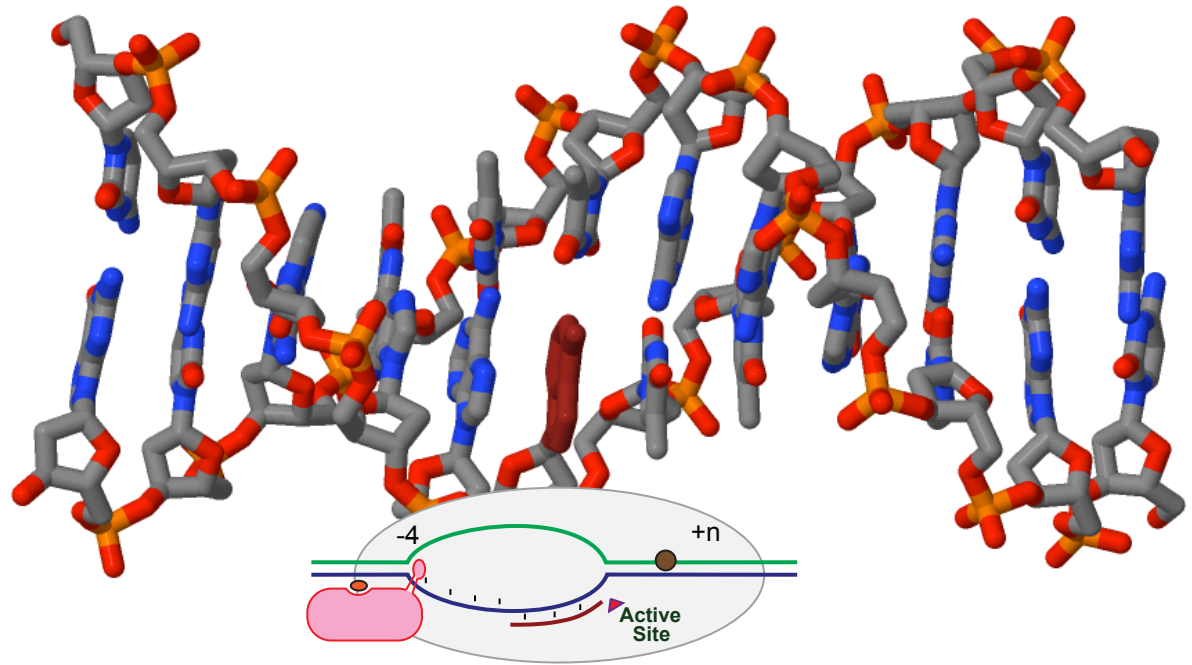
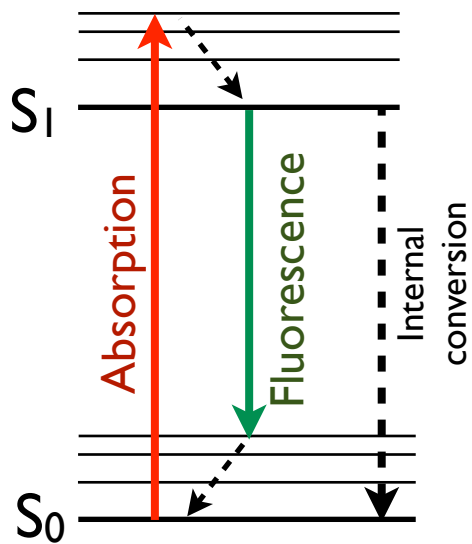
# Electronic Energy Levels

→ Radiative (photon)

