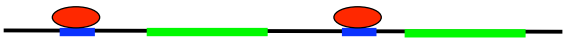
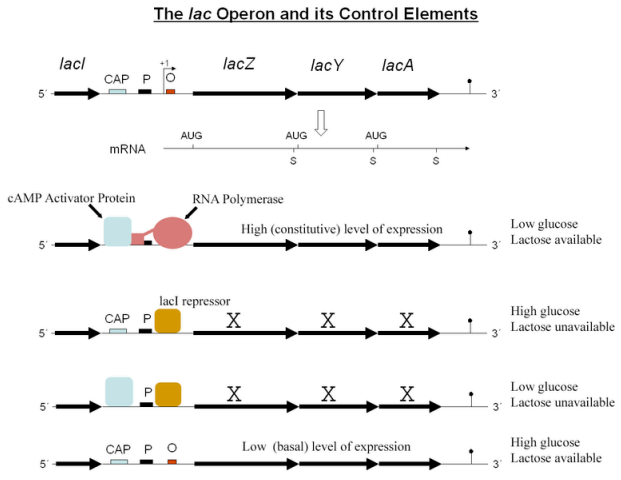
Protein-DNA interactions

Introduction:
DNA, genes and regulation



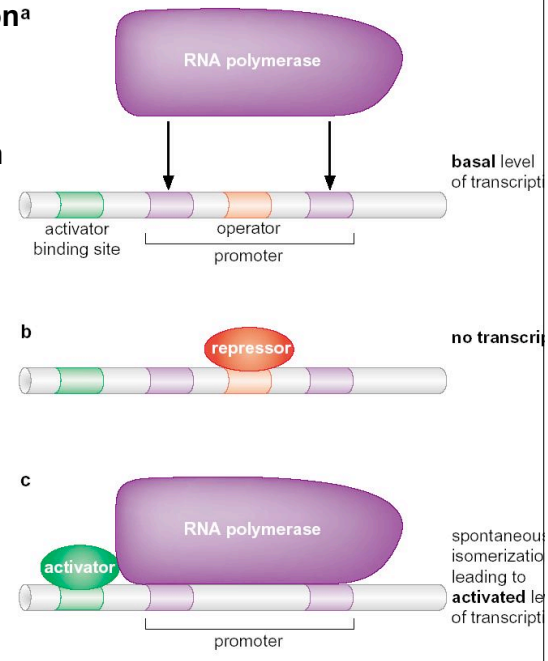
- DNA contains **genes**
- genes need to be turned on and off
- genes are regulated by proteins that bind to specific **regulatory sequences** on DNA.
- proteins that regulate genes are called **transcription factors** (TFs)



http://en.wikipedia.org/wiki/Lac_operon

Introduction:
DNA, genes and regulation[a]

- TF can either repress or activate gene expression



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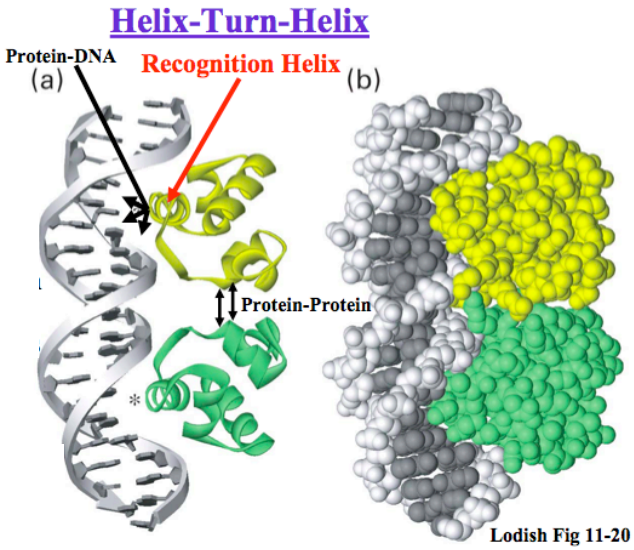
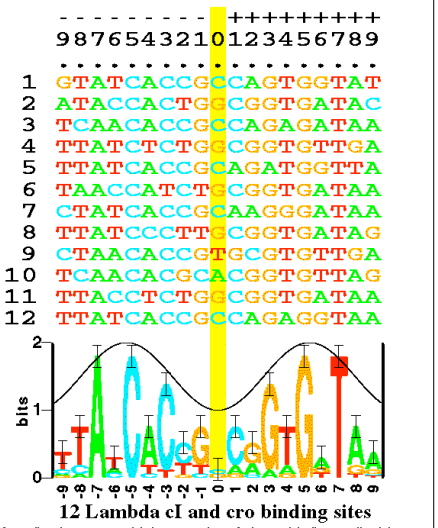


