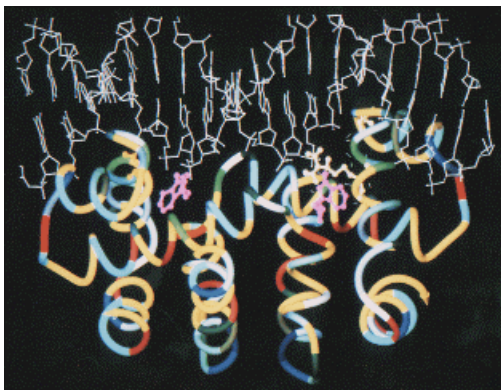
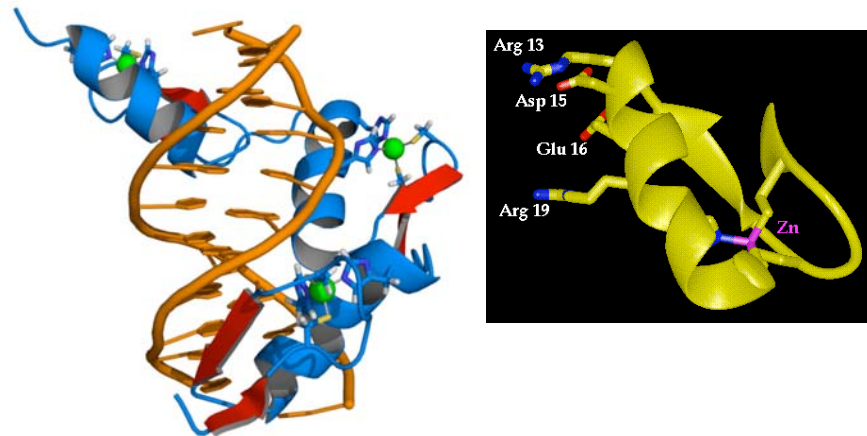


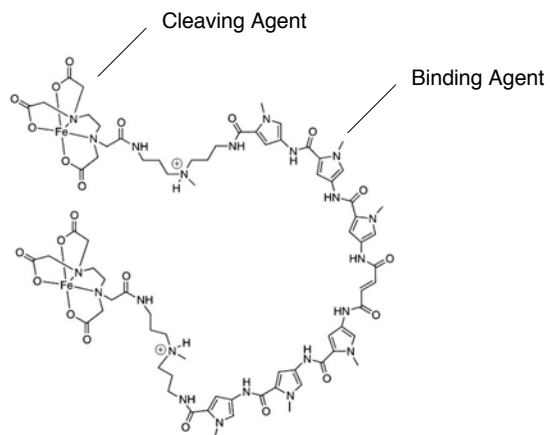
Trp Repressor



Zn²⁺ Finger Recognition

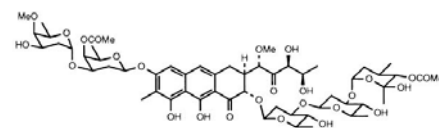


Modularity in Chemical Biology

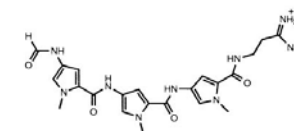


Natural DNA-Binding Proteins Are Typically Modular

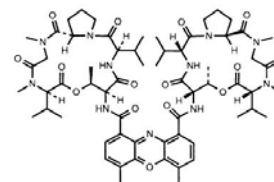
DNA-Binding Natural Products



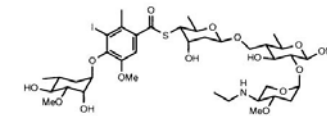
Chromomycin • 5'-GGCT-3'



Distamycin • 5'-(A,T)₅-3'



Actinomycin D • 5'-GC-3'



Calicheamicin oligosaccharide • 5'-TCCT-3'

Dickerson Structure

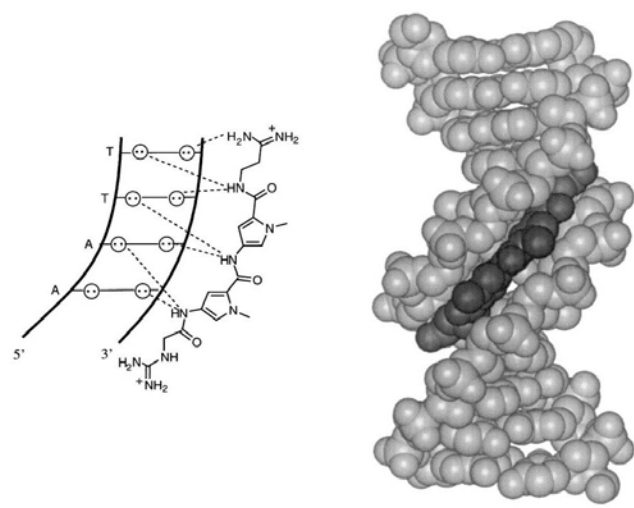


Figure 9. X-ray crystal structure of a 1:1 complex of netropsin: DNA.

