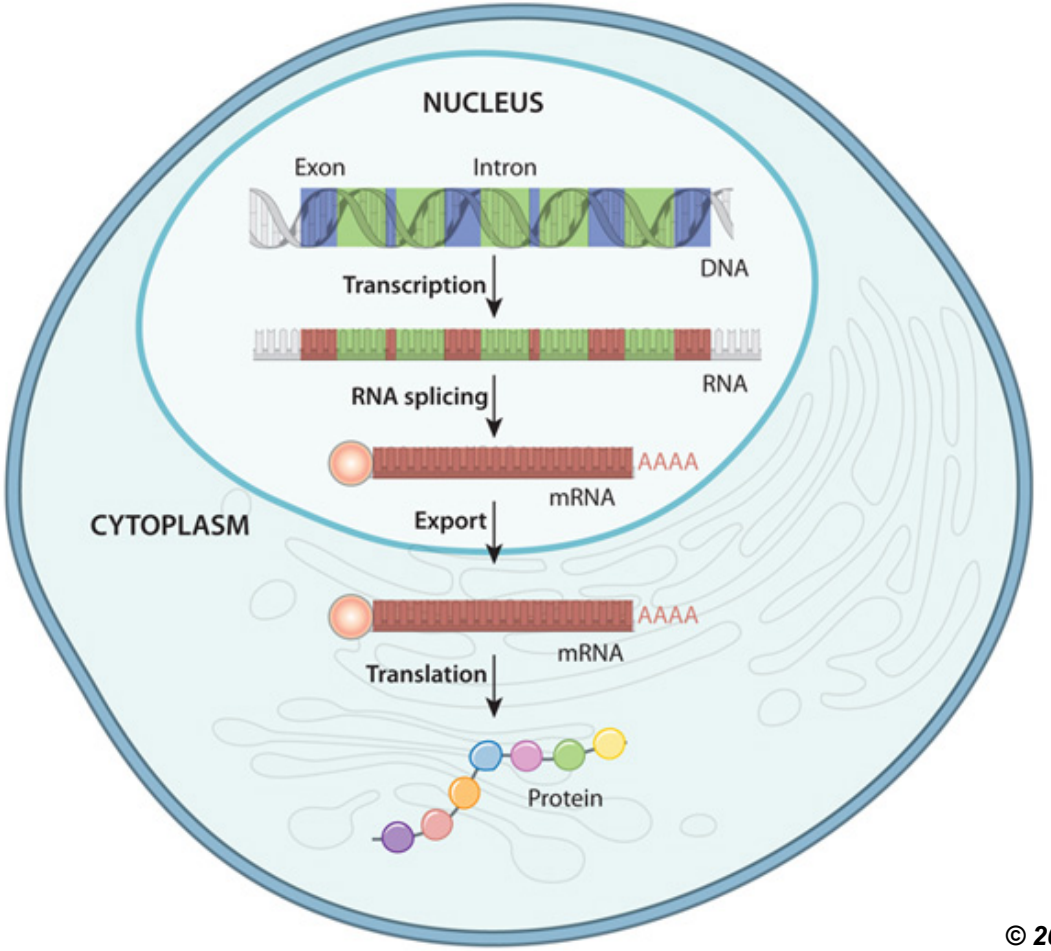
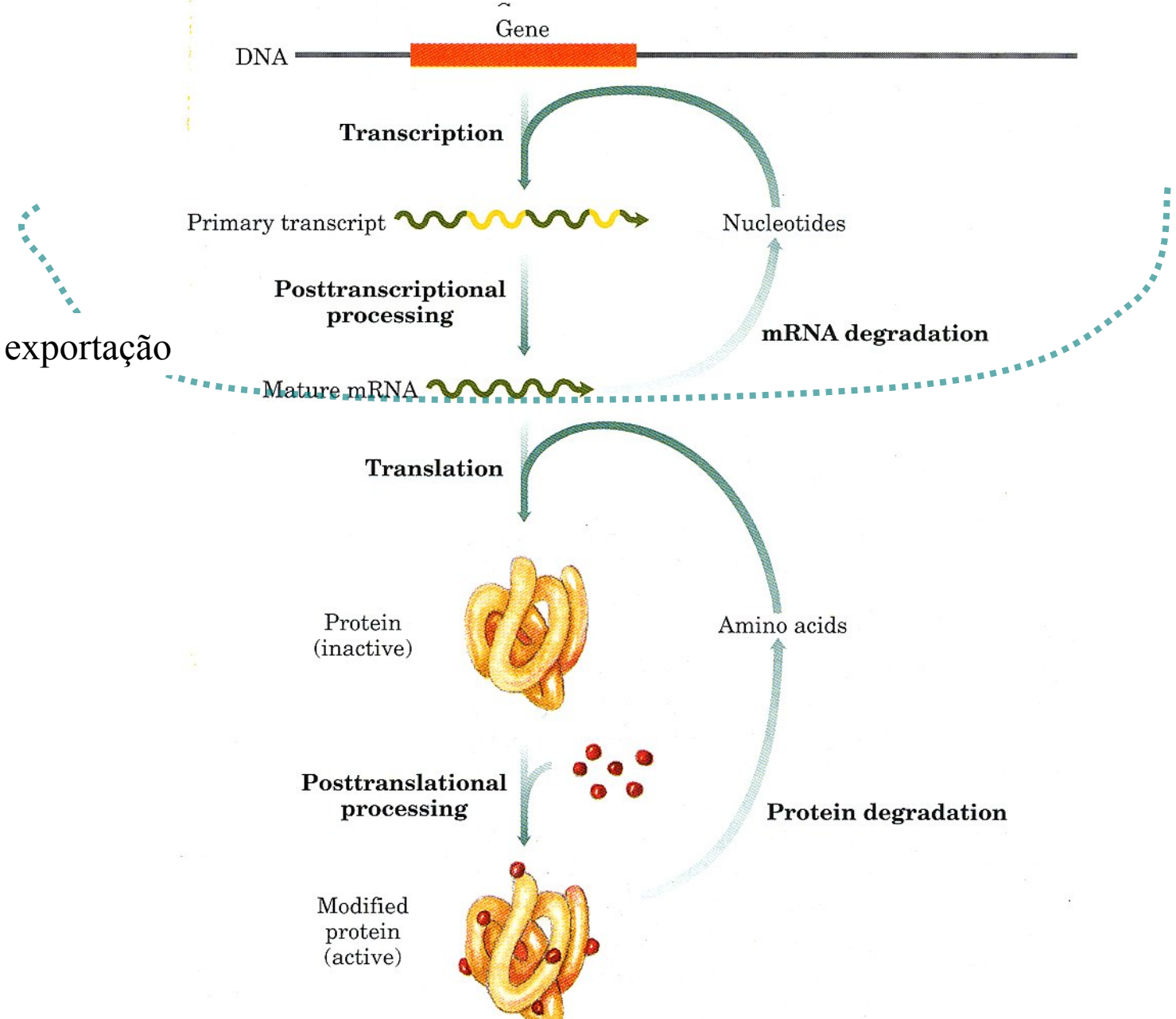
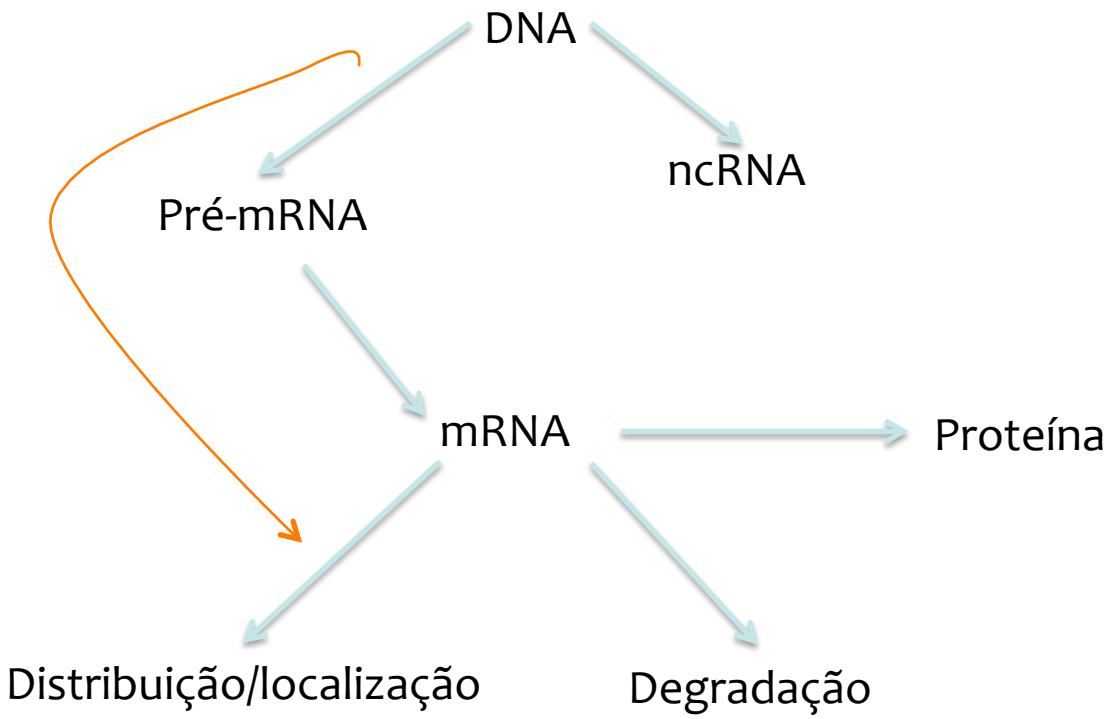
# Regulação da Expressão Gênica



