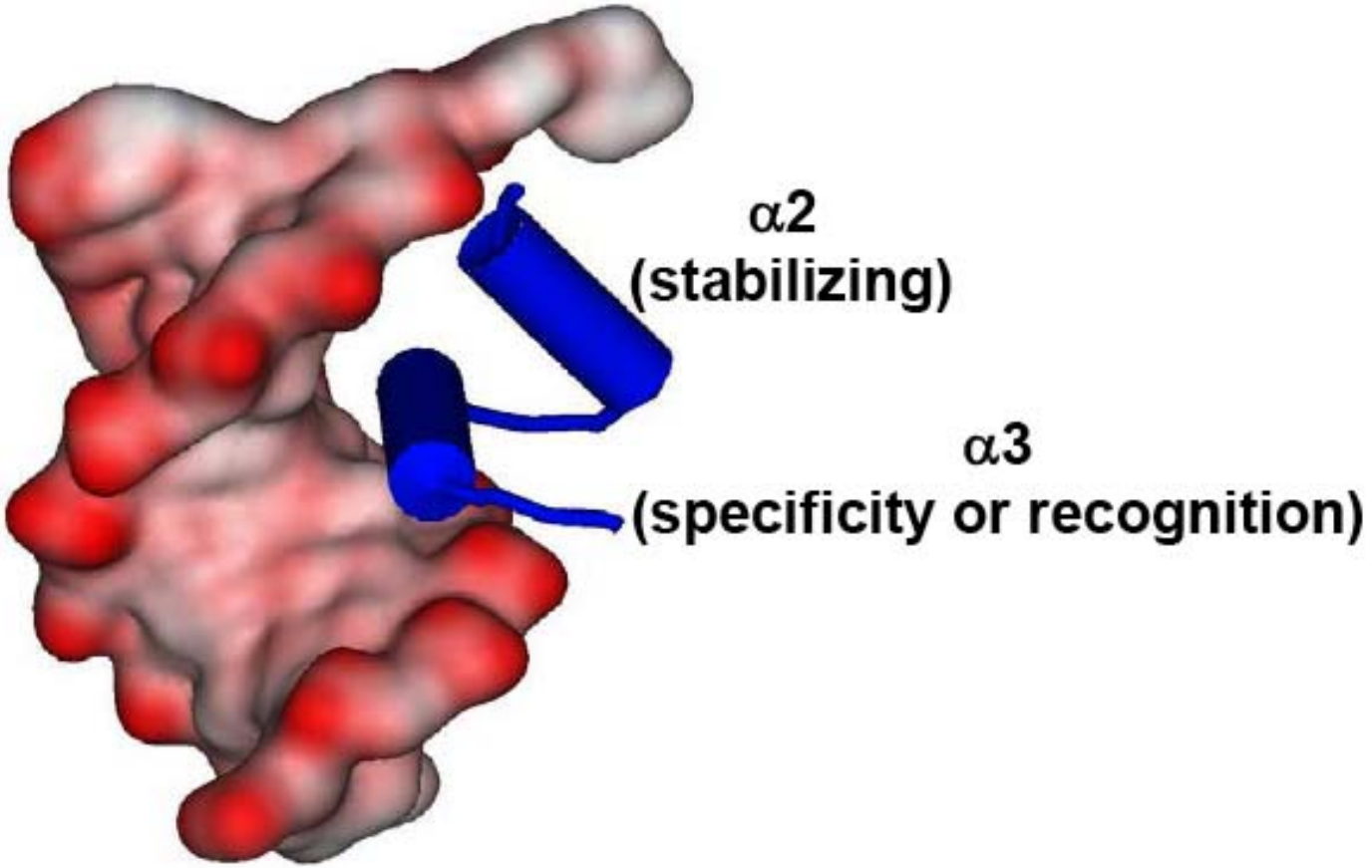
Protein Nucleic Acid Interactions

Different types of recognition motifs

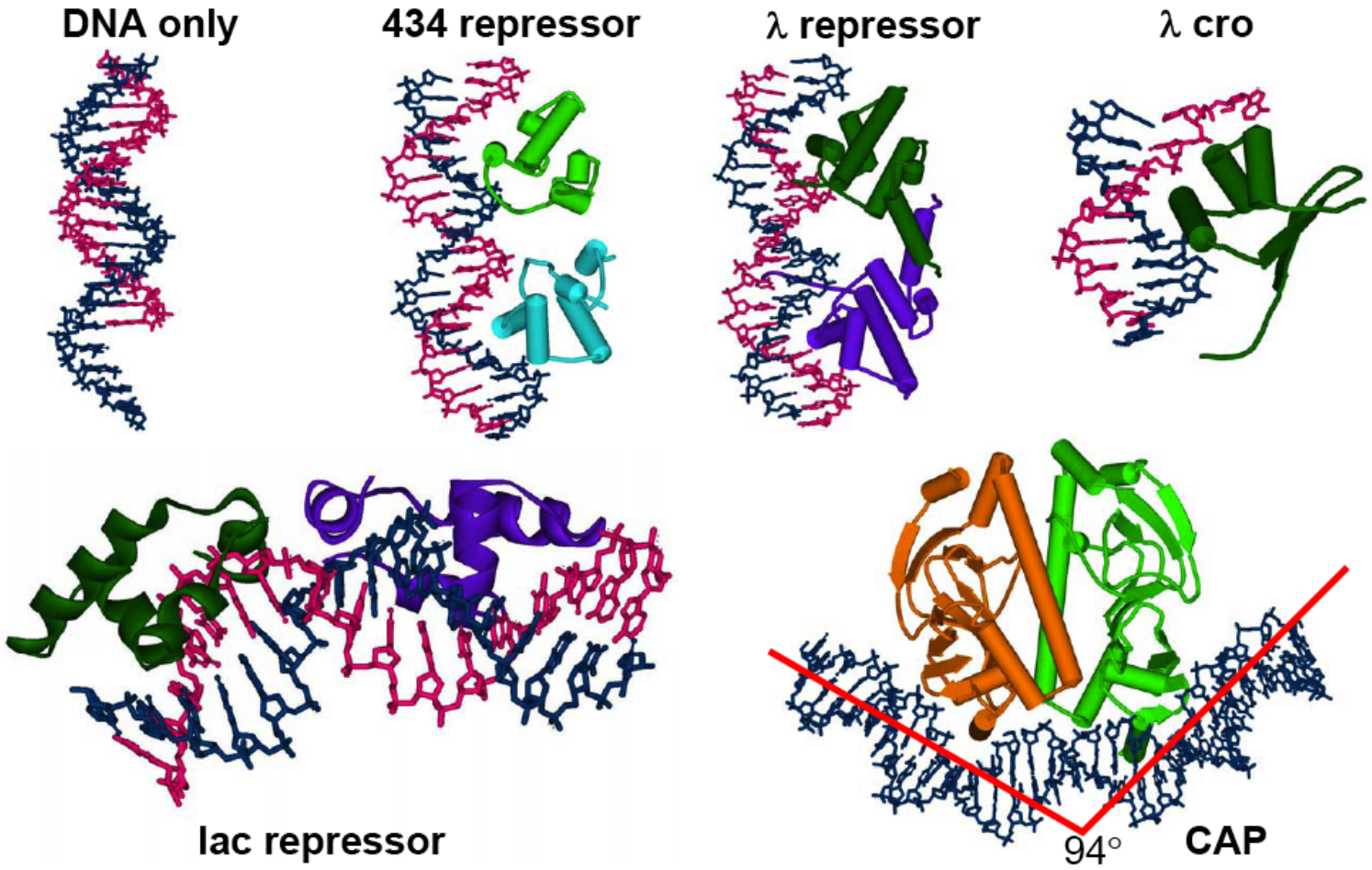
1. Helix turn helix
2. Homeodomains
3. Zinc finger
4. Leucine zipper
5. Winged helix
6. Beta ribbon

1. Helix turn helix
HTH