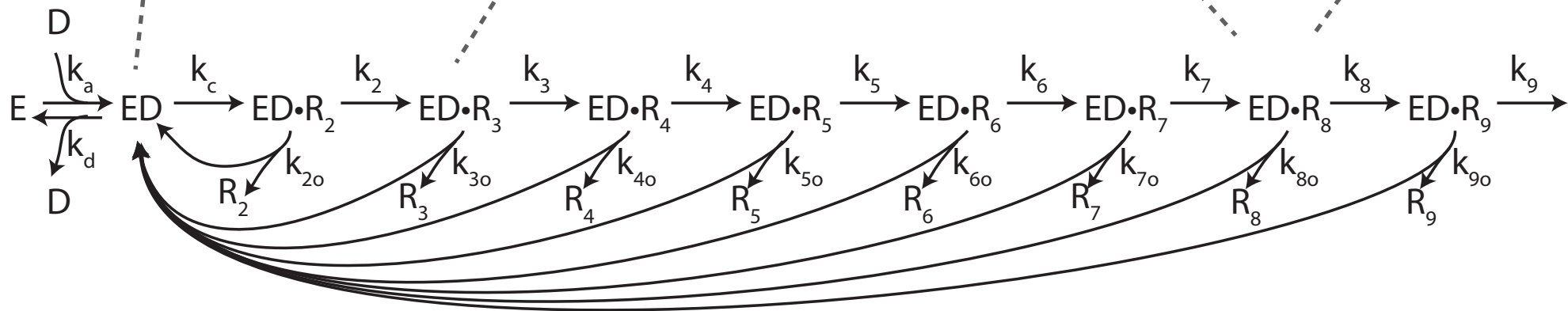
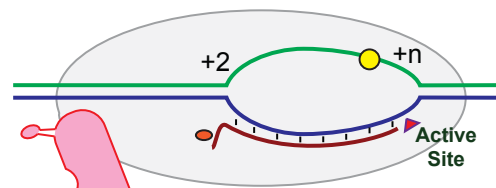
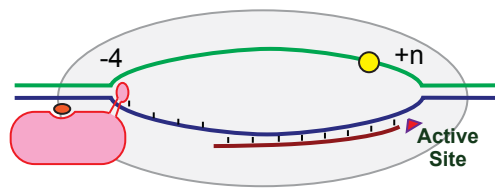
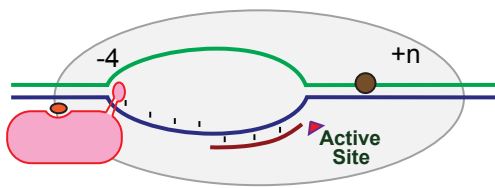
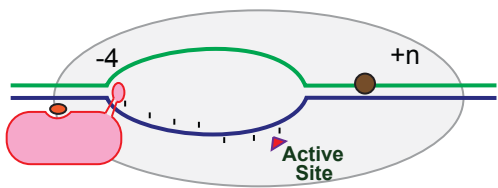
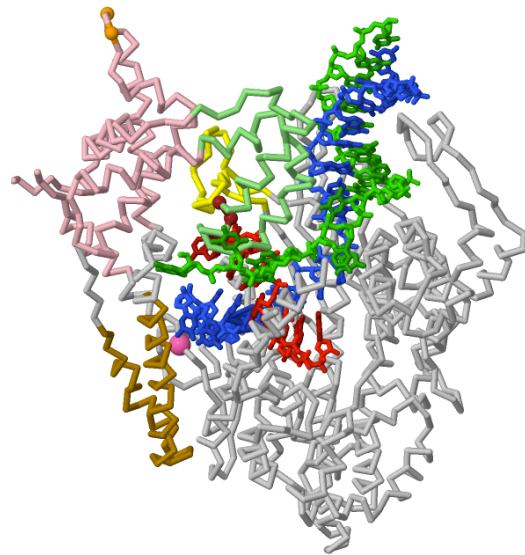
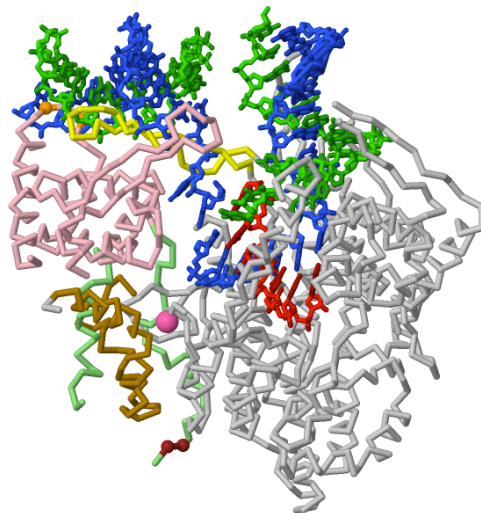
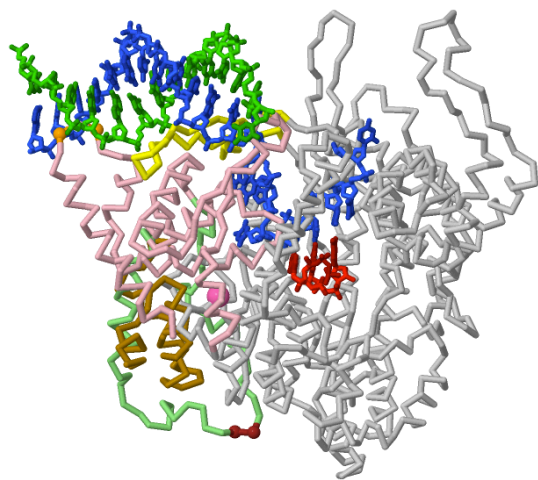
-----> Nonradiative (phonon/lattice vibrations)