# Transcrição: controle de expressão de genes

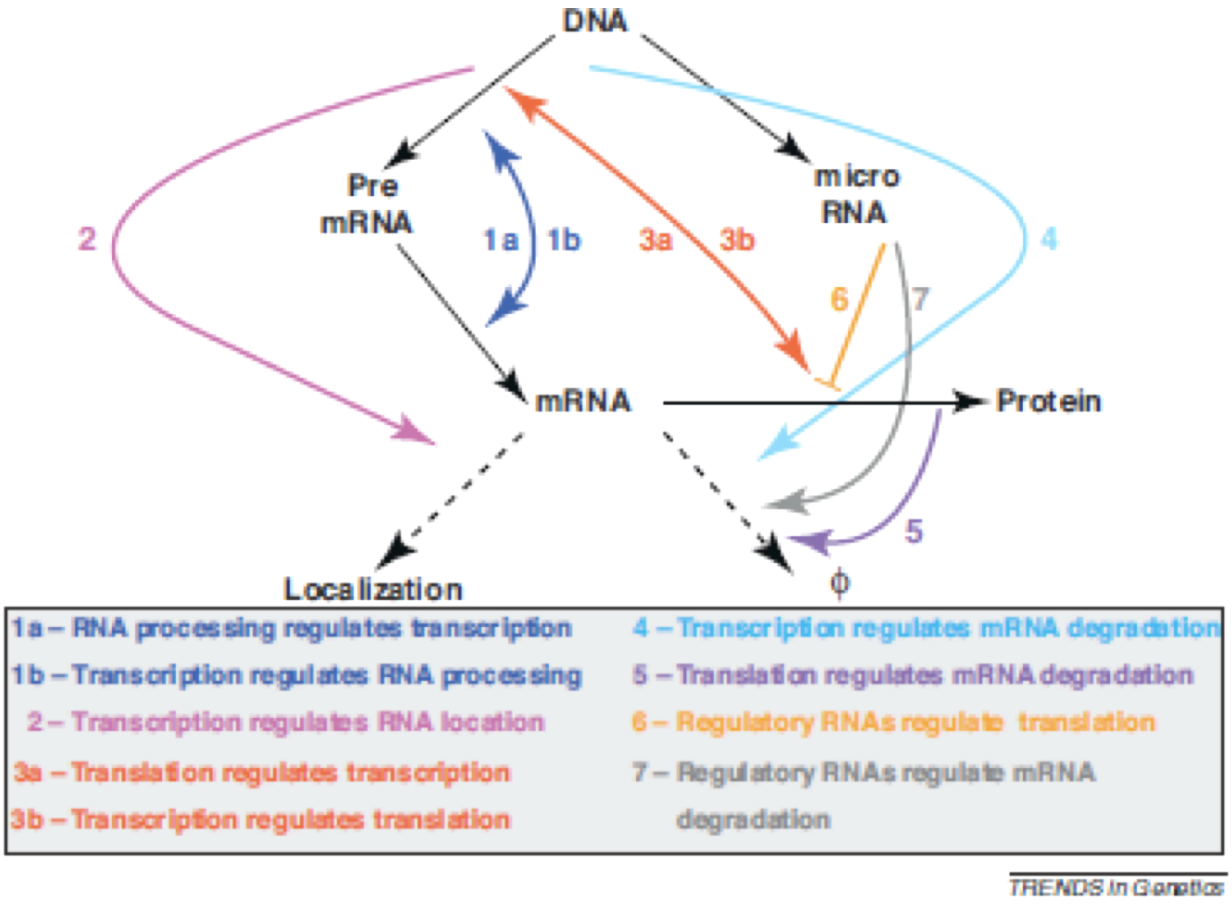


# Os destinos dos transcritos



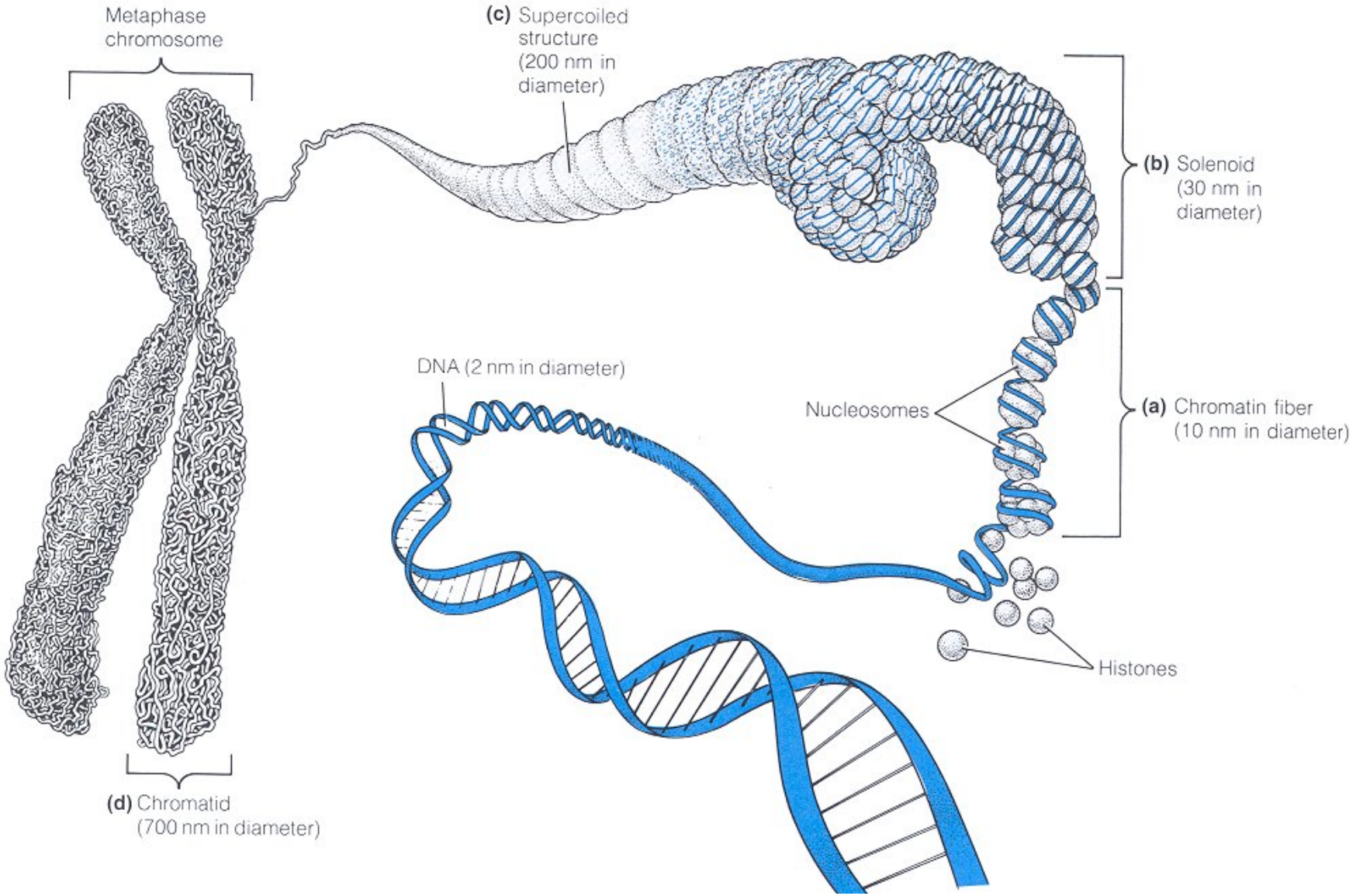

O. Dahan et al, Trends in Genetics 27: 316, 2011

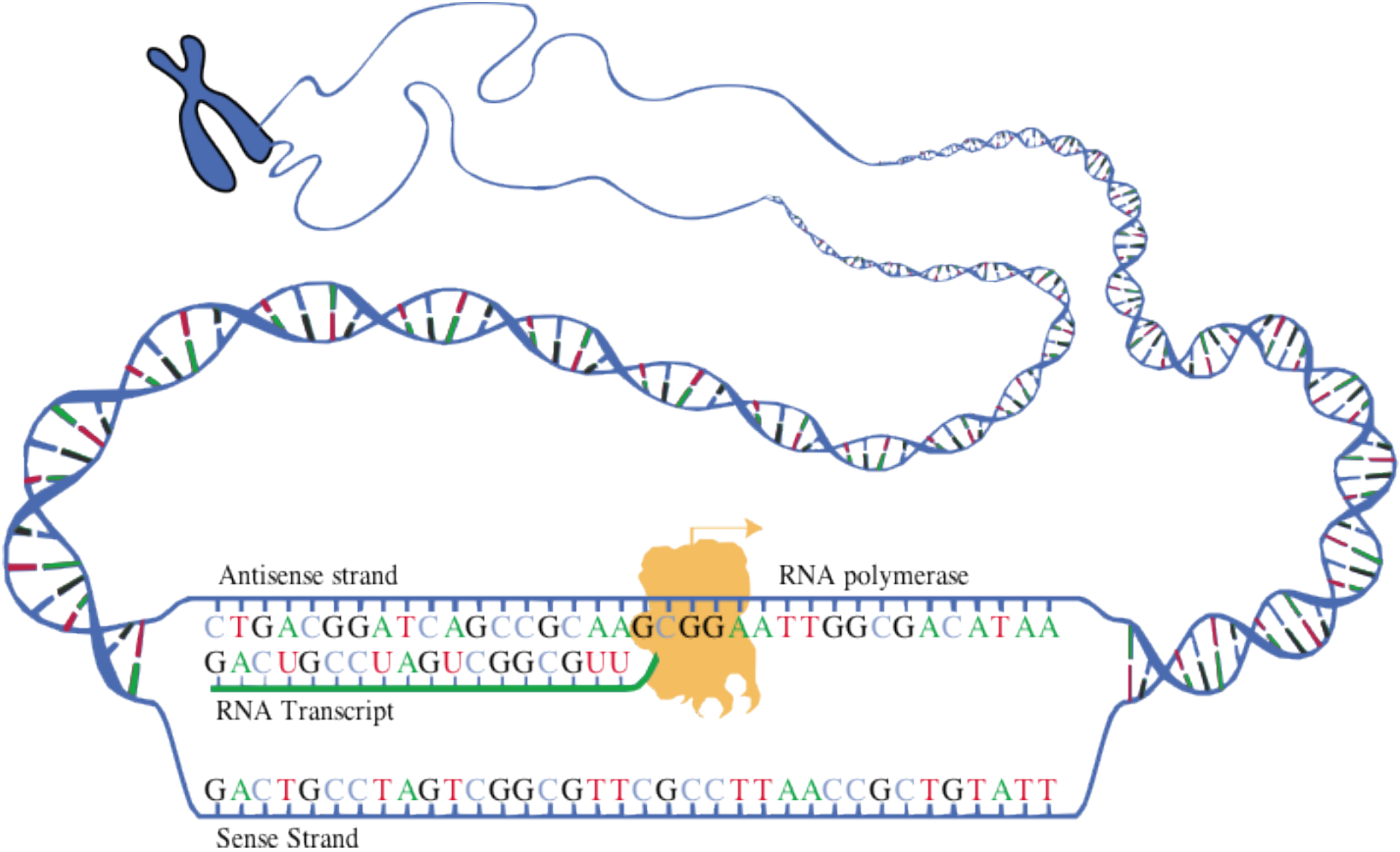
# Acoplamento e redes de controle



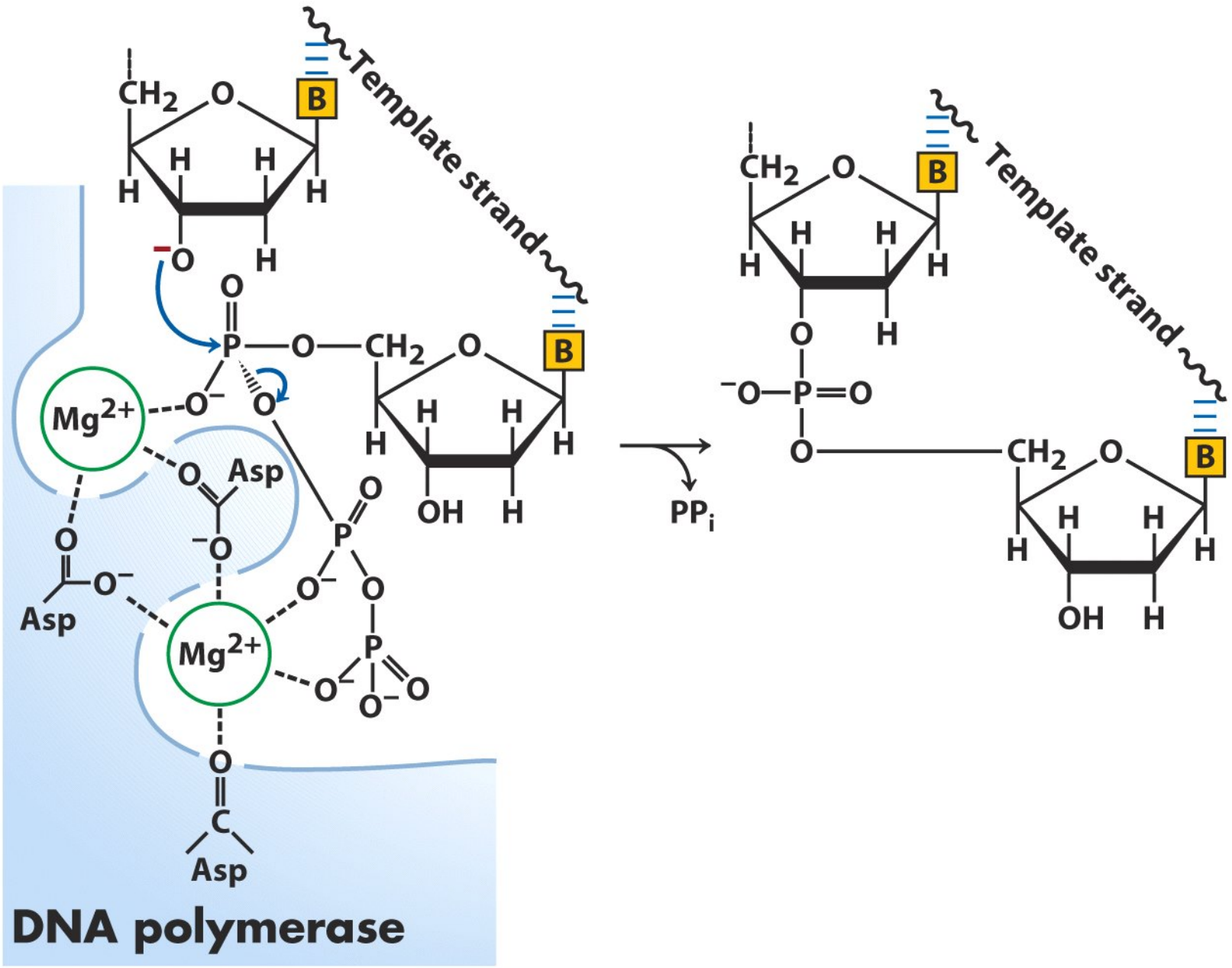

O. Dahan et al, Trends in Genetics 27: 316, 2011

# Cromatina & Transcrição

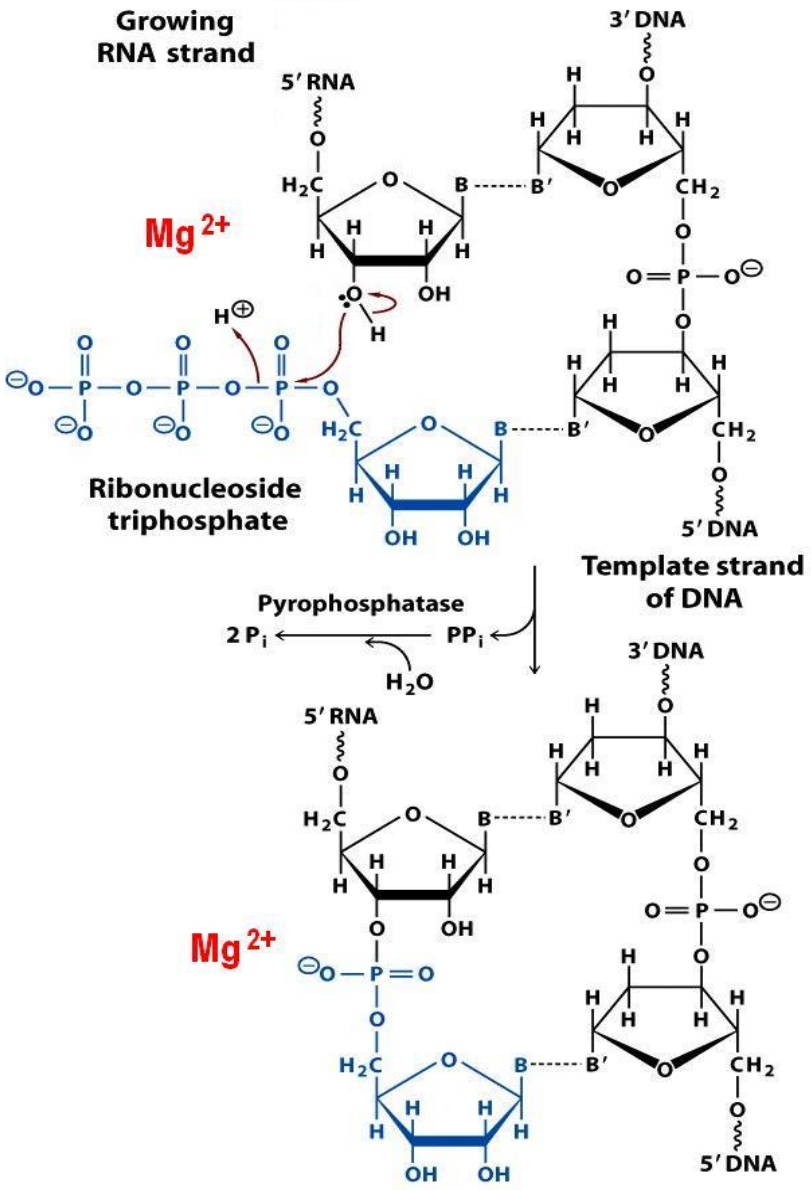



Antisense strand
RNA polymerase
CTGACGGATCAGCCGCAAGCGGAATTGGCGACATAA
GACUGCCUAGUCGGCGUU
RNA Transcript
GACTGCCTAGTCGGCGTTCGCCTTAACCGCTGTATT
Sense Strand

# Síntese do polímero: ligações fosfodiéster



# O que é Transcrição?




-Dependente de DNA

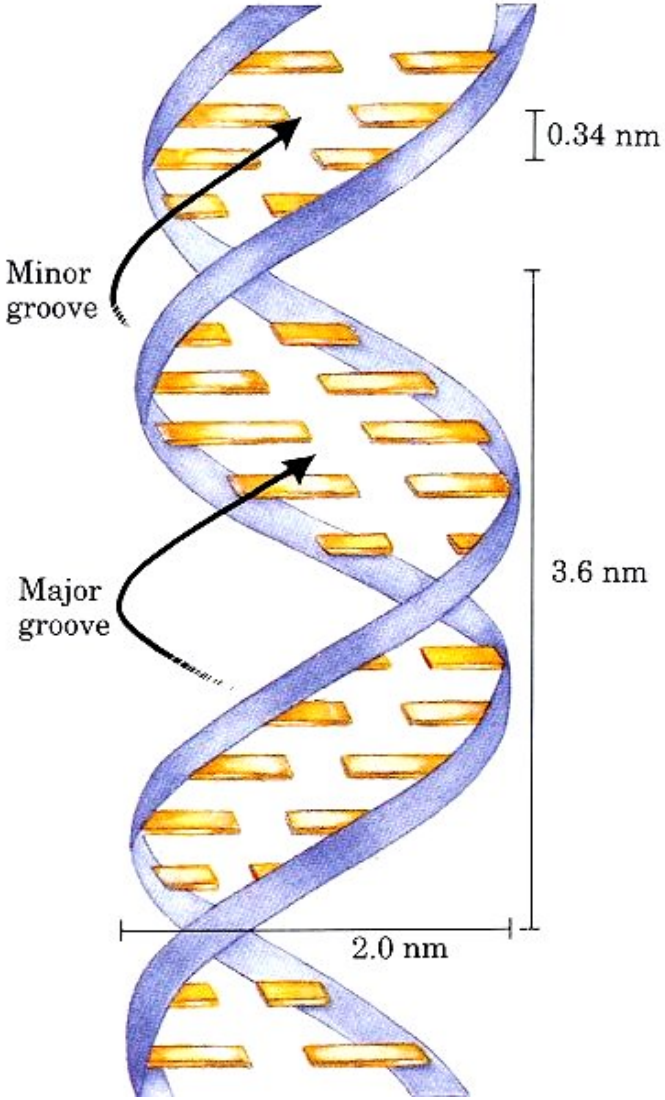
-Reação enzimática (RNA polimerase)