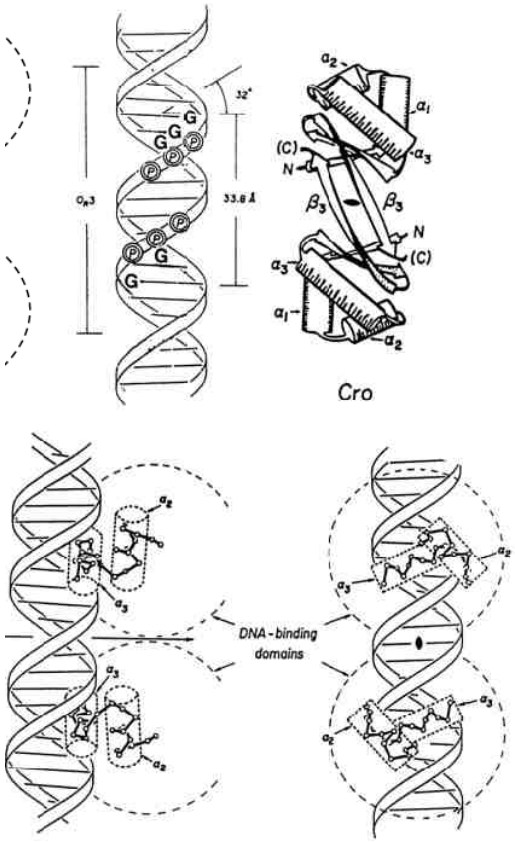
- Most common DNA binding motif
- Procaryotes
- Found in hundreds of DNA binding proteins
- Dimerization required for full activity
- Sequences separated by approximately one turn of helix
- Major groove contact to DNA
- DNA sometimes bent