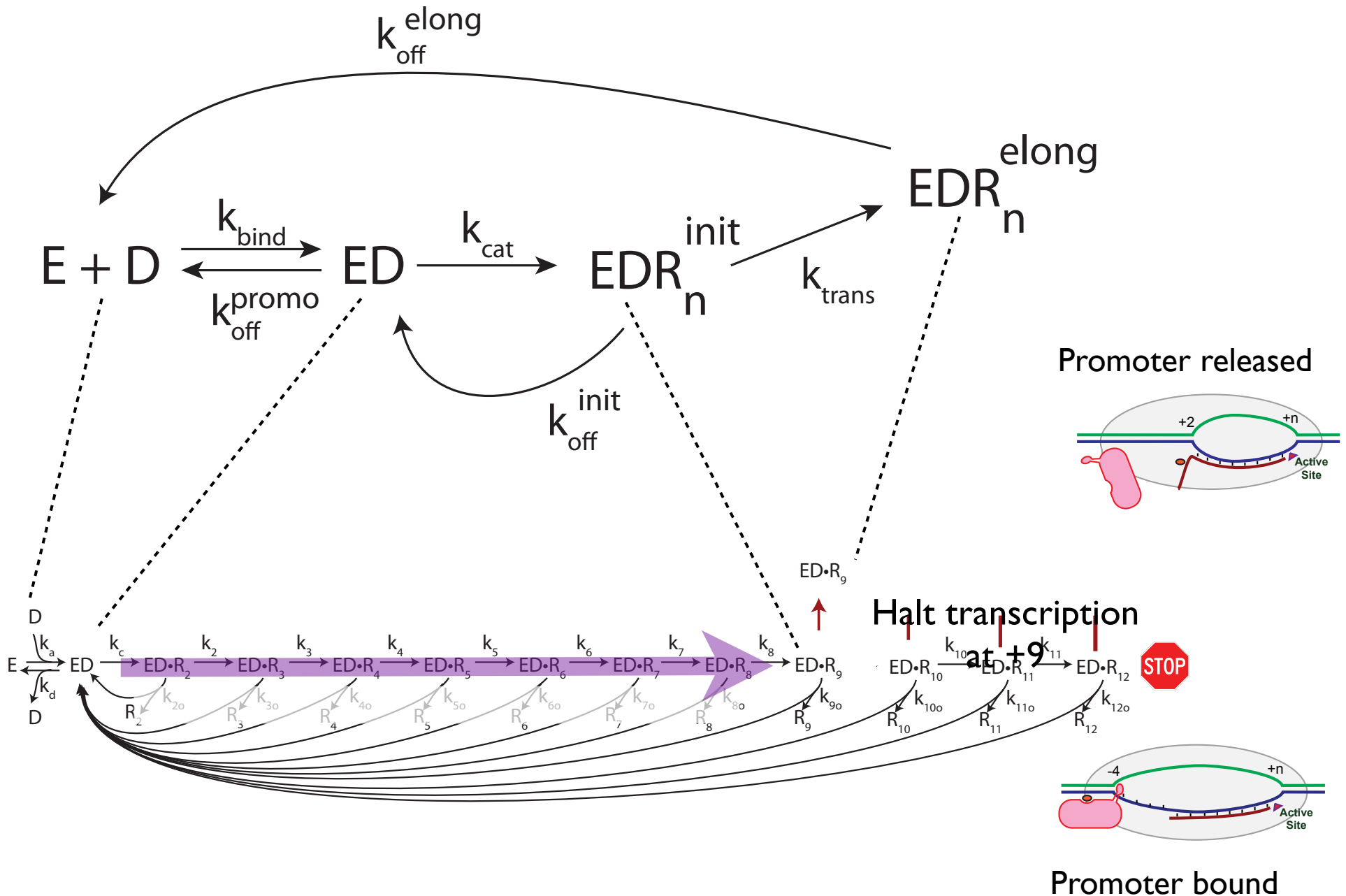
# Fluorescent Base Analog Reporter



