Presentation 3-1:
Regulation of transcription initiation

BIMS 6000 – Block 3 – Day 1
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For starters:
•Handout is available on collab if you want it.
•Download from collab & open in Pymol: Gal11-Gcn4 models.pse
•Let's talk about the assignment (B3a_090414_auble_10)

Goals of this lecture:
•Understand the general regulatory principles of transcription initiation, including the roles of recruitment and chromatin.
•Broader concept: Transcription as a general indicator of cell state.

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What should you do to reinforce the lecture material?

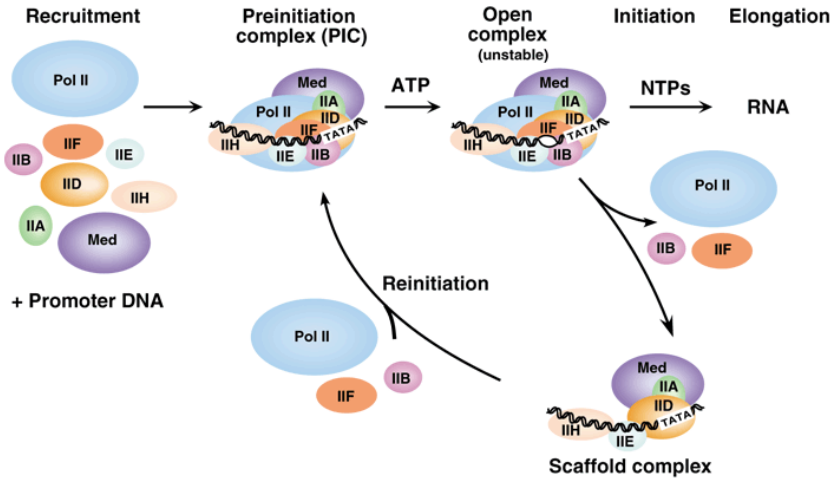
•Look over your notes after class and see me if you have questions.

How will you be tested on today's material?

Incorporate an understanding of transcriptional regulation, as appropriate, into your analysis of high throughput data as part of the assignment due on Monday 9/8.