α2
(stabilizing)
α3
(specificity or recognition)

Proteins with HTH motif



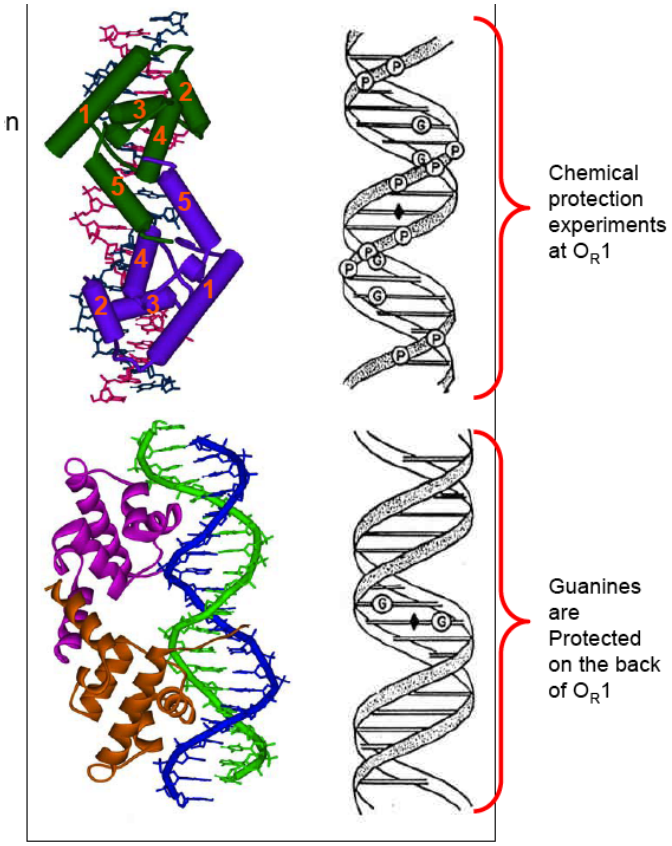
Cro



- HTH 2nd and 3rd helix
- 17bp operator

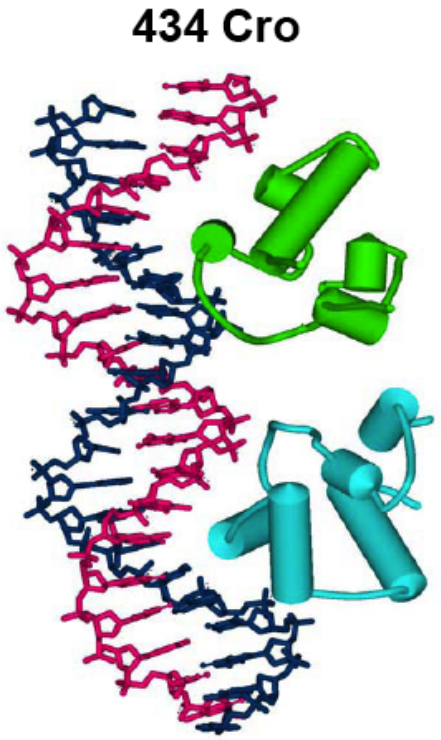
λ

- 2 fold symmetry
- Recognition helices 34 A apart
- DNA slightly distorted



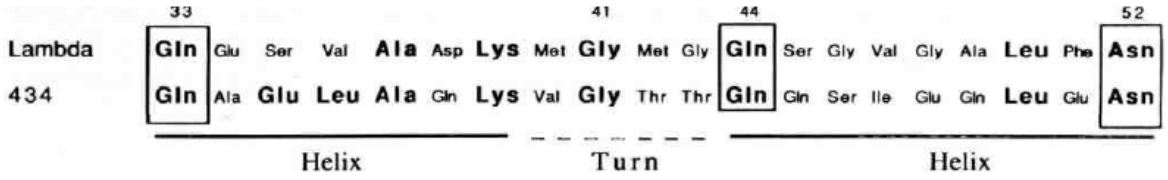
434

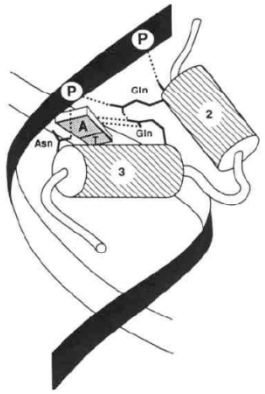
- 4 helix cluster, 2,3 HTH
- 34 A between recognition helices
- Slight distortion