-Independente de *primer*

- 5’ → 3’

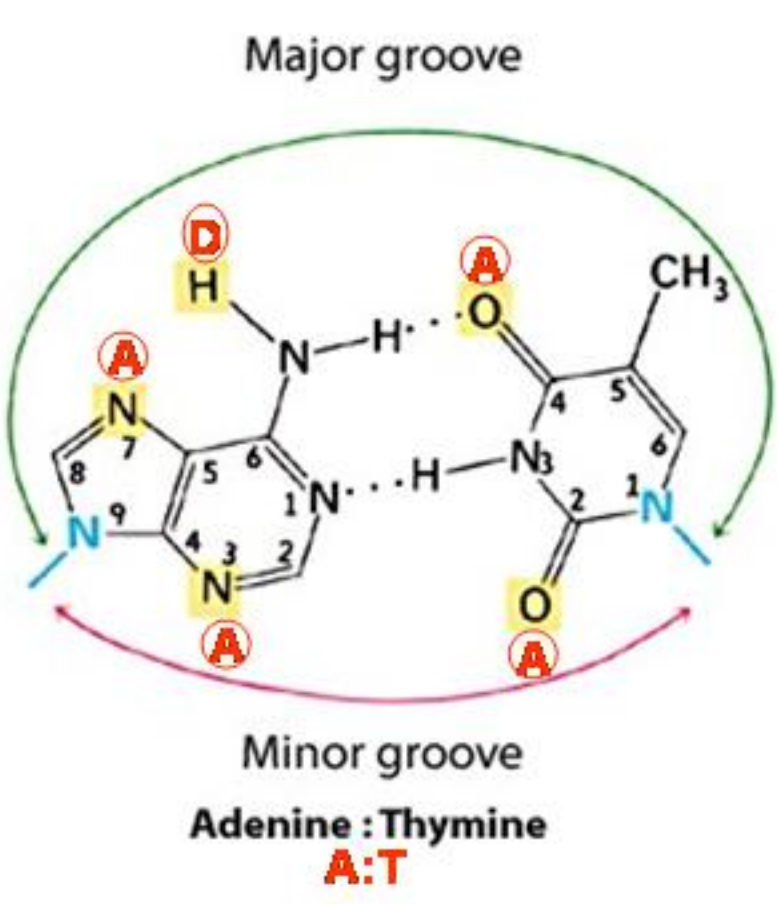
-NTPs: ATP, GTP, CTP e UTP

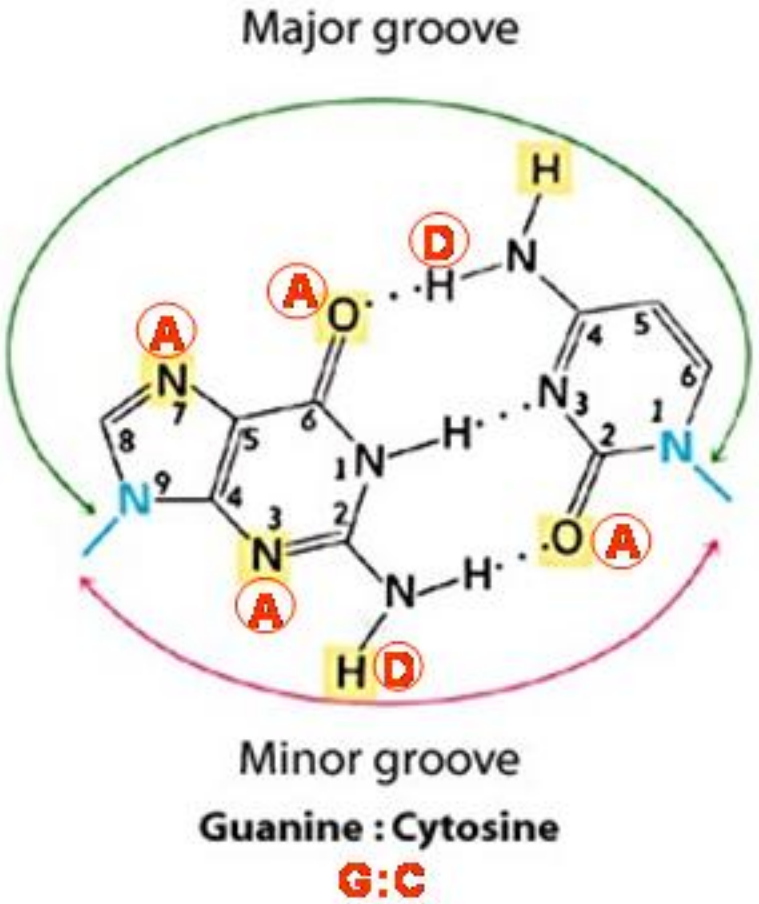
# A dupla hélice




http://upload.wikimedia.org/wikipedia/commons/1/16/DNA_orbit_animated.gif

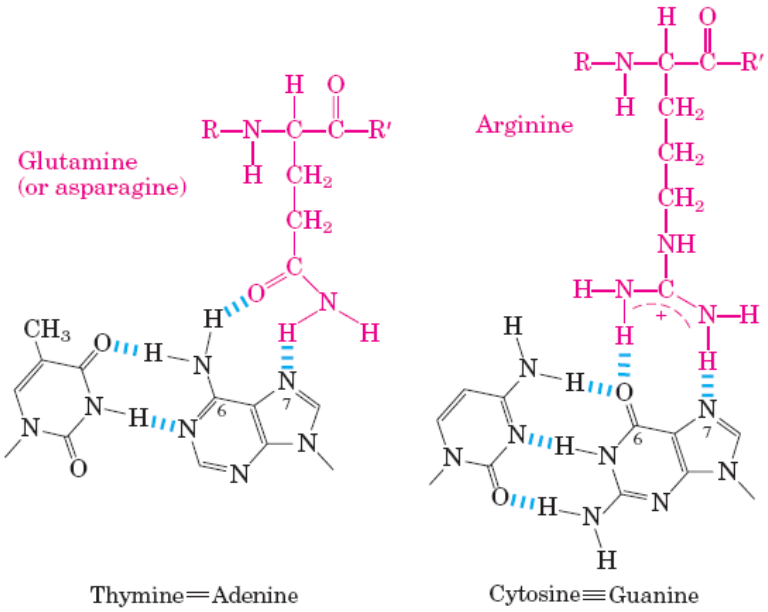
# Base pairs: H-bonding properties



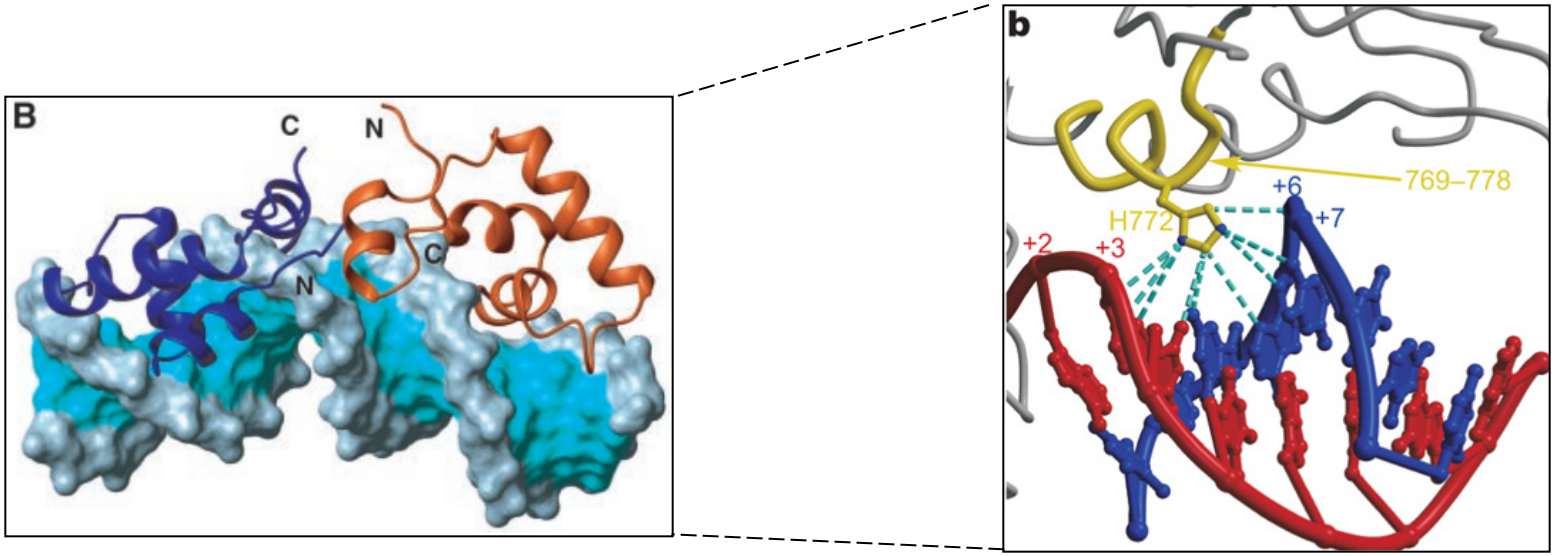




**Bases are H-donors (D) or acceptors (A)**

# Início da Transcrição: Interação DNA-Proteína



# Maquinaria de transcrição: Interação DNA-Proteina

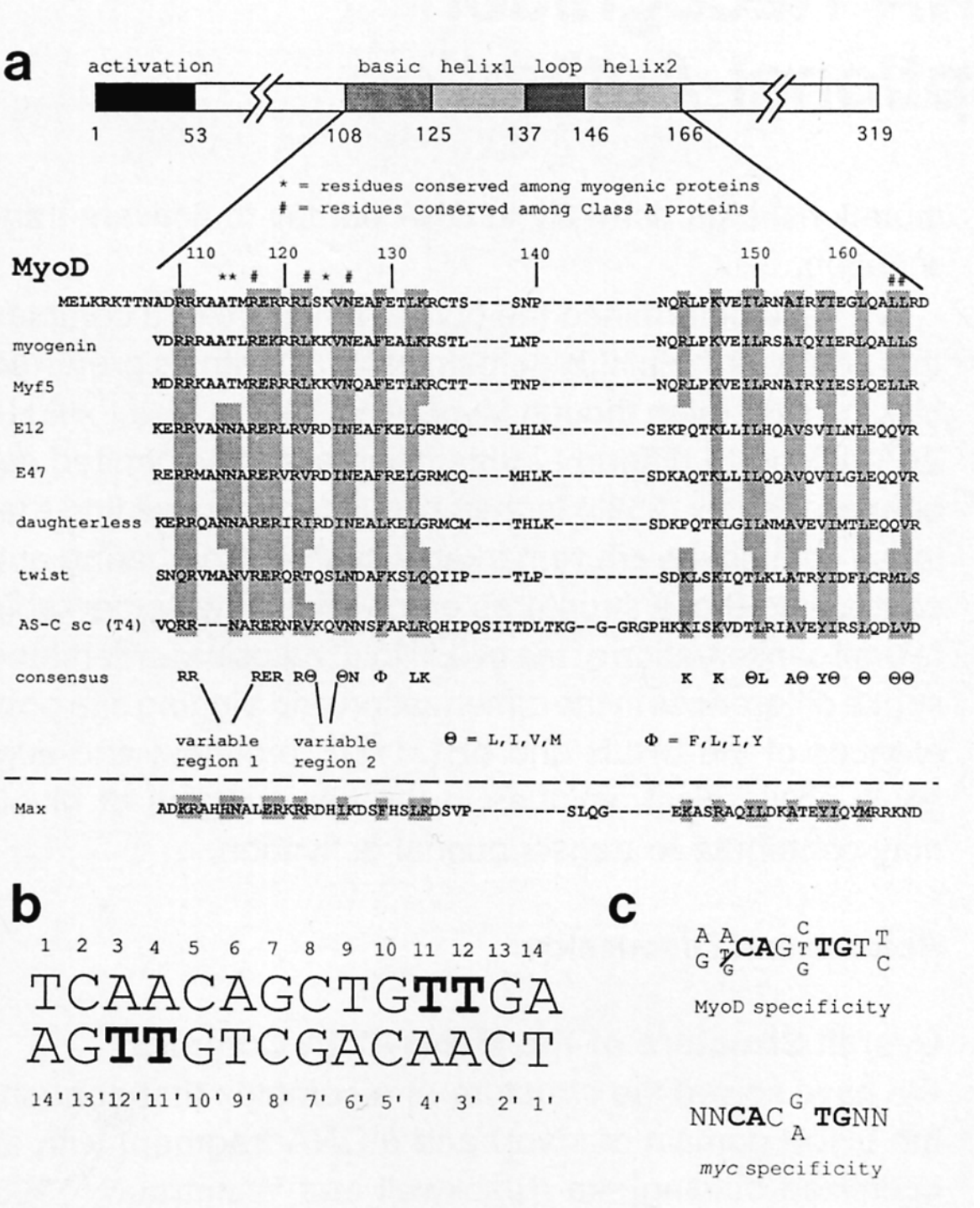



*Kalodimos et al, EMBO 2002*

*Vassylyev et al, Nature 2007*

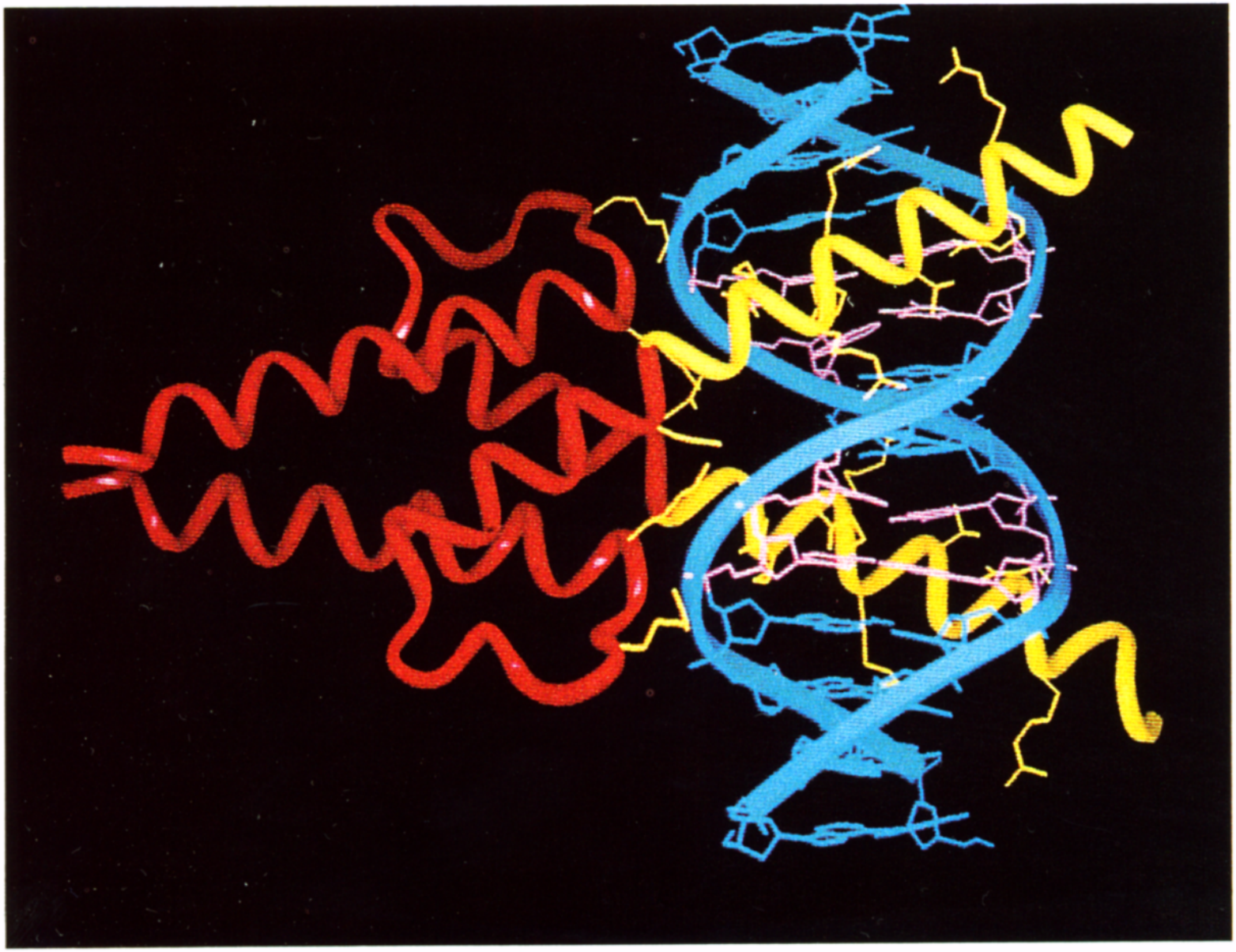
# TFs: Dominios, estruturas e interações

MyoD HLH domain
&