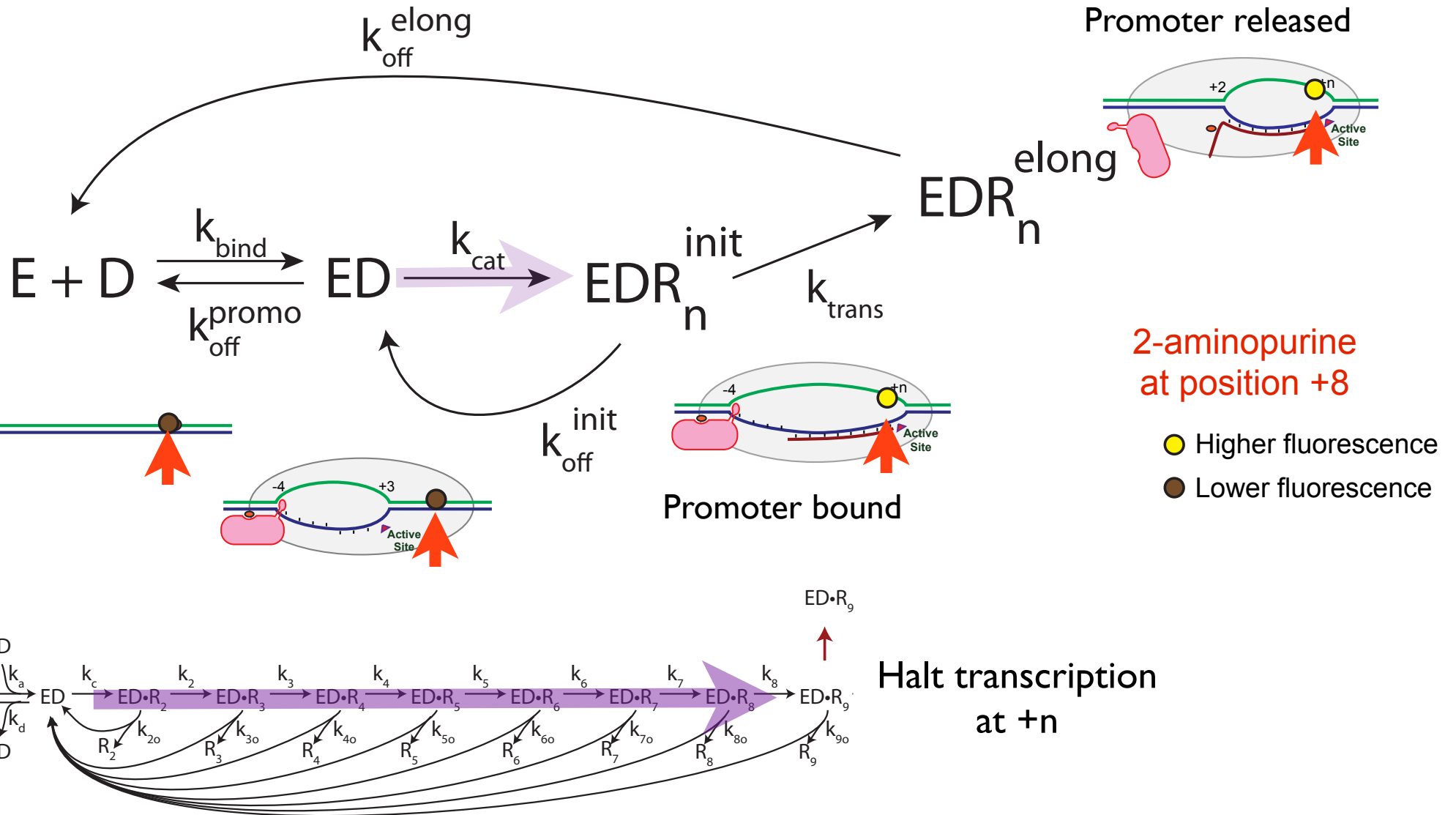




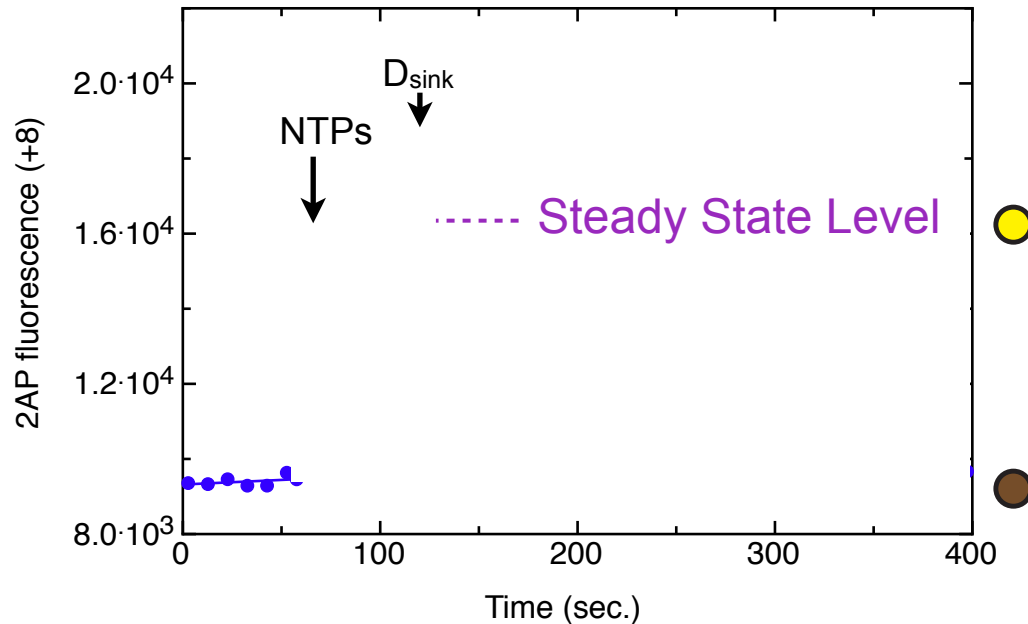