(HARRISON, PDB 2OR1)

Comparison of 434 and λ

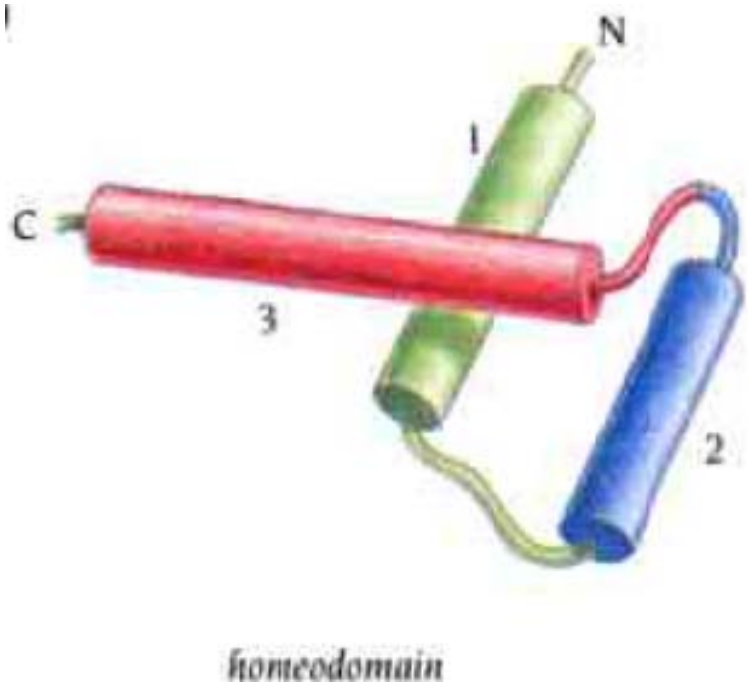




- Gln 33 H bonds to backbone
- Gln 44 H bonds to adenine
- Asn 52 H bonds to backbone

2. Homeodomains

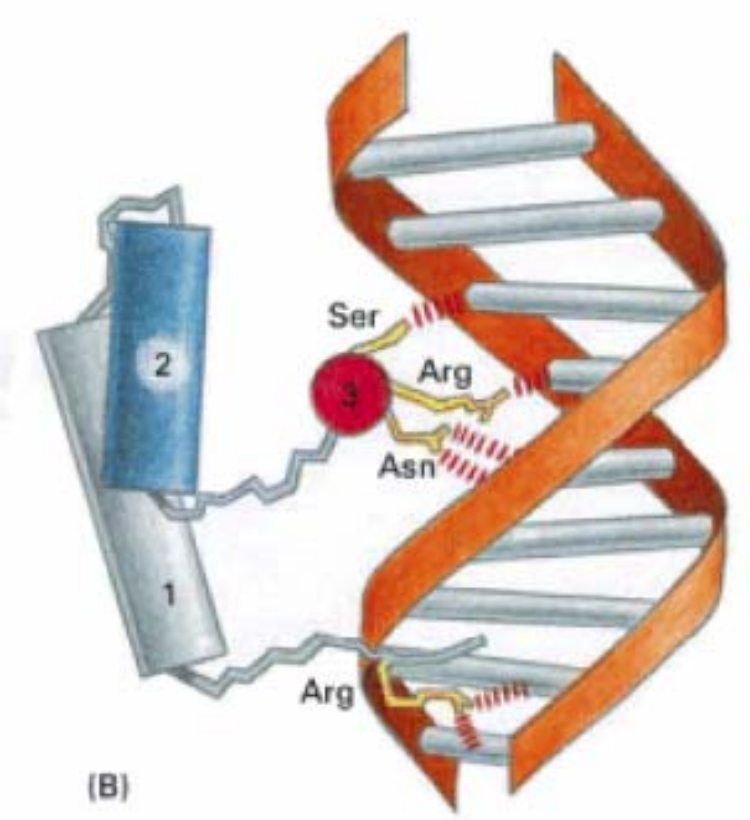
- HTH in eukaryotes
- 60 amino acids
- Helix-loop-helix-turn-helix