DNA fragment



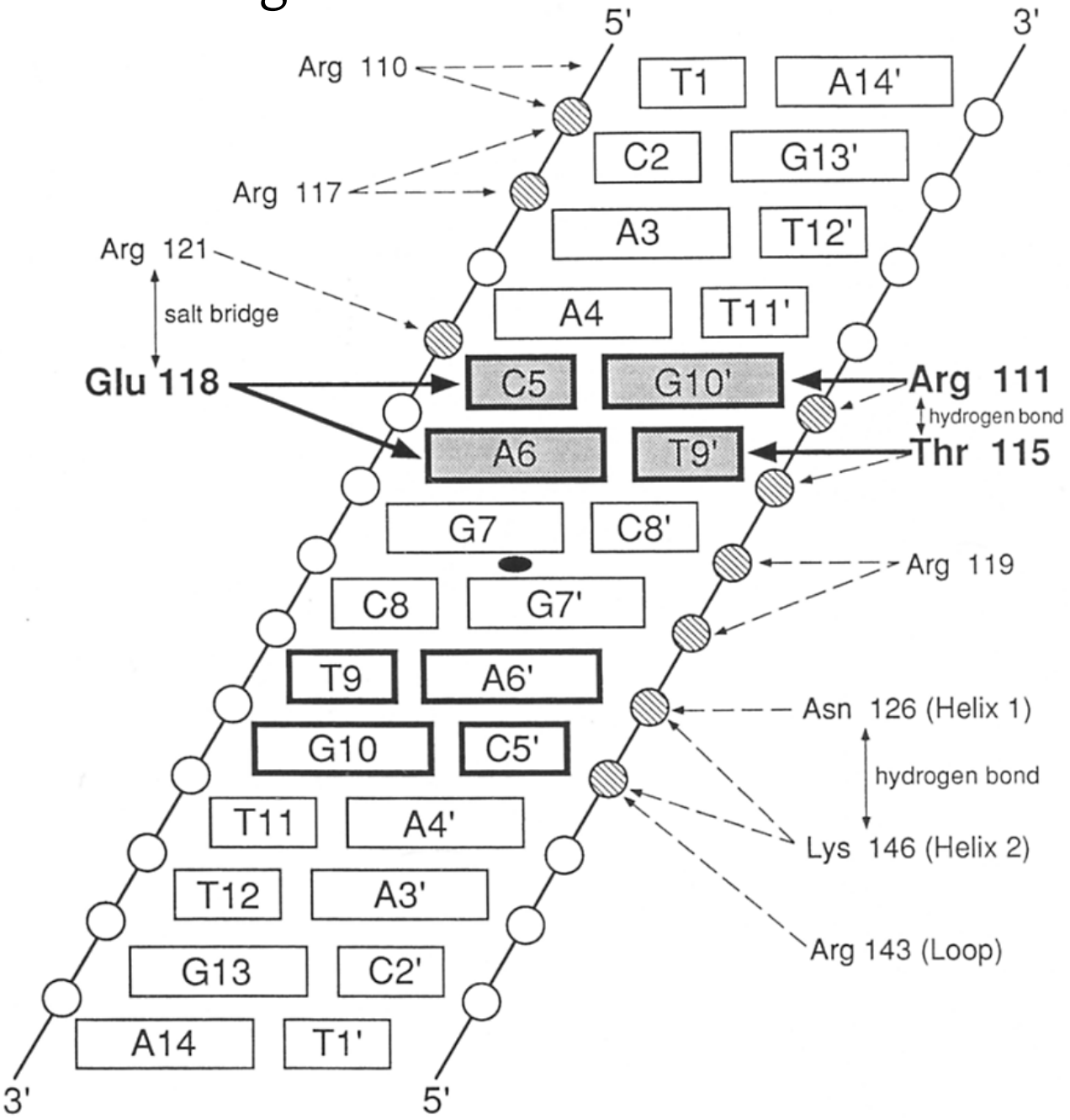

PCM Ma, Cell 77, 1994

# MyoD HLH domain & DNA fragment



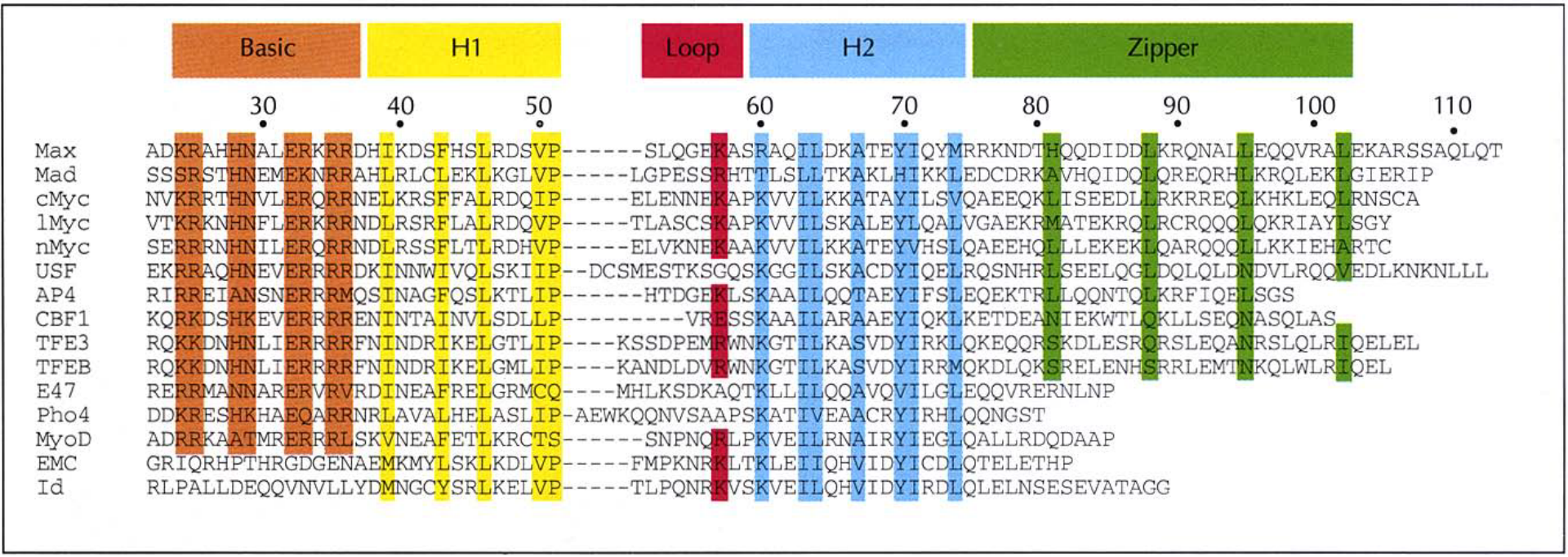
PCM Ma, Cell 77, 1994

# MyoD HLH domain & DNA fragment



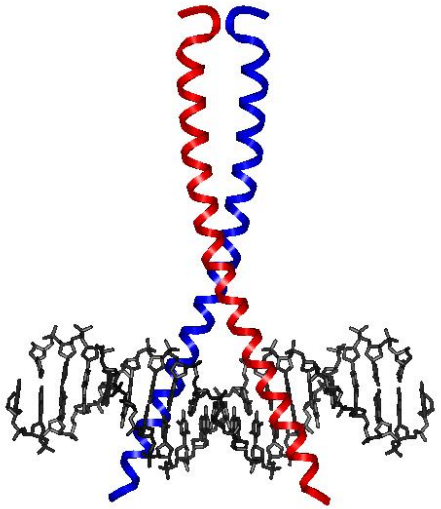

PCM Ma, Cell 77, 1994

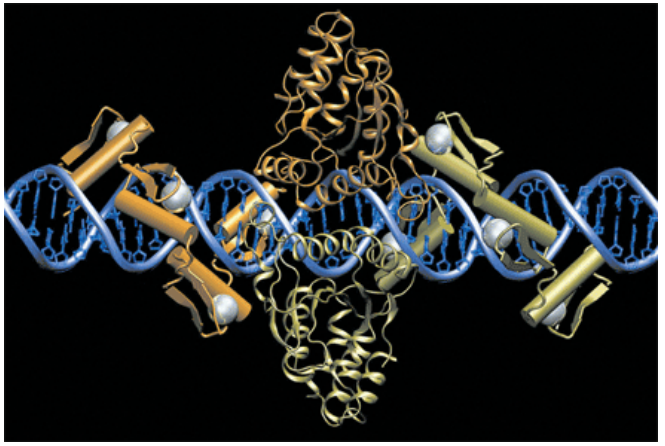
# Início da Transcrição: Interação DNA-Proteína

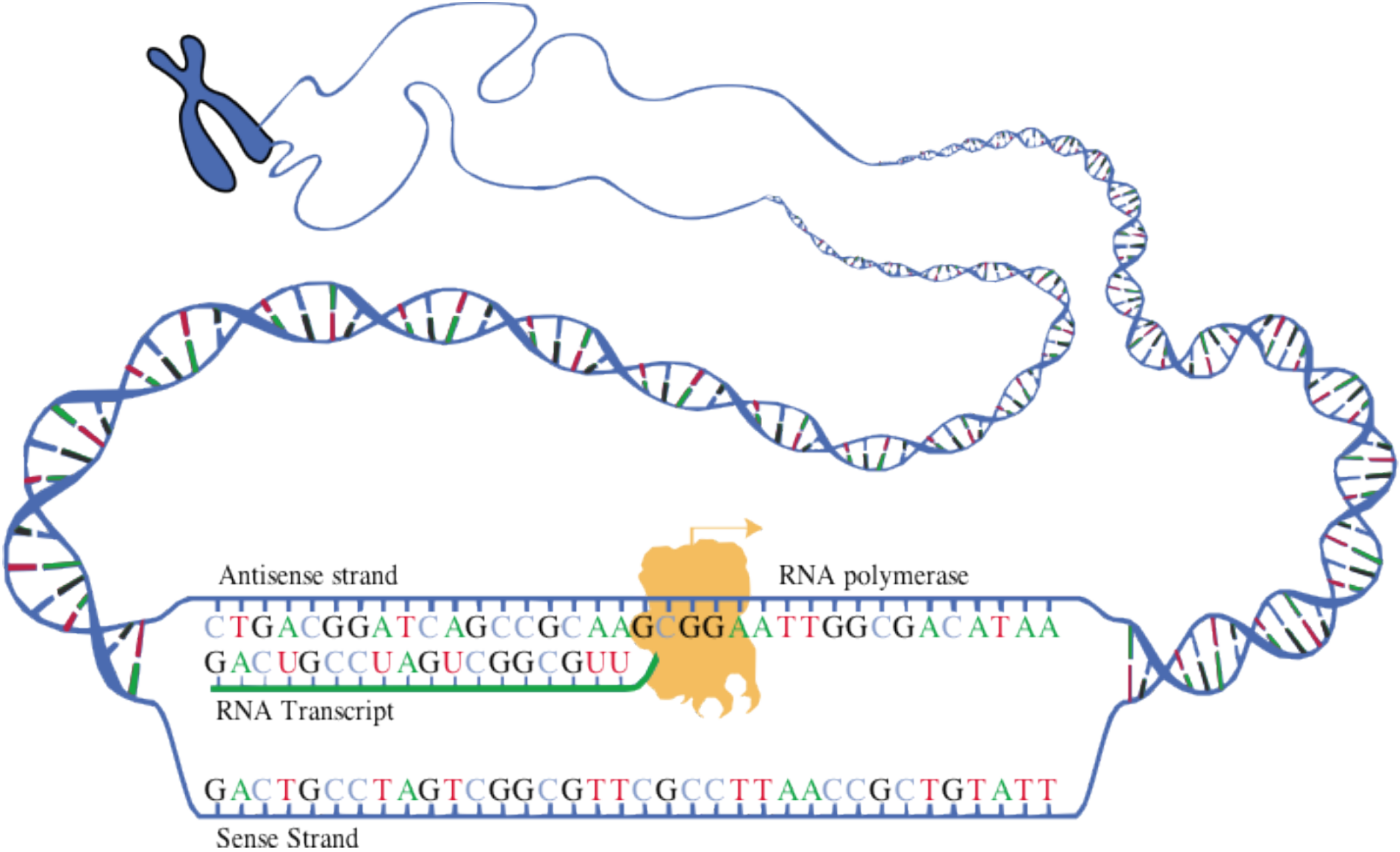


# Início da Transcrição: Interação DNA-Proteína

Leucine Zipper:
GCN4

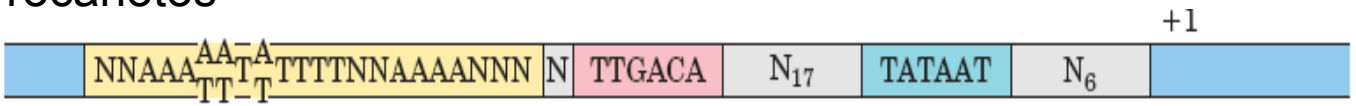




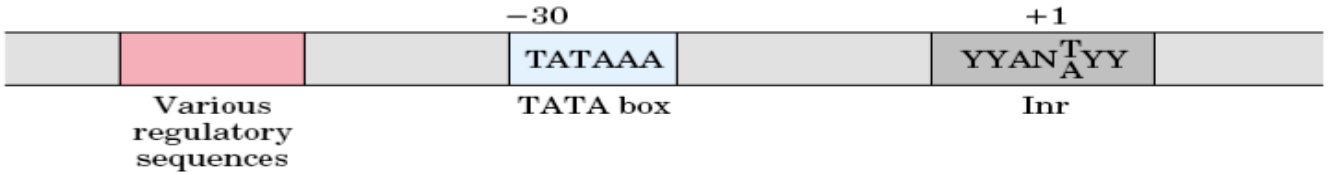

Antisense strand
RNA polymerase
CTGACGGATCAGCCGCAAGCGGAATTGGCGACATAA
GACUGCCUAGUCGGCGUU
RNA Transcript
GACTGCCTAGTCGGCGTTCGCCTTAACCGCTGTATT
Sense Strand