Wemmer Structure

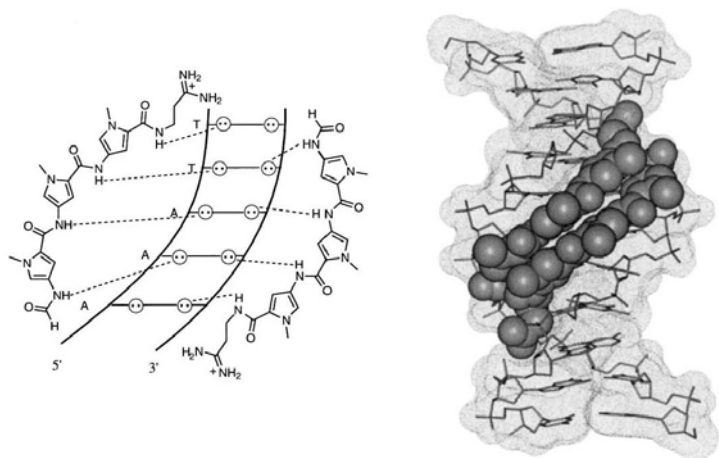
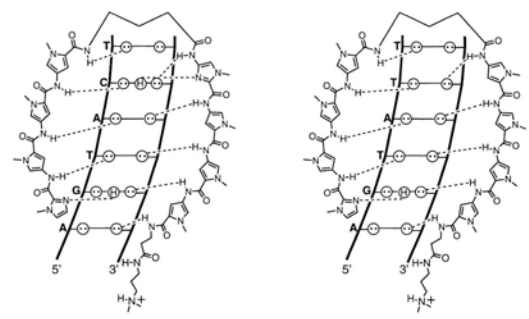


Figure 10. NMR structure of 2:1 complex of distamycin-DNA complex.

Recognition of All 4 Base Pairs

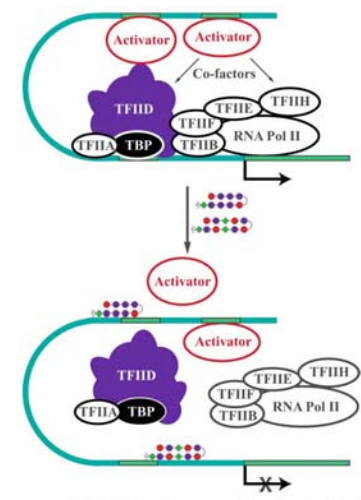


Equilibrium Association Constants (M⁻¹)

Binding Site	ImPyPyPy-γ-ImPyPyPy-β-Dp	ImPyPyPy-γ-PyPyPy-β-Dp
5'-AGTACT-3'	3.7 x 10 ¹⁰	5.0 x 10 ⁸
5'-AGTATT-3'	4.1 x 10 ⁸	3.5 x 10 ⁹

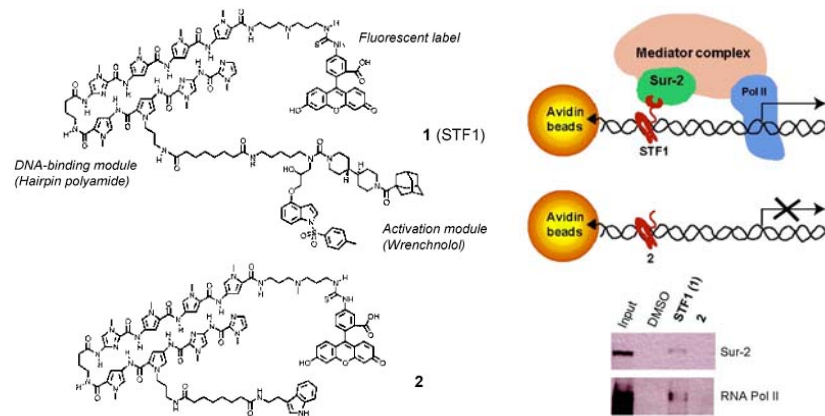
Conditions: 10 mM Tris+HCl, 10 mM KCl, 10 mM MgCl₂, and 5 mM CaCl₂, pH 7.0, 22°C

Inhibiting Transcription



Activating Transcription

Scheme 1



See: J. Am. Chem. Soc. **2004**, *126*, 10504