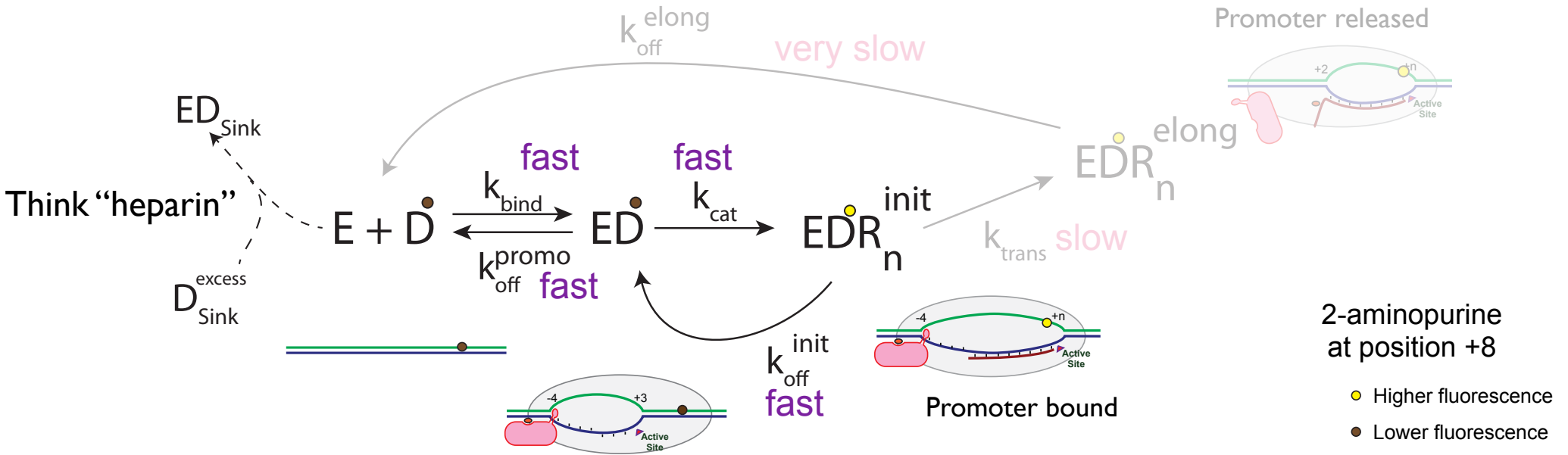
# Kinetics of Initial Transcription