# Início da Transcrição Depende de Promotores

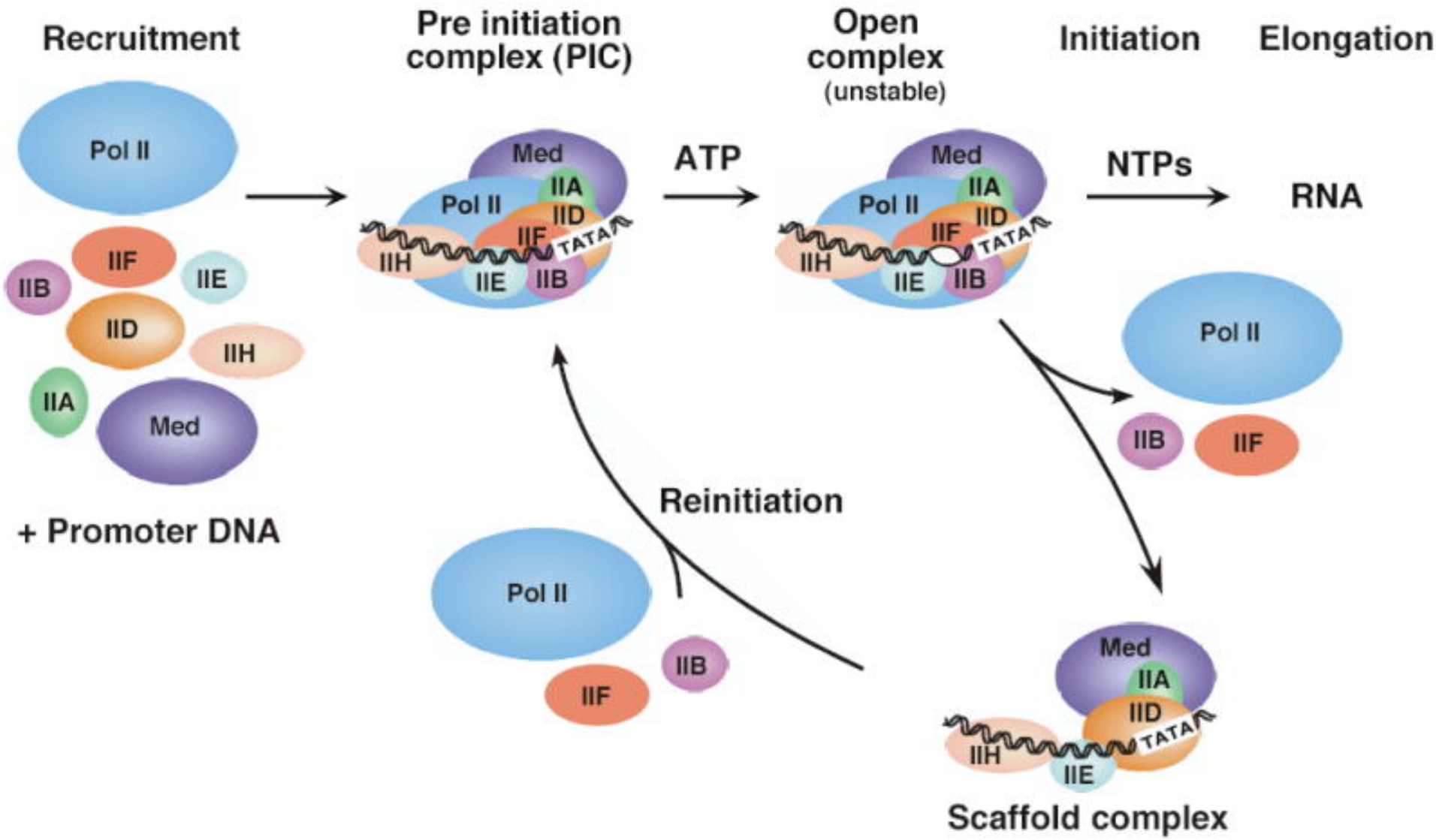
Procariotos




Eucariotos



# Iniciação e reiniciação da Transcrição




S.Hahn Nature Struct & Mol Biol 11, 2004

# Da complexidade de interações de um fator de transcrição

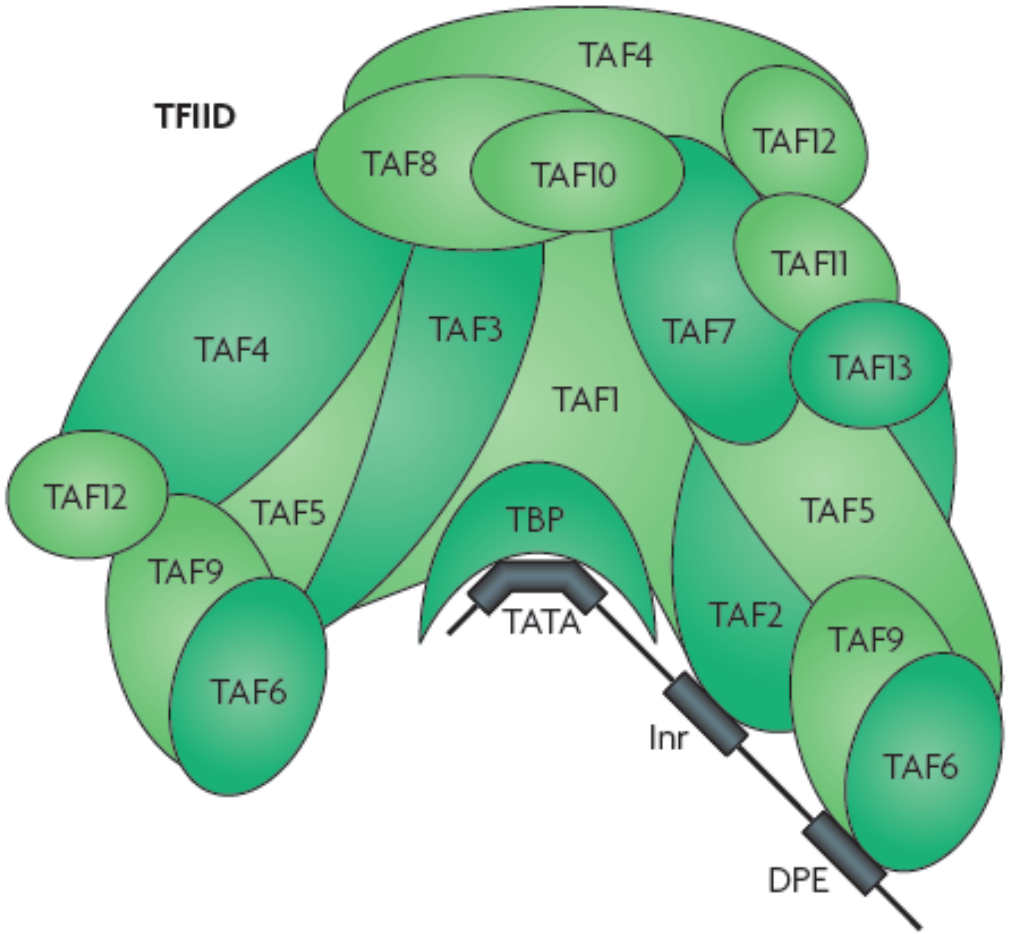
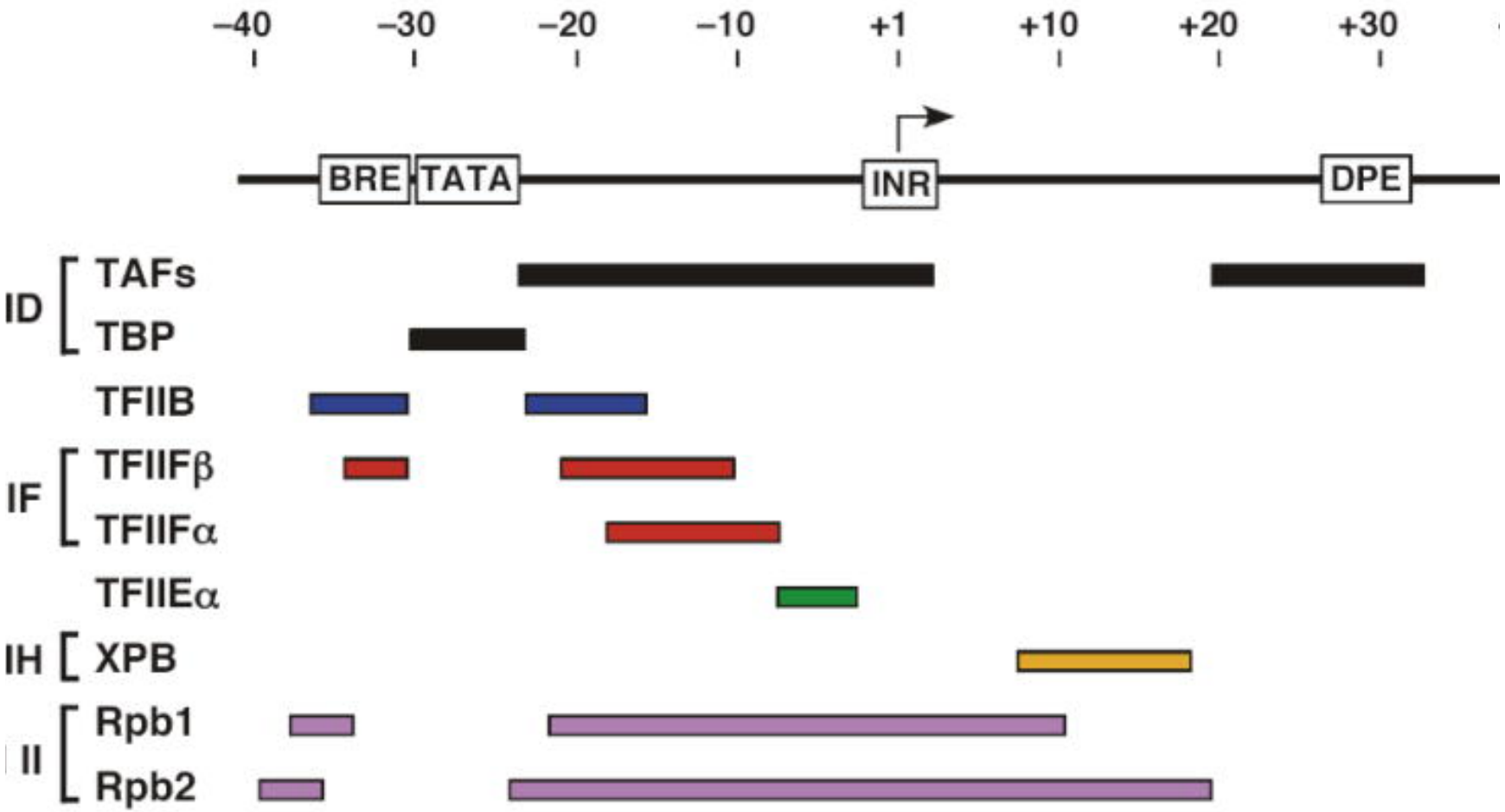
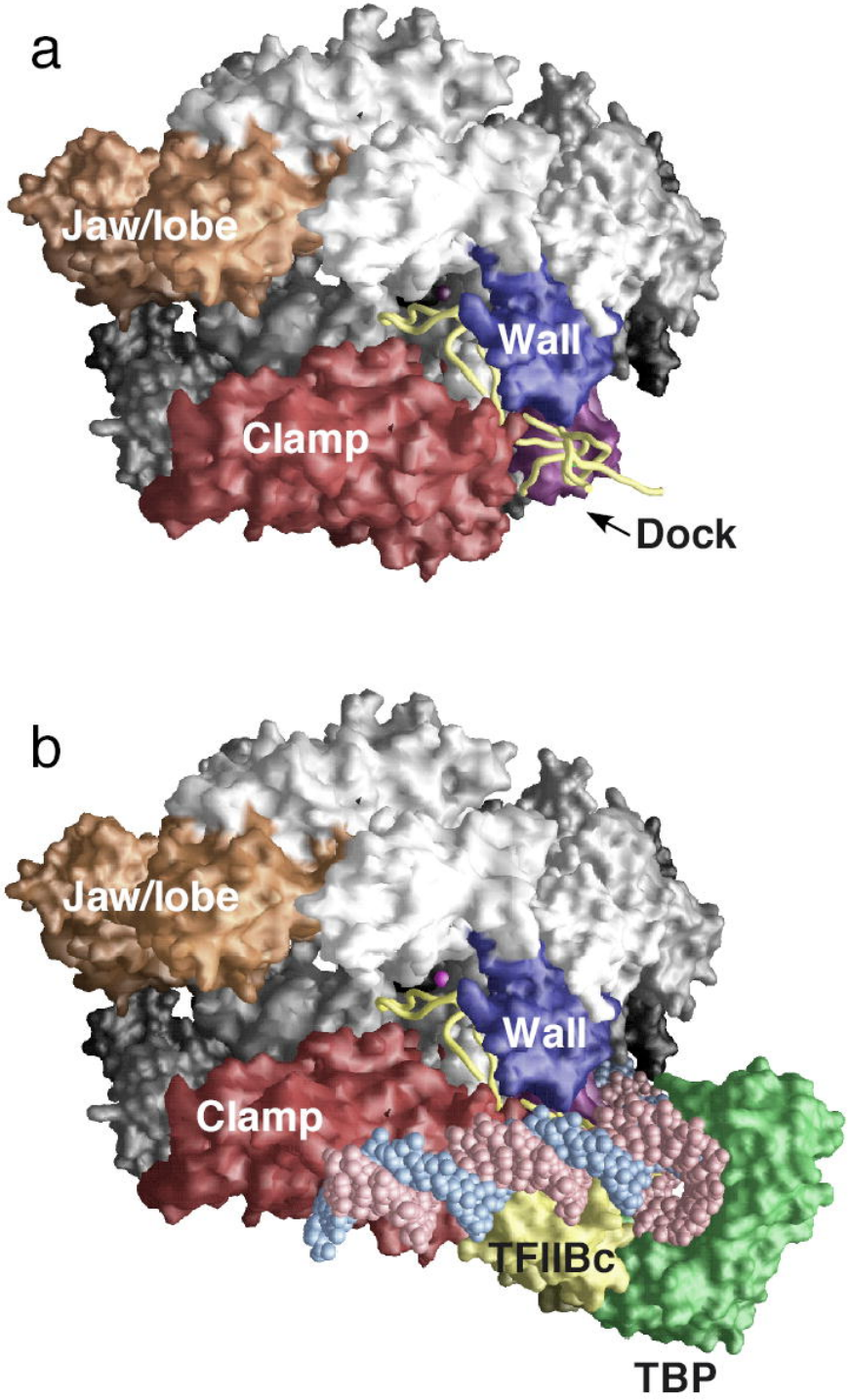