homeodomain

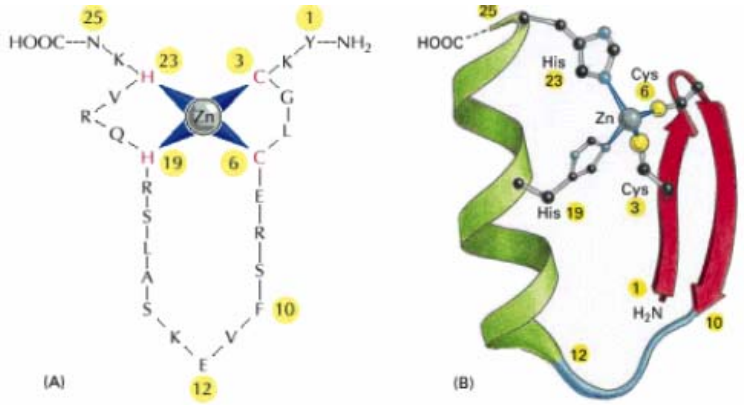
DNA Binding

- Helix 2 and 3 similar to HTH
- Recognition helix (3) makes key contacts with major groove
- Flexible arm in helix 1 contacts minor groove



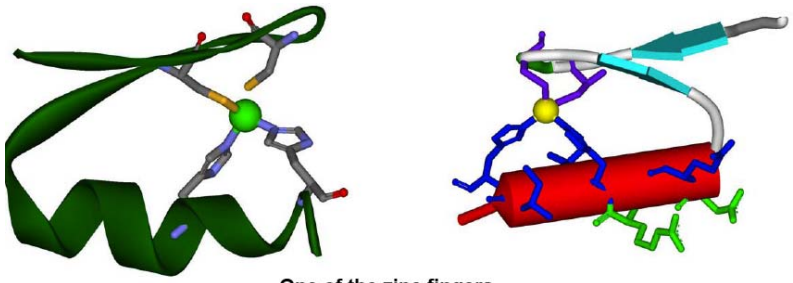
3. Zinc Finger

α) ββα
b) Hormone receptor
c) Gal4
d) Loop sheet helix



a. ββα

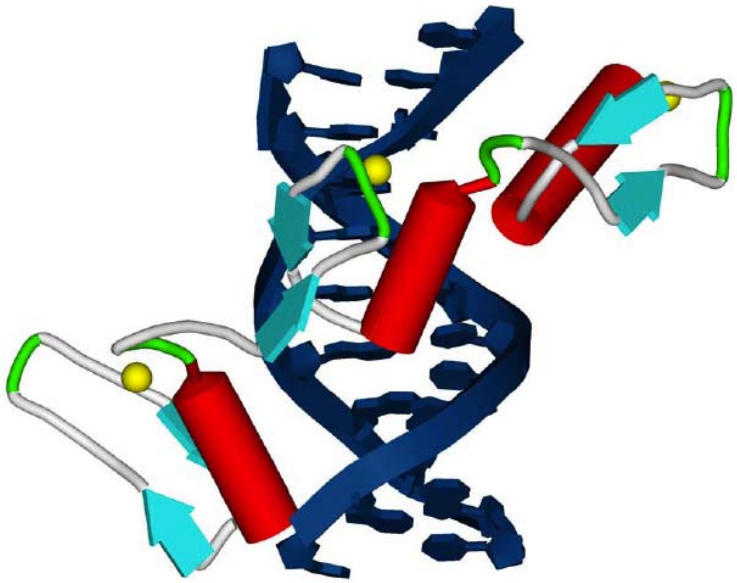
- Part of transcription regulatory proteins
- 30 residue motif coordinating one zinc via 2 cysteines and 2 histidines



One of the zinc fingers from the mouse Zif268 protein (1ZAA)