# Kinetics of Initial Transcription



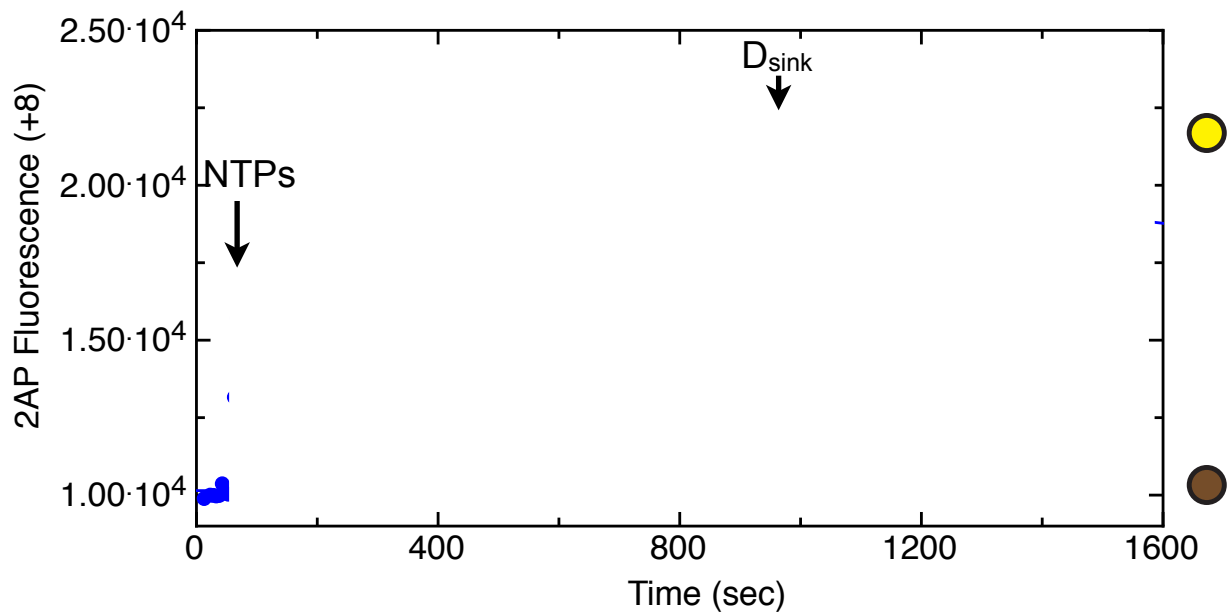
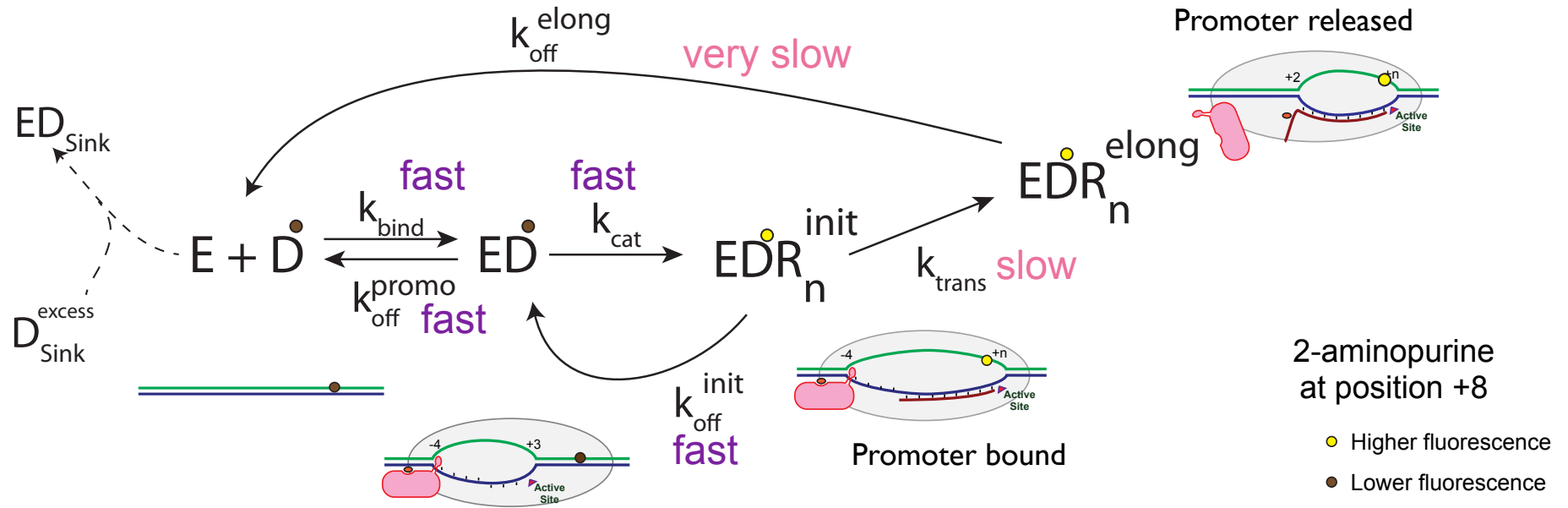
# Kinetics of Initial Transcription