Figure 1 | **Core promoter recognition by TFIID.**

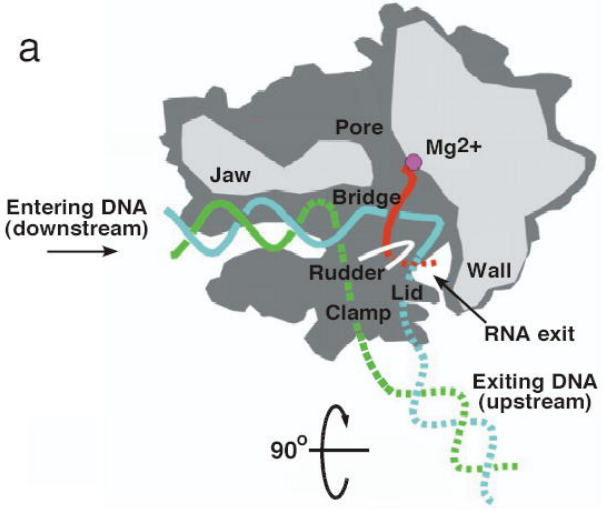

–40
–30
–20
–10
+1
+10
+20
+30
BRE
TATA
INR
DPE
ID
TAFs
TBP
TFIIB
IF
TFIIFβ
TFIIFα
TFIIEα
IH
XPB
II
Rpb1
Rpb2

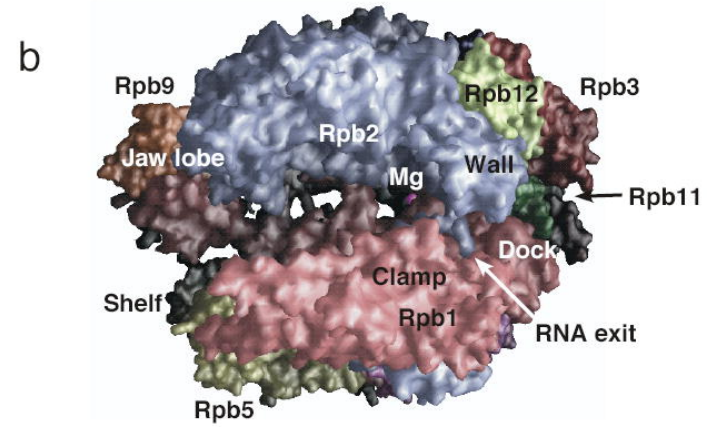
# RNA polimerase II

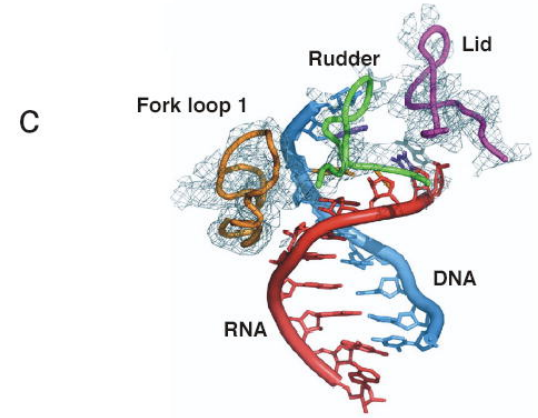



S.Hahn Nature Struct & Mol Biol 11, 2004

# RNA polimerase II
# &
# Complexo de elongação



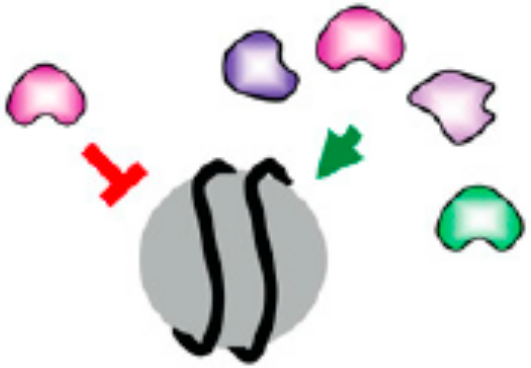

S.Hahn Nature Struct & Mol Biol 11, 2004

# Pioneer transcription factors

- Eventos iniciais na cromatina: Pioneer TFs ligam-se primeiro
- Podem ser determinantes de destino celular
- Permitem respostas mais rápidas
- Diferentes associações = destinos celulares diversos
  - Perspectivas de reprogramação celular