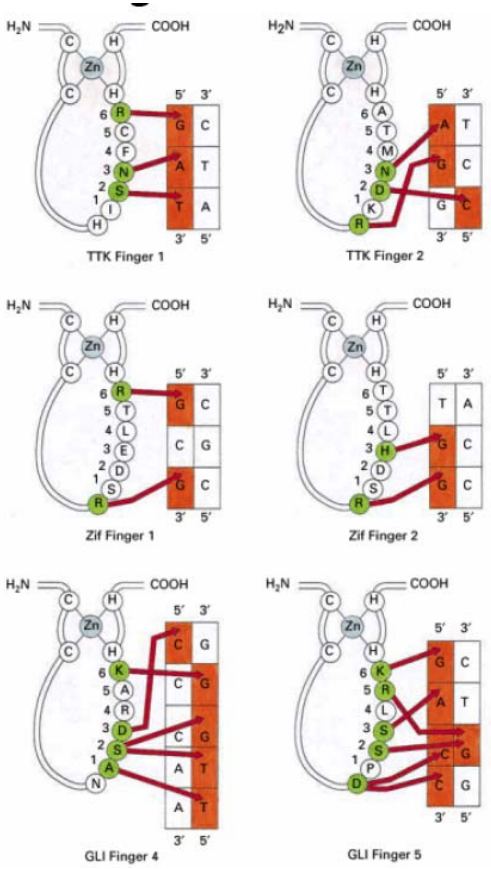
DNA binding of Zif268

- Monomer
- Major groove
- Finger bind to 3 base pair subsites



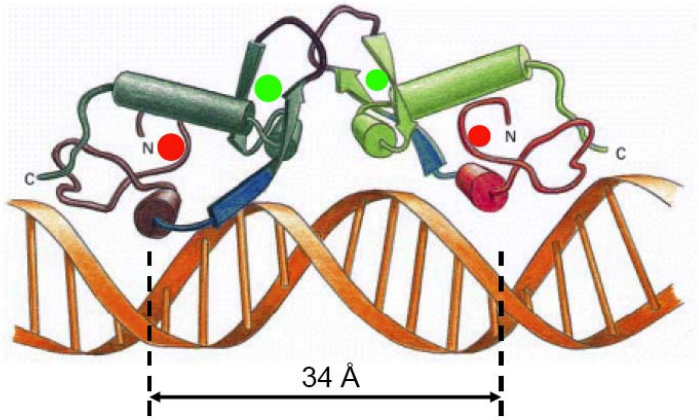
Different Zinc finger binding to DNA

- Zn fingers all have similar structure
- Different contacts to DNA
- Arginine guanine contacts are common



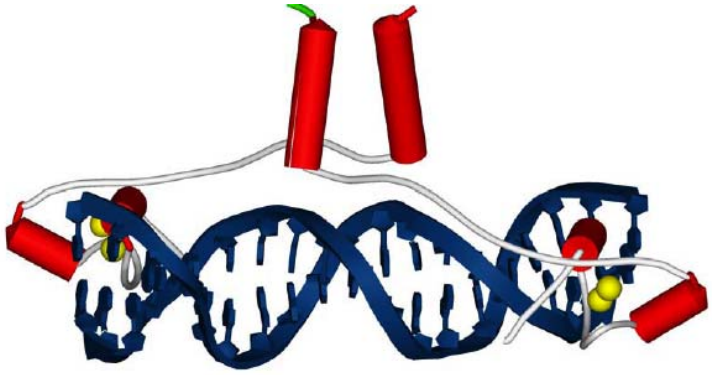
b. Hormone receptor

- Pseudosymmetric homo or heterodimer
- 2 Zn coordinating modules
  - 1 Zn stabilizes DNA recognition helix, other Zn involved in dimer formation
- Zn coordinated by 4 cysteines
- Major groove contacts



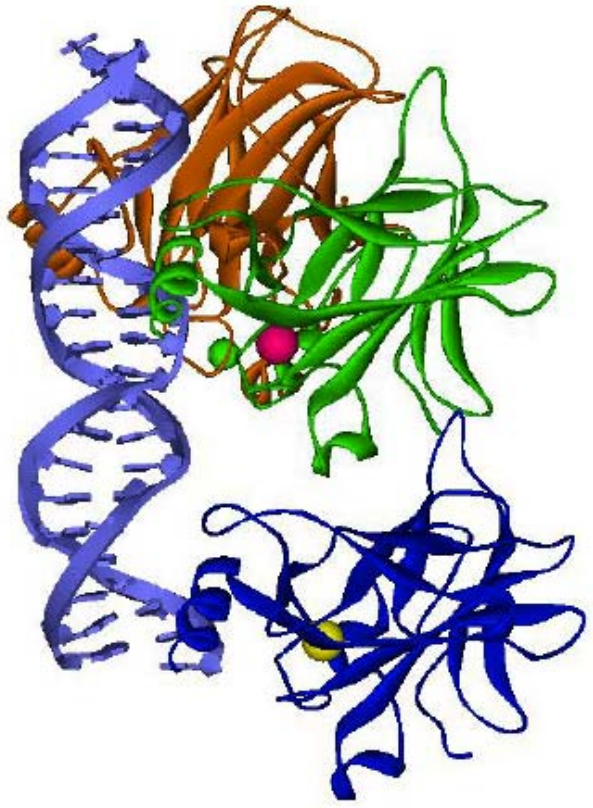
c. Gal4

- Found in yeast transcriptional activators
- 65 residue regions binds as dimer (C terminus)
- 2 Zn coordinated by 6 cysteines (N terminus)
- Major groove binder