Walk to position +8  
with G, A, U

$\rightarrow$   
 GGGAUUAUACCA...

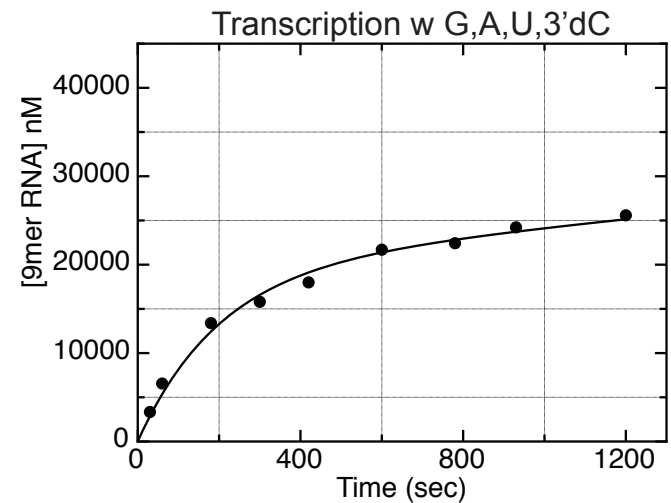
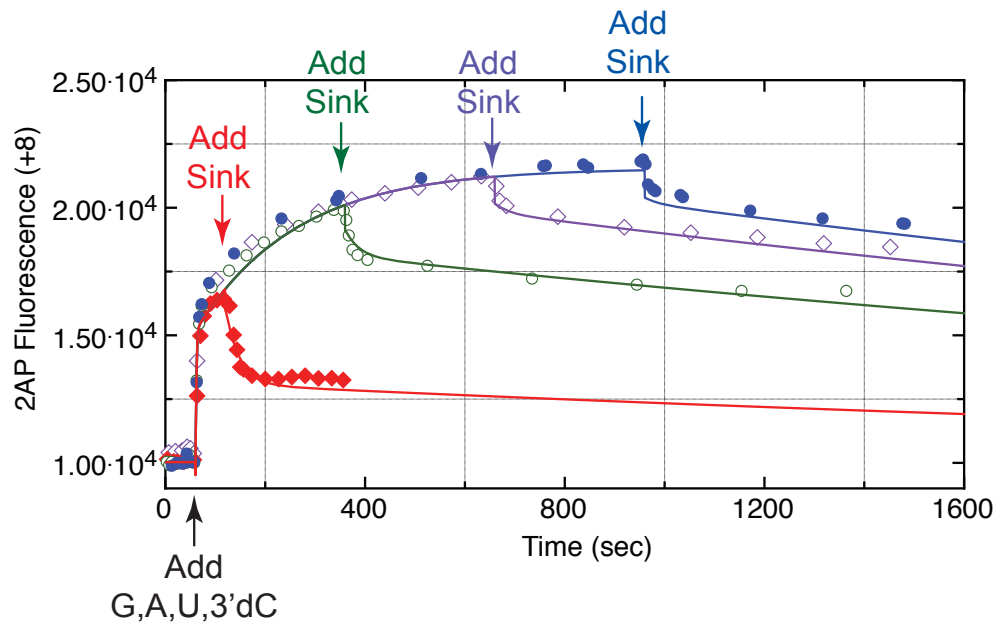
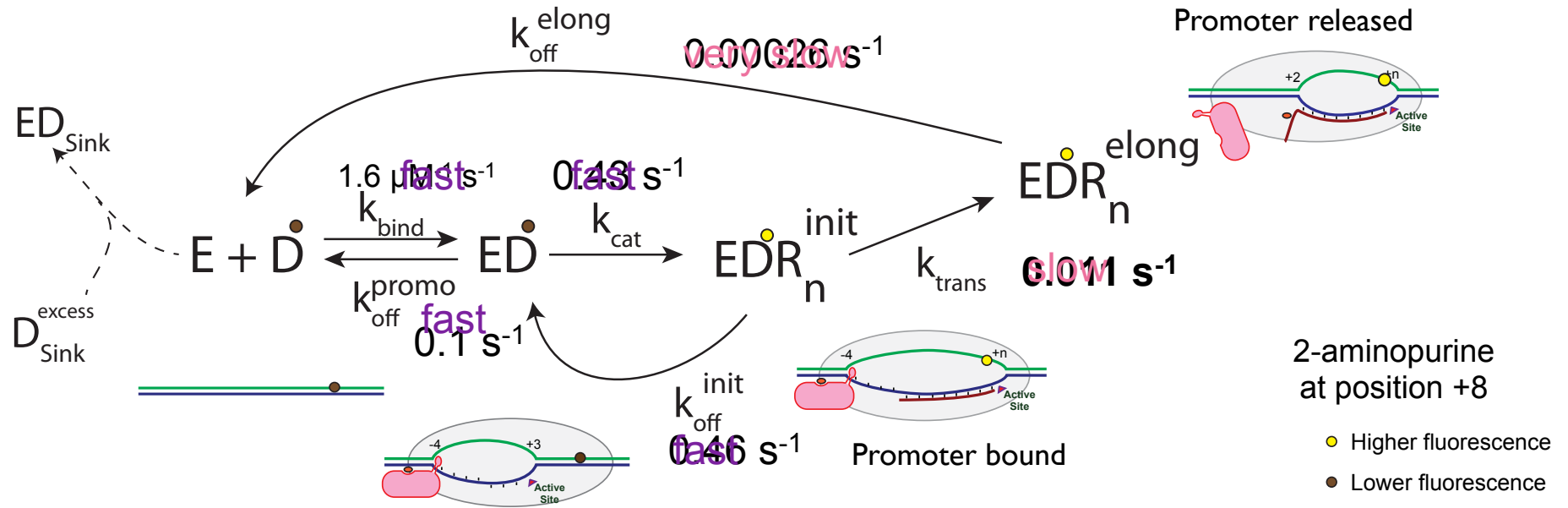
# Kinetics of Initial Transcription