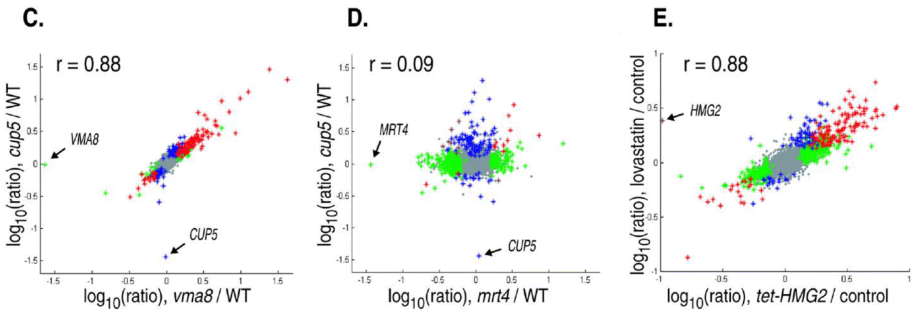
2

RNA polymerase II transcription pathway



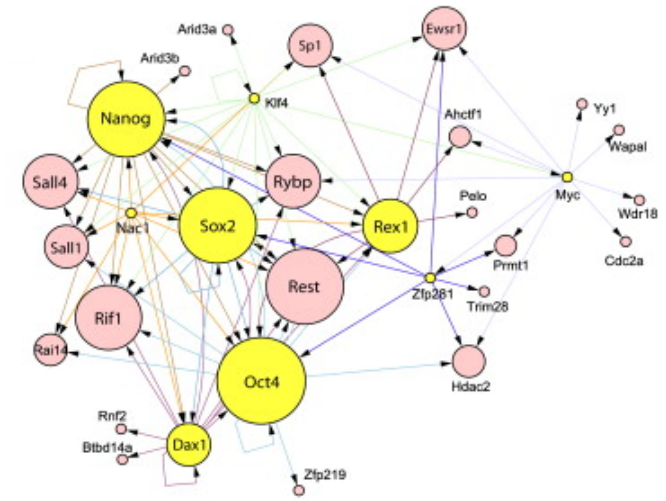
3

Transcriptional analysis can provide a precise signature of cell state



4

Example: a network of transcription factors can define cell state



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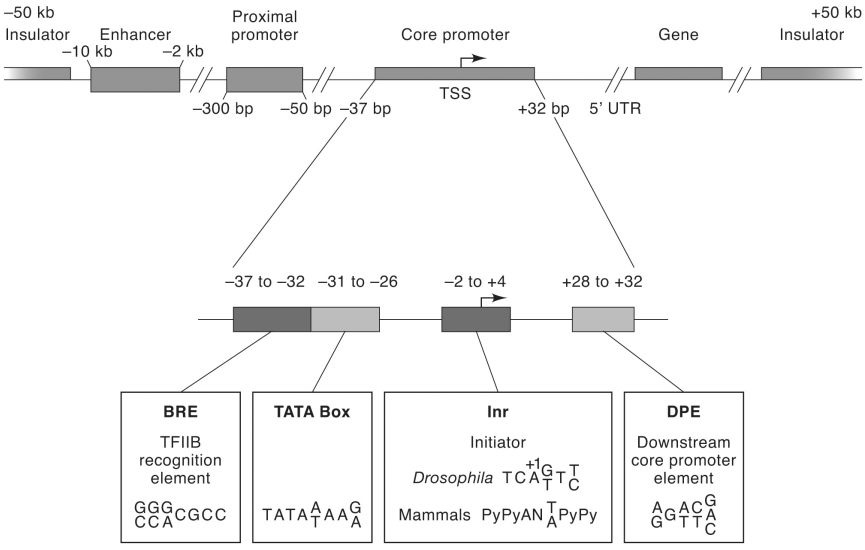
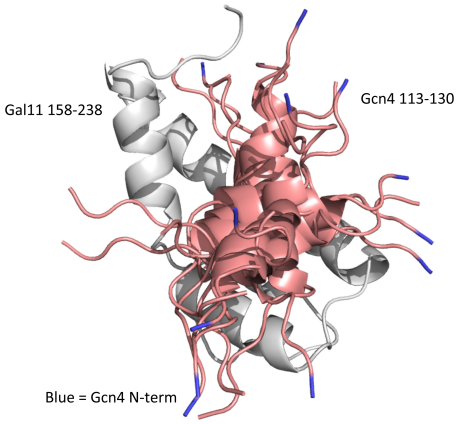
Promoter region of a regulated gene



Regulation by recruitment



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Regulation by chromatin

- Histone modification (e.g. acetylation, methylation, phosphorylation)
- Chromatin remodeling
- Histone variants, exchange
- Nucleosome dynamics (e.g. spontaneous unwrapping, higher order folding)
- Promoter chromatin architecture.

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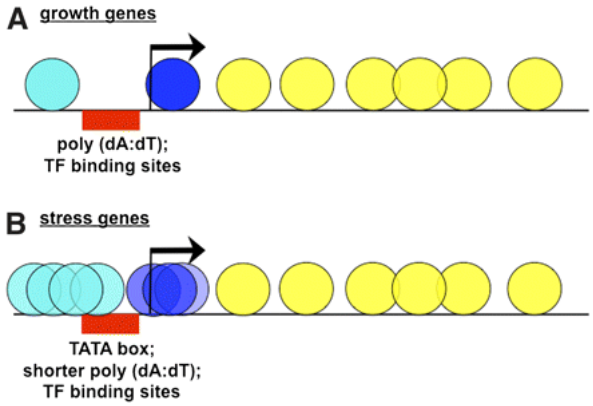
Two stereotypical types of promoter chromatin structure



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Summary: gene activation

Activators can work by two broad classes of mechanism:

- Recruitment
- Modification of chromatin structure

Recruitment occurs by low-affinity, partially redundant, "fuzzy" interactions. "Pioneering" factors bind DNA in the context of the native chromatin state.

Requirements for recruitment and chromatin modification depend on promoter sequence and local chromatin structure

Chromatin modification can facilitate gene activation by:

- altering chromatin structure (e.g. nucleosome movement)
- providing new sites for interaction with chromatin-binding modules in regulatory factors
- other mechanisms not yet discovered (e.g. exchange)

Analysis of a regulatory mechanism

You notice, for example, that a protein is detectable in a cell grown under one set of conditions but not when grown under a different set of conditions.

What steps could we take to determine experimentally how the regulation is occurring?

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