

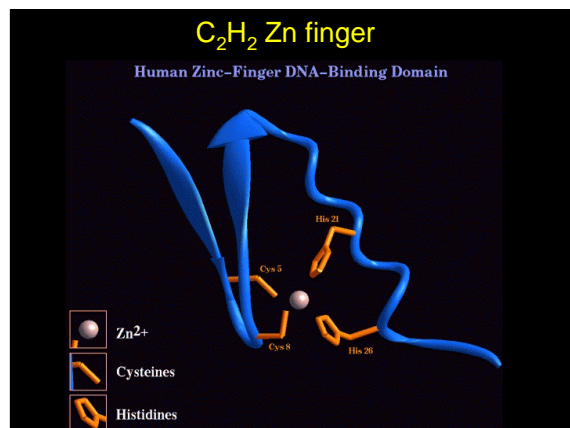
DNA binding domains and Activation domains of transcription factors

A survey of DNA binding domains

- Zn -containing domains
 - 6 Cys and 2 Zn: Gal4
 - Zn fingers
 - Many eukaryotic transcription factors
- Basic-leucine zipper proteins
 - (hetero)Dimers, eukaryotic activators
- Helix-turn-helix
 - Many bacterial regulators, e.g. repressor
 - Homeodomain proteins involved in segment determination in eukaryotes
- Basic-helix-loop-helix proteins
 - (hetero)Dimers, differentiation factors

Zinc fingers

- Cys or His amino acids donate electron pairs to a tetrahedral configuration organized by a Zn^{++} ion
- Several different types TFIIIA
 - C_2H_2 (e.g. TFIIIA)
 - C_2C_2 (e.g. Glucocorticoid receptor)
 - C_6
 - GATA
- Different functions
 - DNA binding
 - Protein-protein interactions
- Each finger contacts 3 consecutive bp in major groove



C2-C2 Zn Finger

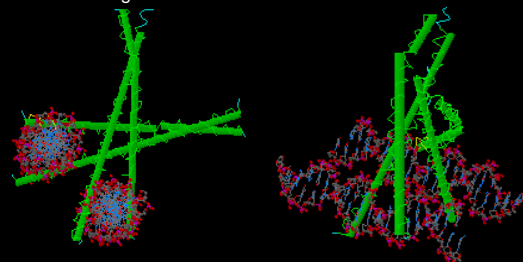
- Found in steroid receptors
- Glucocorticoid receptor (p. 644)
 - Three functions in central domain
 - DNA binding (Zn finger)
 - Dimerization (Zn finger)
 - Activation domain
 - C terminus binds steroid hormone
 - N terminus activates transcription



Basic-leucine zipper proteins

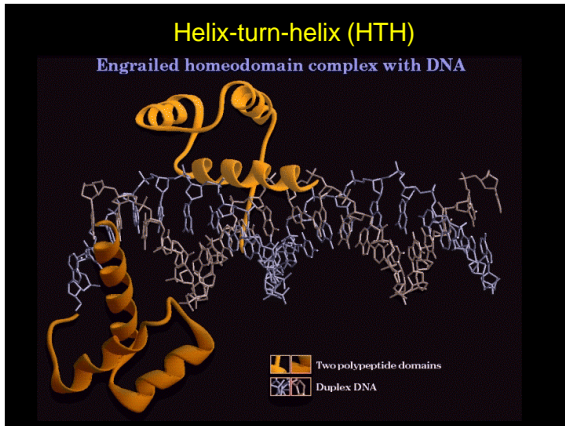
View down long axis of DNA

Lateral view of DNA

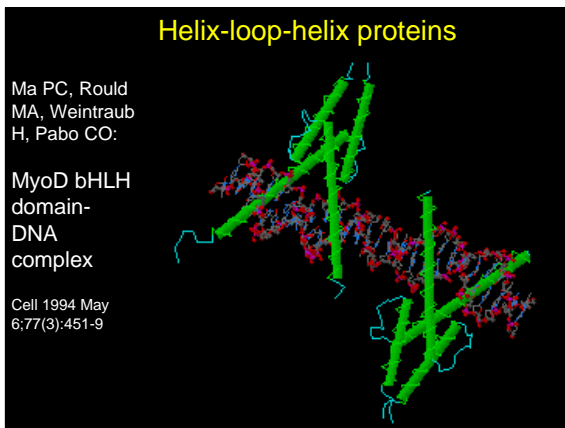


S. Harrison lab: cFos-cJun heterodimer, DBD, 2 complexes
 Nature 1995 Jan 19;373(6511):257-61

Images via NCBI and their Cn3D program.



View Chime tutorial of lambda repressor-operator co-crystals



Use Dr. T. Nixon's "Chime tutorials"

<http://www.bmb.psu.edu/pugh/514/mdls/default.htm>

Transcriptional activator domains (ADs)

- 3 general types of activator domains
- Acidic
 - Amphipathic helix, acidic amino acids on one face
 - No consistent secondary or tertiary structure has been identified
 - Glutamine-rich (Q-rich)
 - Pro-rich (P-rich)

No correspondence between type of DBD and type of AD

- Examples of proteins with acidic AD
 - GAL4 (Zn₂Cys₆)
 - AP1 (bZIP)
 - VP16 (no DBD)
 - repressor (HTH)
- Examples of proteins with Q-rich AD
 - Sp1 (Zn finger)
 - Antp (homeodomain)
 - Oct (POU-homeo)

Lack of fixed structure in activator domains

- DBDs of transcription factors form discrete structures that can be analyzed by X-ray crystallography and NMR
- The ADs do **not** generate identifiable electron density in the crystallographic analysis.
- This indicates that they do **not** form discrete structures.
- One hypothesis is that the ADs are unstructured until they interact with their targets.
- This is an induced fit model.