Walk to position +9\*  
with G, A, U, dC

GGGAUAUACCA...

# Kinetics of Initial Transcription



## Current Group Members



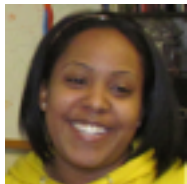
**Ketan  
Mathavan**



**Luis  
Ramirez**



**Satamita  
Samanta**



**Christina  
Chisholm**



## Recent Group Members



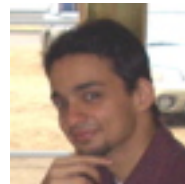
**Peng Gong**  
Ph.D. '06  
Postdoc - Colorado State



**Yi Zhou**  
Ph.D. '06  
Altus Pharmaceuticals  
Dicerna Pharmaceuticals



**Eddie Esposito**  
Ph.D. '05  
BlueSky Biotech



**Ankit Vahia**  
Ph.D. 2009  
Postdoc - Harvard Med



**Cuihua Liu**  
Senior Research Scientist  
Momenta Pharmaceuticals



**Selase Enuameh**  
Ph.D. '08  
Intelligent Biosystems



**Rosemary  
Turingan**  
Ph.D. '06  
Senior Scientist  
Network Biosystems



**Han Gang**  
Ph.D. '07 joint with Rotello  
Lawrence Berkeley Labs  
Asst Prof: UMass  
Medical School

  
**Xiaoqing Liu**  
Ph.D. 2008  
Educator - Suzhou, China