# Pioneer Transcription Factors

Most transcription factors



1- cooperativity allows nucleosome/chromatin binding

2 - simultaneous binding with other factors

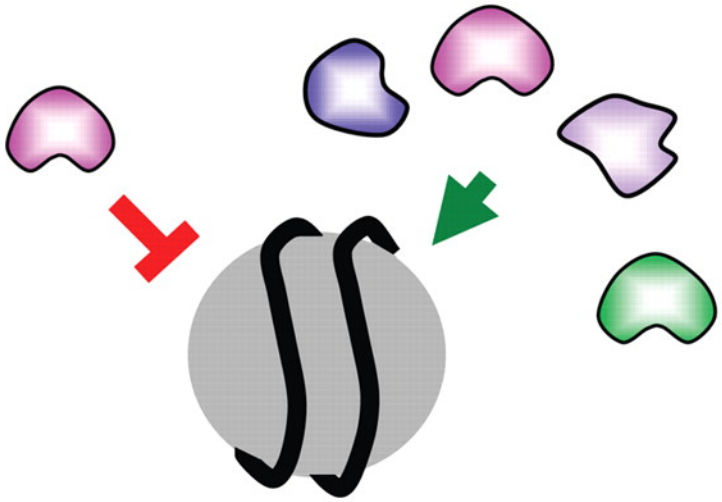
Pioneer transcription factors

1 - independent nucleosome/chromatin binding

2 - precedes other factors binding

**Properties that distinguish pioneer factors from other transcription factors.**

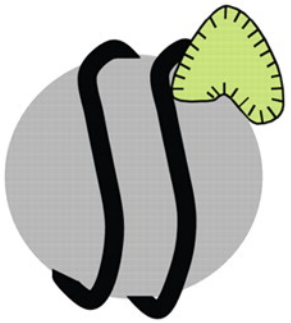
## Most transcription factors



1- cooperativity allows nucleosome/chromatin binding

2 - simultaneous binding with other factors

## Pioneer transcription factors

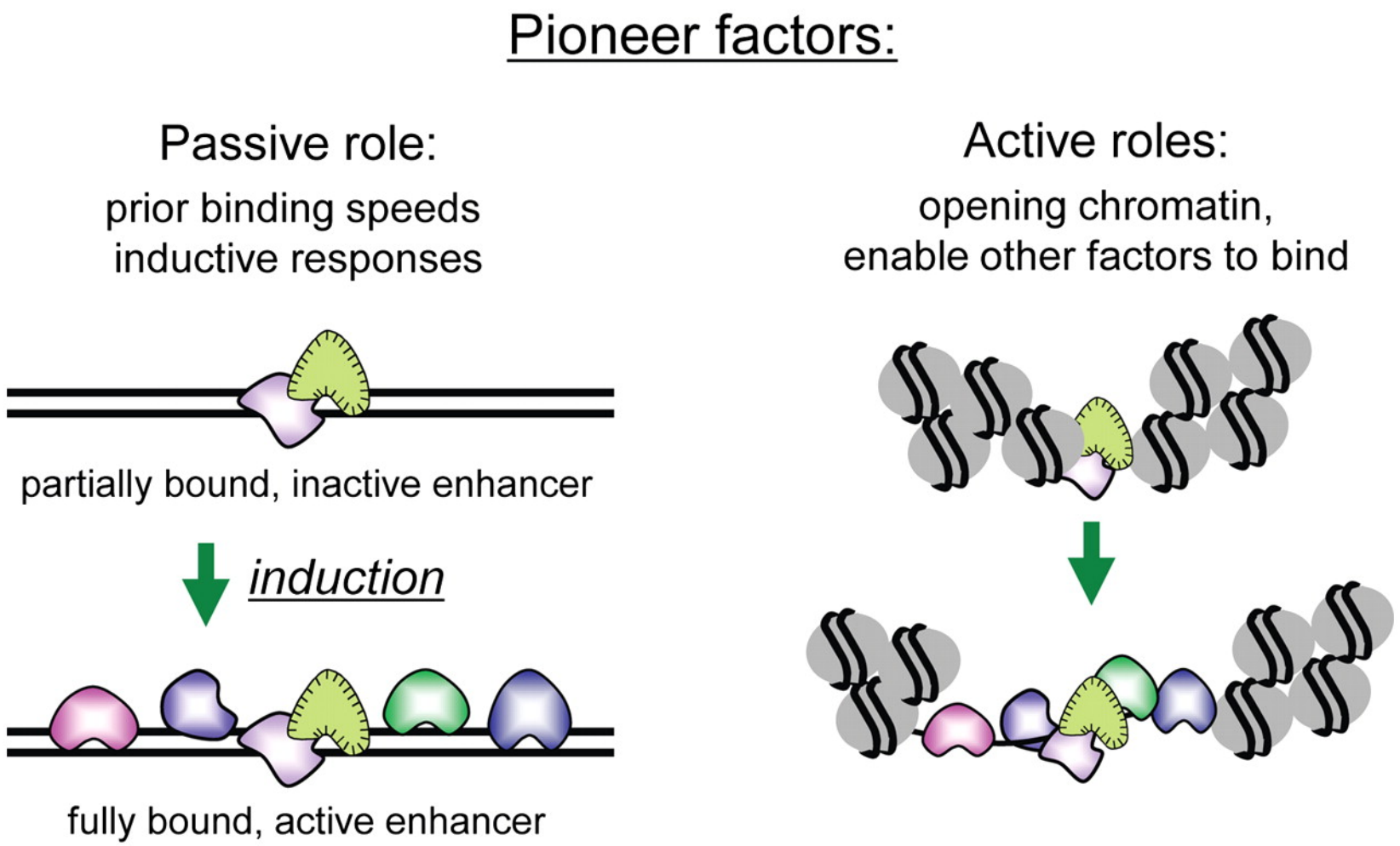


1 - independent nucleosome/chromatin binding

2 - precedes other factors binding

**Zaret K S , Carroll J S Genes Dev. 2011;25:2227-2241**

**Passive and active roles for pioneer factors in endowing transcriptional competence.**




Zaret K S , Carroll J S Genes Dev. 2011;25:2227-2241

OPEN ACCESS Freely available online

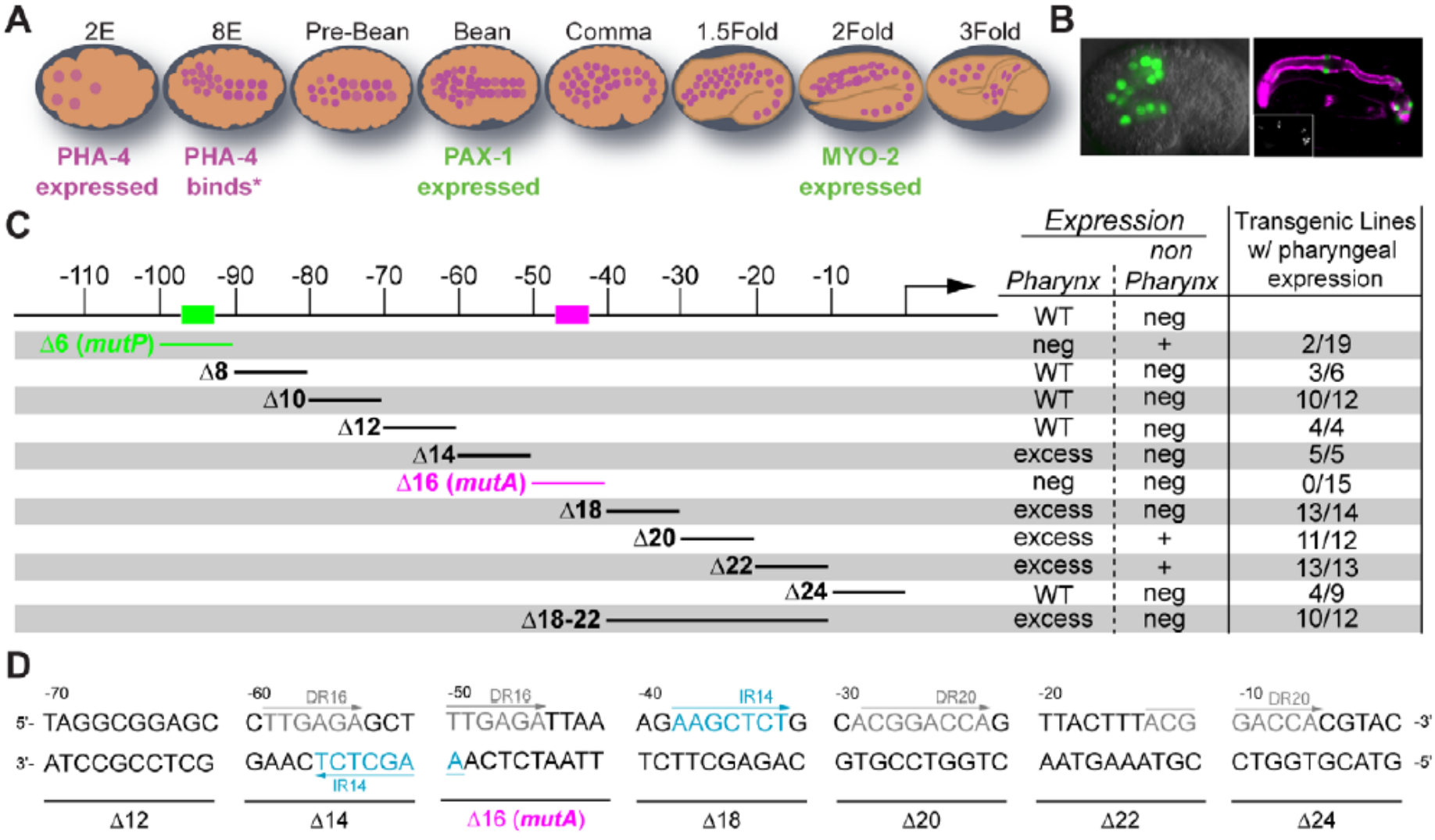
PLoS GENETICS

# Dynamic Chromatin Organization during Foregut Development Mediated by the Organ Selector Gene PHA-4/FoxA

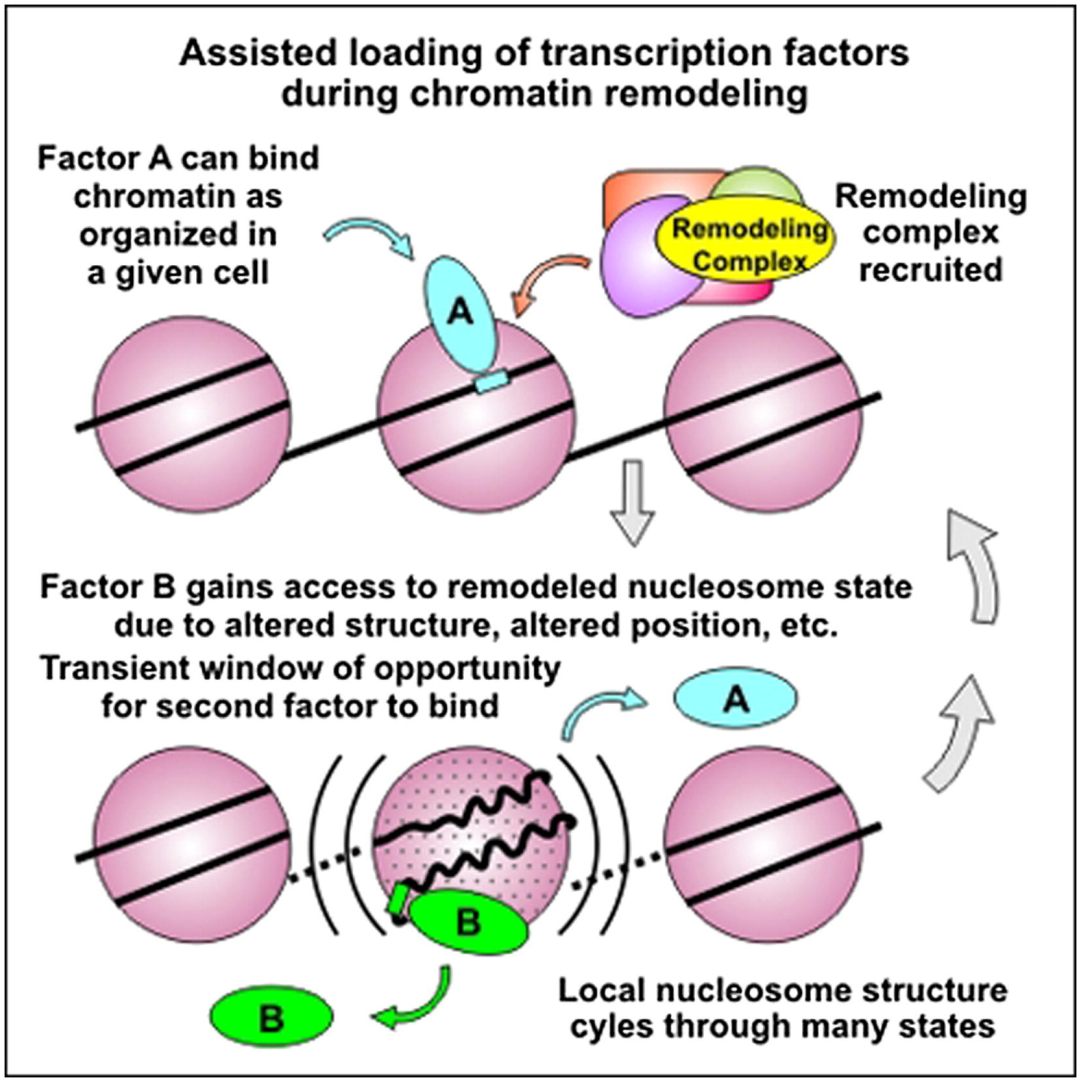
Tala H. I. Fakhouri, Jeff Stevenson[¤a], Andrew D. Chisholm[¤b], Susan E. Mango*

Selector genes govern the fates of groups of cells related to each other by virtue of their cell type, position or affiliation to an organ [1]. Genomic methods have revealed that selector genes directly control hundreds, even thousands, of target genes, which define the characteristics of a particular cell type [2–6]. For example, the

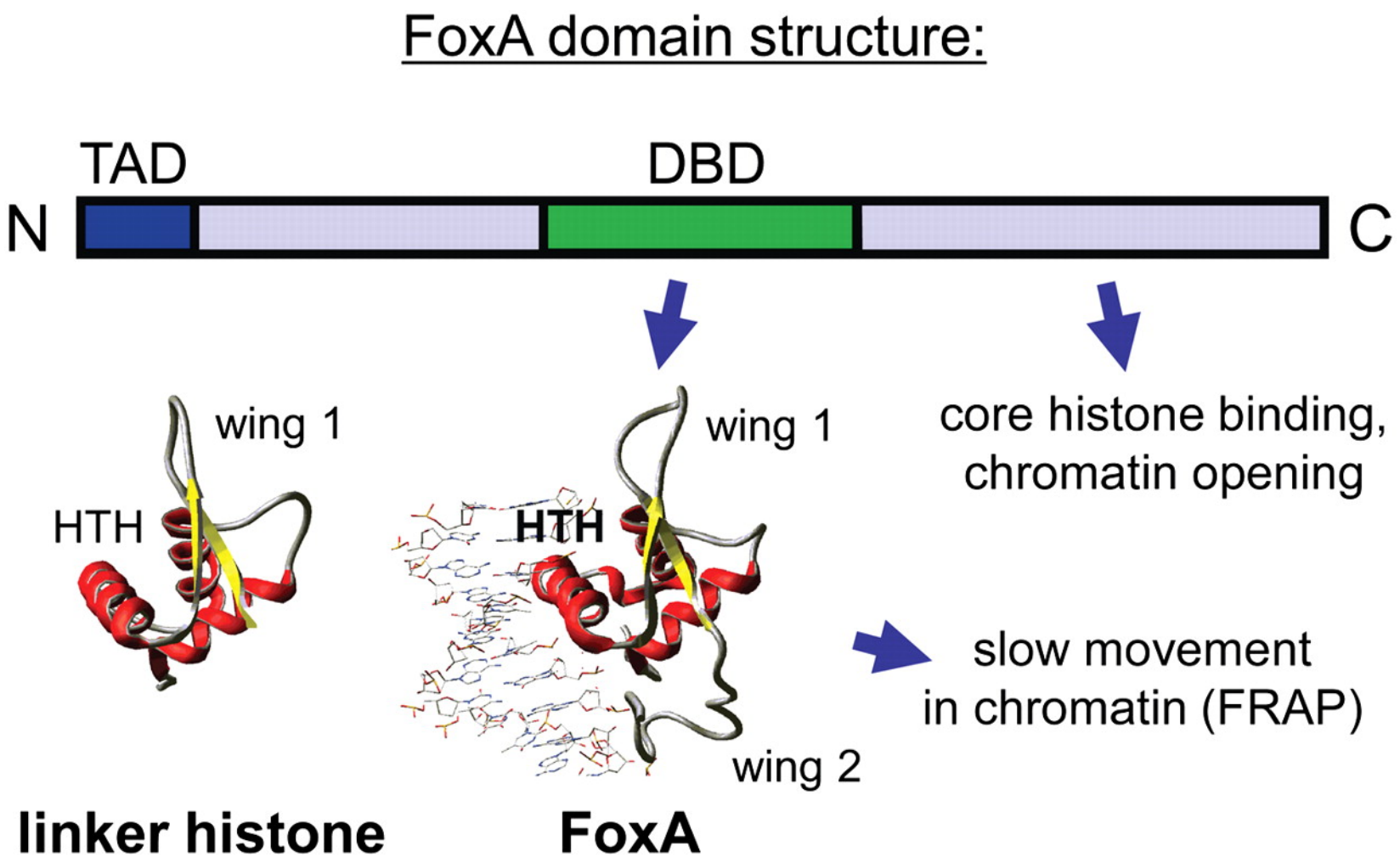
**Figure 1. Scanning mutagenesis of the *pax-1* promoter.** (A) A cartoon depicting the pattern of PHA-4 expression during different stages of embryogenesis. Embryonic events that occur at specific developmental stages are annotated.



# Pioneer TFs: access of target sites on nucleosomes

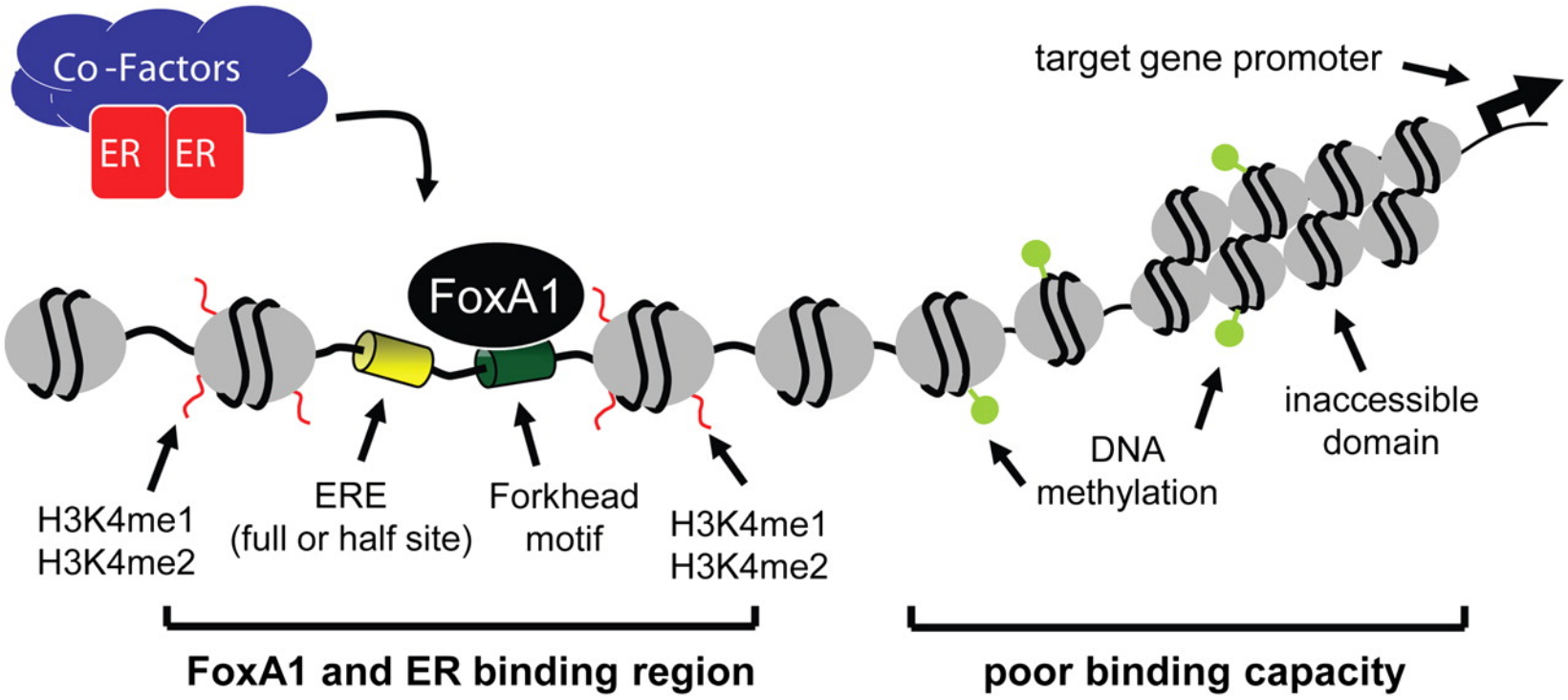


**FoxA factors possess features of linker histones and conventional transcription factors.**

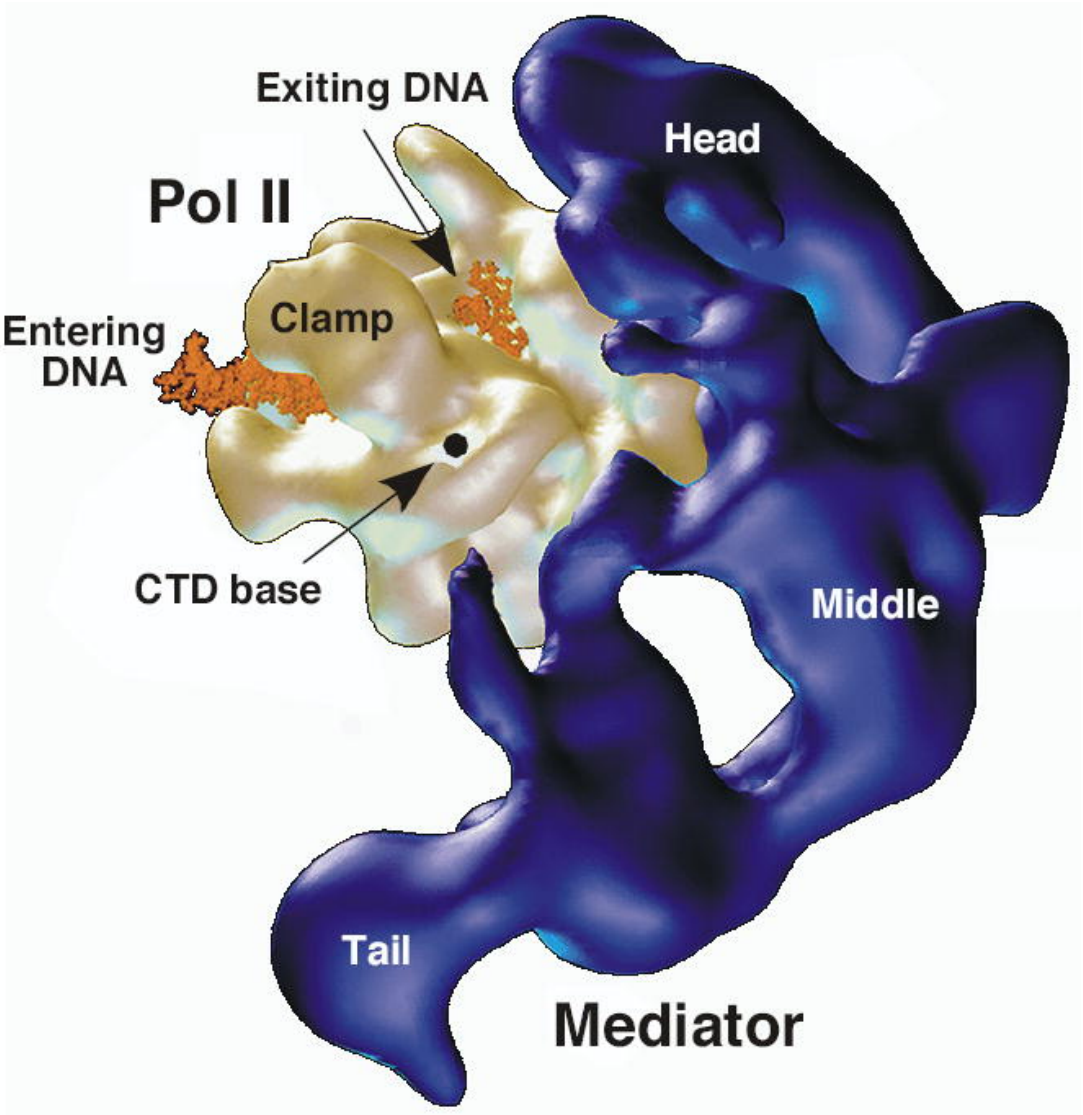



Zaret K S , Carroll J S Genes Dev. 2011;25:2227-2241

**Optimal chromatin features for FoxA1 binding to chromatin in breast cancer cells.**




Zaret K S , Carroll J S Genes Dev. 2011;25:2227-2241


Exiting DNA
Head
Pol II
Clamp
Entering DNA
CTD base
Middle
Tail
Mediator

GENE EXPRESSION

# The coherent Mediator

**Enhancer sequences increase gene transcription with the help of a co-activator complex, the Mediator. Another protein complex — cohesin — seems to work with Mediator to bring together enhancers and promoters.** SEE ARTICLE P. 430