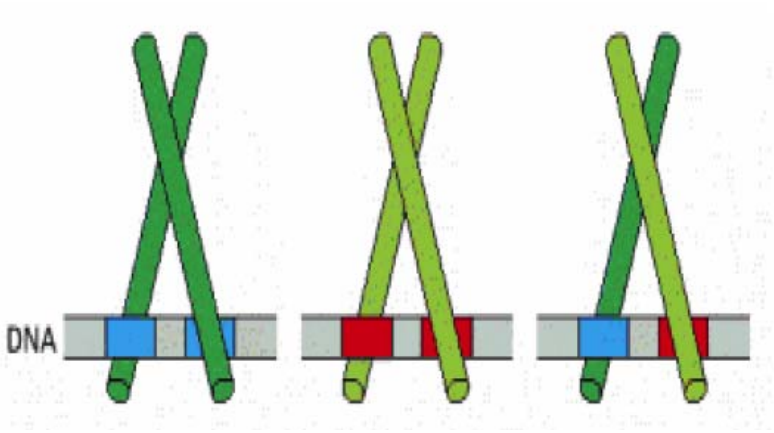
d. Loop sheet helix

- P53-transcriptional activator involved in tumor suppression
- Zn coordinated by 3 cysteines and a histidine
- Tetramer-5bp recognition helix one after another
- Helix in major groove, loop in minor groove



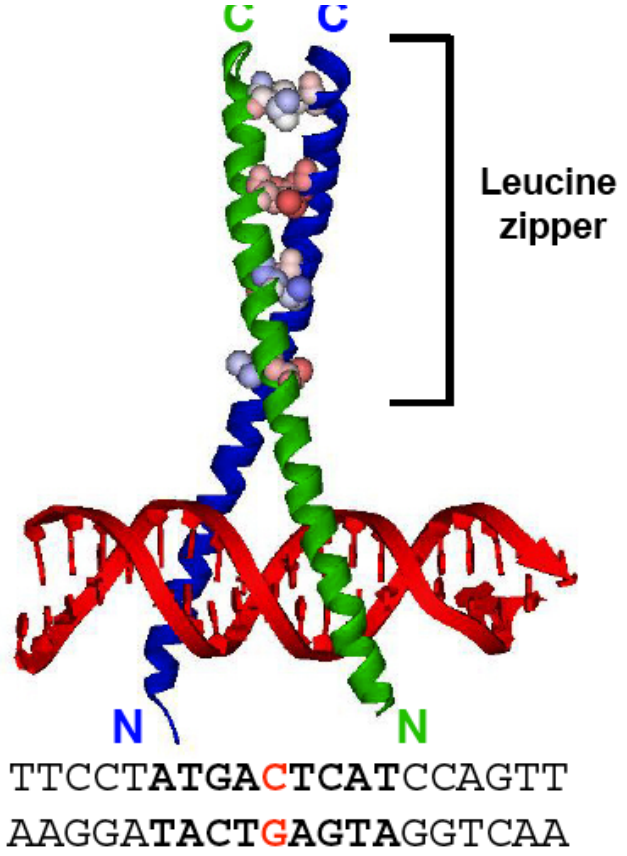
4. Leucine zipper

- Dimer (homo or hetero)
- Two a helices wound around one another
- Grip DNA like a clothespin



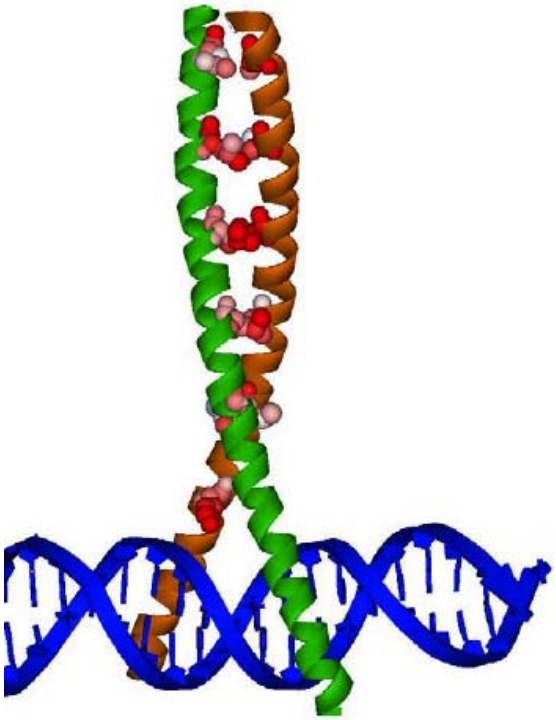
GCN4

- Yeast transcriptional activator
- Coiled coil packing of helices (knobs in hole)
- homodimer