Introduction:
DNA, genes and regulation

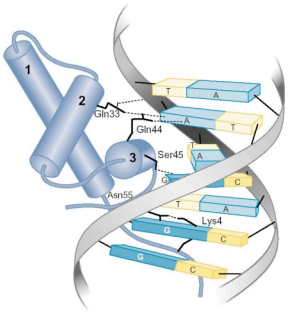
- TFs recognize specific DNA motifs
- protein-DNA complexes are very stable (life time ~10^3 sec)
- stabilized by interactions betwee DNA base-pairs and protein amino acids.



12 Lambda cI and cro binding sites

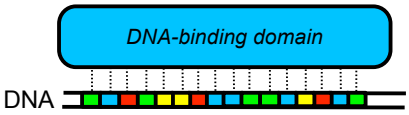
Fig. 1. Some aligned sequences and their sequence logo. At the top of the figure are listed the

Protein-DNA interaction energy



- Specific (sequence-dependent) and non-specific interactions
- Specificity is achieved by formation of local interactions with DNA

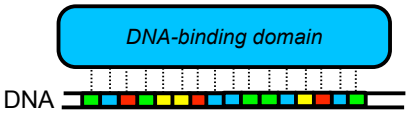
Model



Assumption:
Independent contributions of individual base-pairs.

Protein-DNA interaction energy

Model



$$E = \sum_{i=1}^{l} e(i, b_i)$$

Example: *Mnt* protein weight matrix
(*Stormo & Fields, TIBS 23, p. 109, 1998*)

(a)

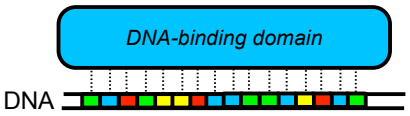
	11	12	13	14	15	16	17	18	19
	–	–	–	–	–	–	–	–	–
A	0.26	0.37	0.91	0.31	0.058	**–0.29**	0.55	0.14	0.39
C	–0.16	0.87	0.58	1.90	0.74	–0.11	**–0.72**	**–0.33**	–0.33
G	**–0.16**	**–0.68**	0.36	**–0.68**	**–0.56**	0.45	1.30	0.30	0.45
T	0.26	1.20	**–0.63**	0.68	0.85	0.13	0.74	0.11	**–0.16**

(b)

3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
a	*g*	*g*	*t*	*c*	*c*	*a*	*c*	*g*	*g*	*t*	*g*	*g*	*a*	*c*	*c*	*t*

Protein-DNA interaction energy

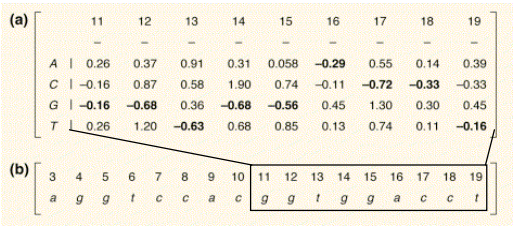
Model



$$E = \sum_{i=1}^{l} e(i, b_i)$$

CGATGGACTT
CCATGGCCCT
GGATGGGCTT
GGATGGTCCT
GGATGCACCT

$$e(i,x) = -\beta \log\left(f(i,x)/g(x)\right)$$



GIVEN THIS ENERGETICS, CAN A PROTEIN FIND ITS SITE?