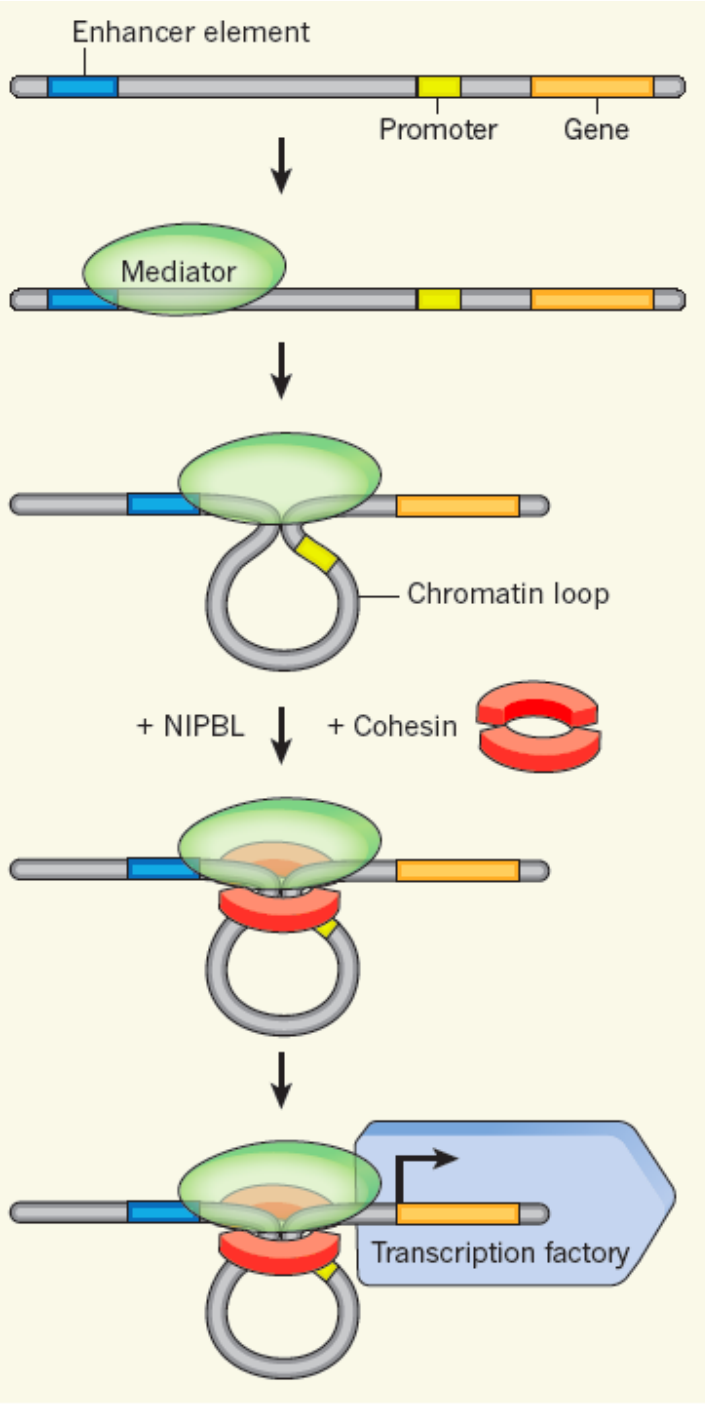
ROLF OHLSSON

GENE EXPRESSION

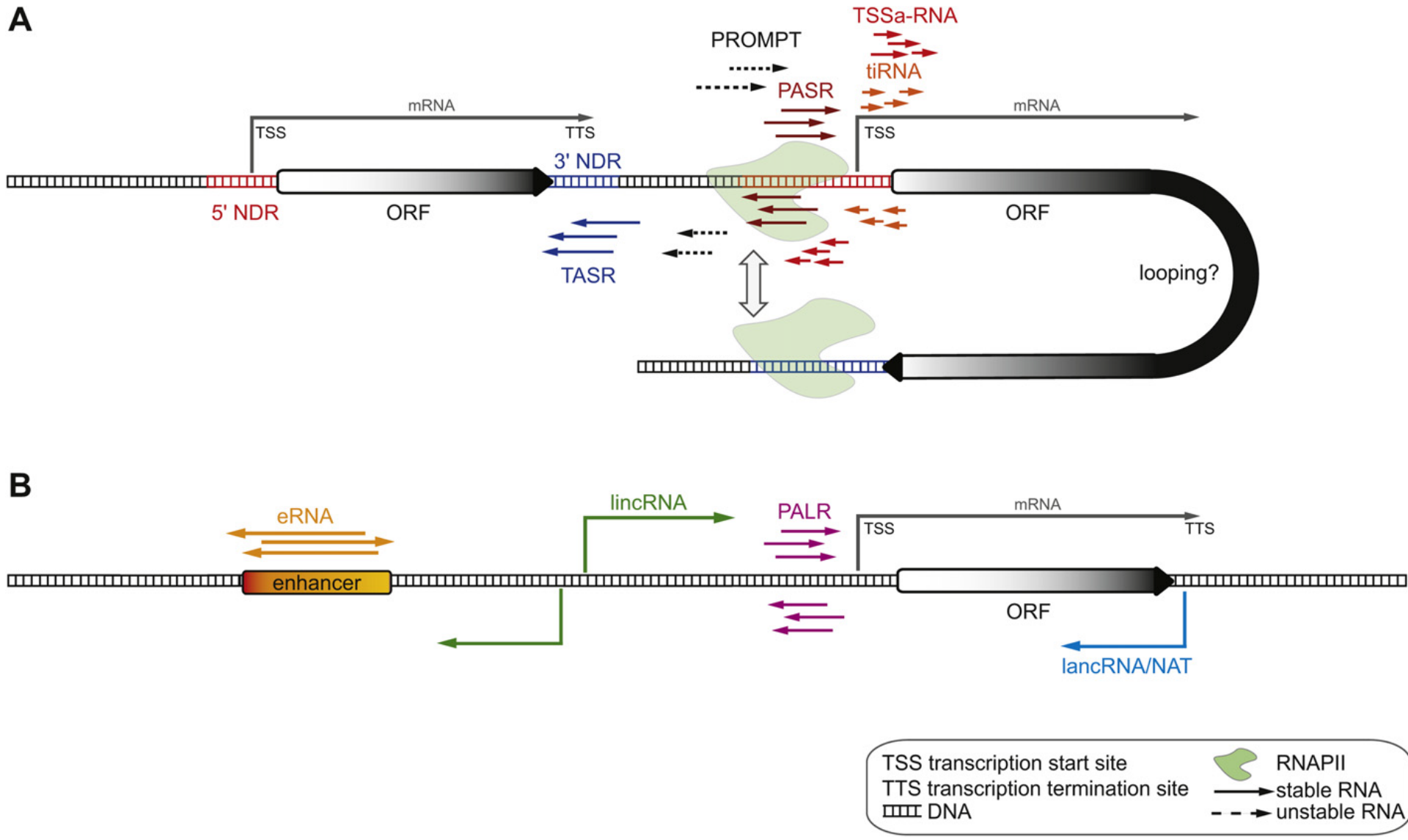
# The coherent Mediator

do this? A paper[2] in this issue describes the discovery that the Mediator complex recruits another protein complex, cohesin, to provide coherence between enhancer and promoter sequences (Kagey *et al.*, page 430).

# The coherent Mediator

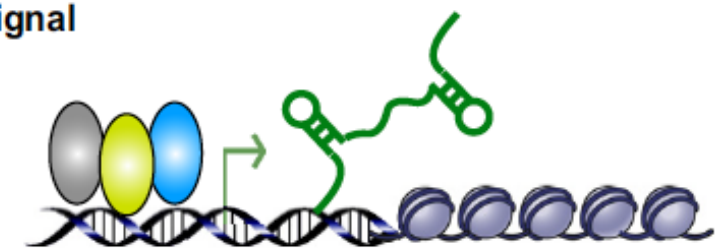


# ncRNAs diversos & controle de expressão

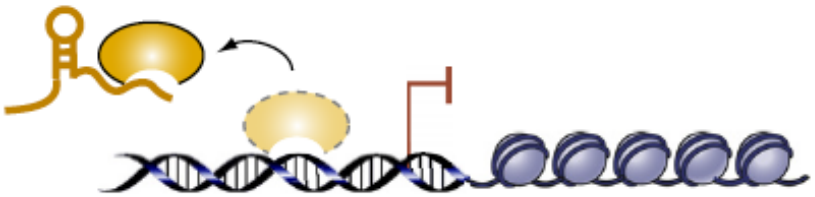


# lncRNA mecanismos diversos: Controle de expressão

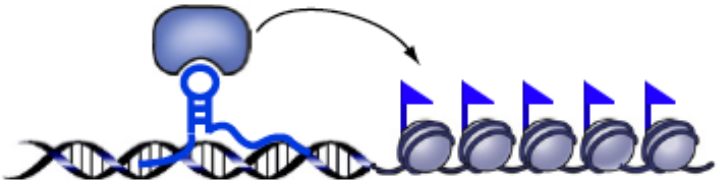
I. Signal



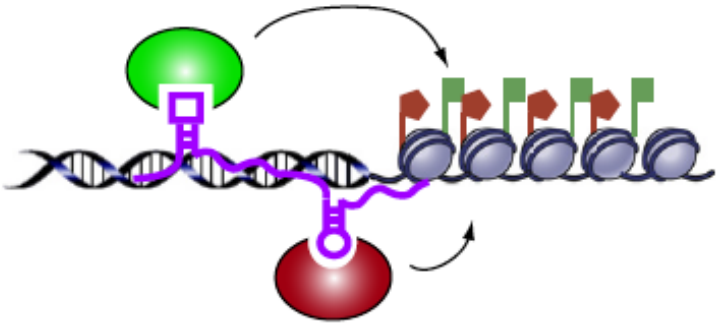
II. Decoy



III. Guide

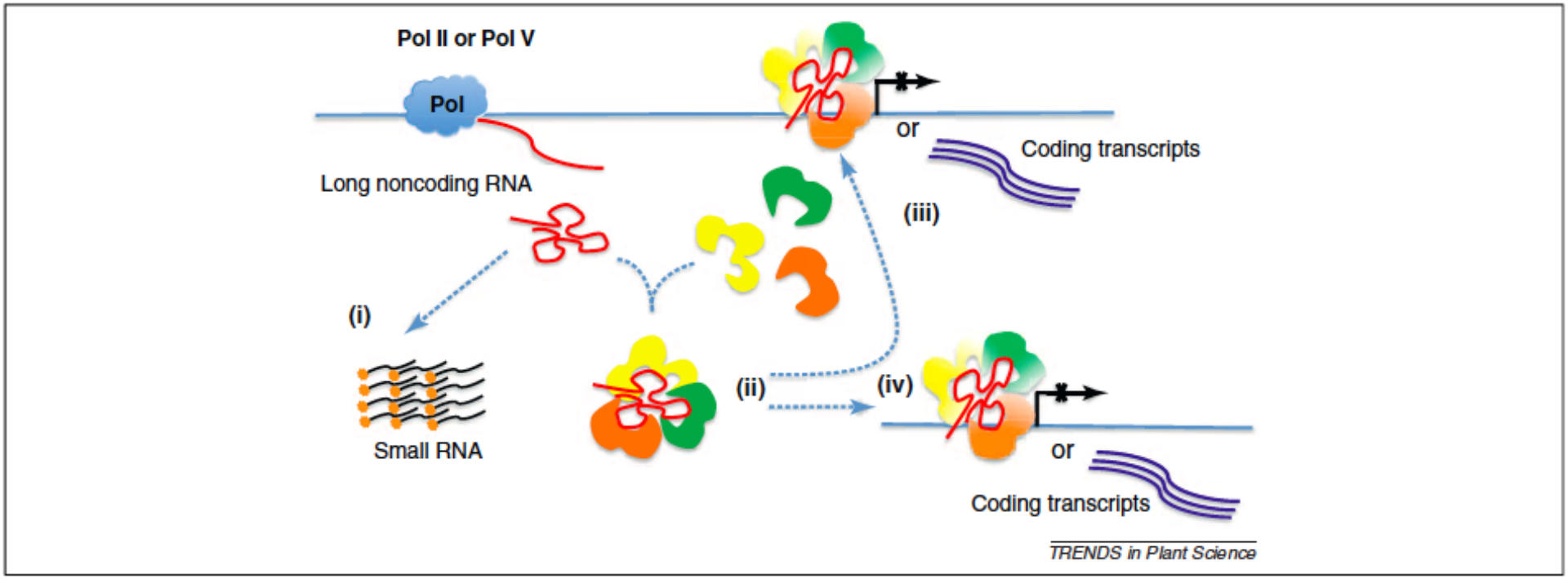


IV. Scaffold



Wang & Chang
Molecular Cell *43*, September 16, 2011

# ncRNAs diversos & controle de expressão



# O RNA como molécula regulatória