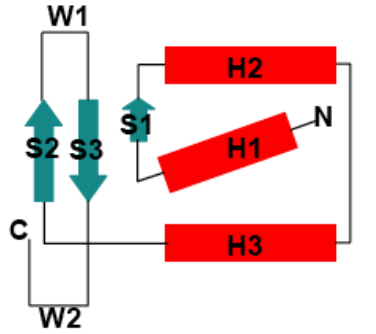
AP-1 Fos Jun

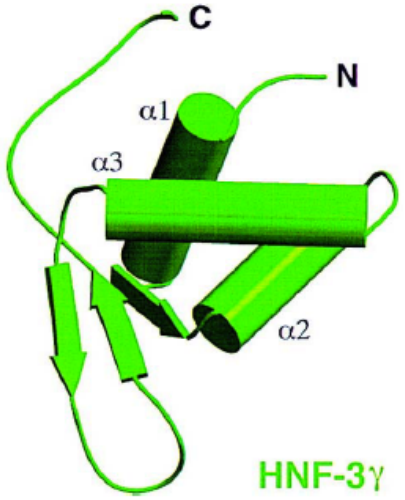
- heterodimer



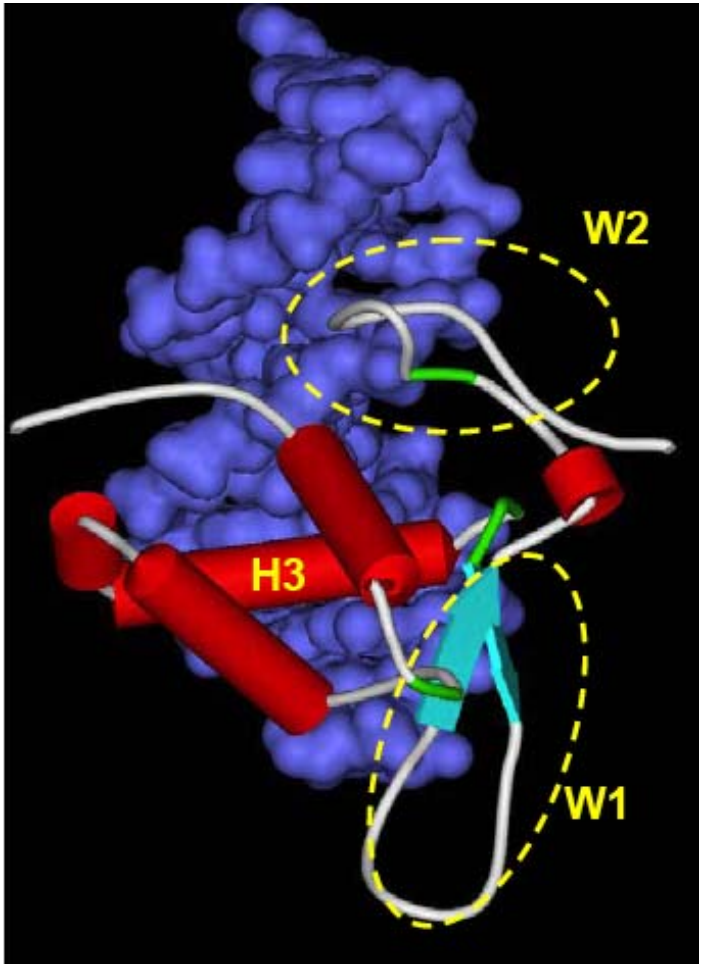
5. Winged helix

- Compact α/β structure
- 2 wings, 3 helices and 3 strands
- Helix 3 is recognition helix



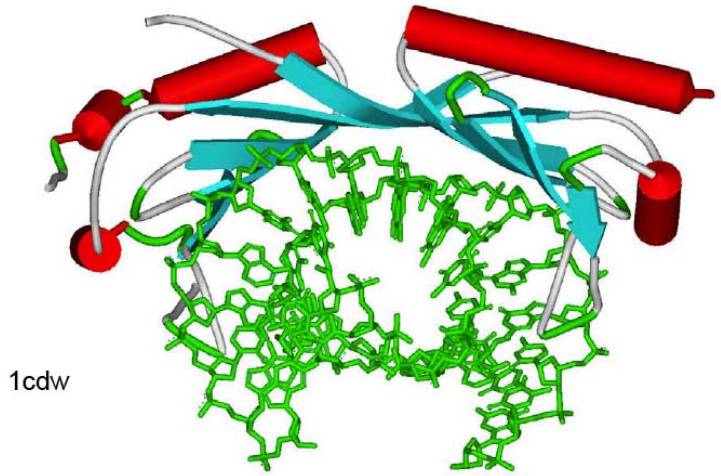


HNF 3



TATA binding protein

- Specifically recognize AT rich DNA seqeunces
- 8 stranded β sheet binds to DNA
- Hydrophobic side chains intercalate in minor groove
- DNA kinked



DNA-Binding Sites on Proteins

Computational analysis of

- Size (ASA)
- Packing
- Polarity
- Hydrogen Bonding
- Bridging Water Molecules
- Residue Propensities