"You will think this looks complicated,

and you are right - it is complicated.

But wouldn't you rather me tell you it

is complicated than tell you it is

mysterious'? ”

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Homer Kelly, The Golfing Machine

Treating a complex subject as though it were simple multiplies its complexity because of the difficulty of systematizing missing and unknown elements or factors.

Treating a complex subject as though it were simple multiplies its complexity because of the difficulty of systematizing missing and unknown elements or factors.

Homer Kelly, The Golfing Machine

All really original achievements make us sharply rethink things we supposed we knew well.

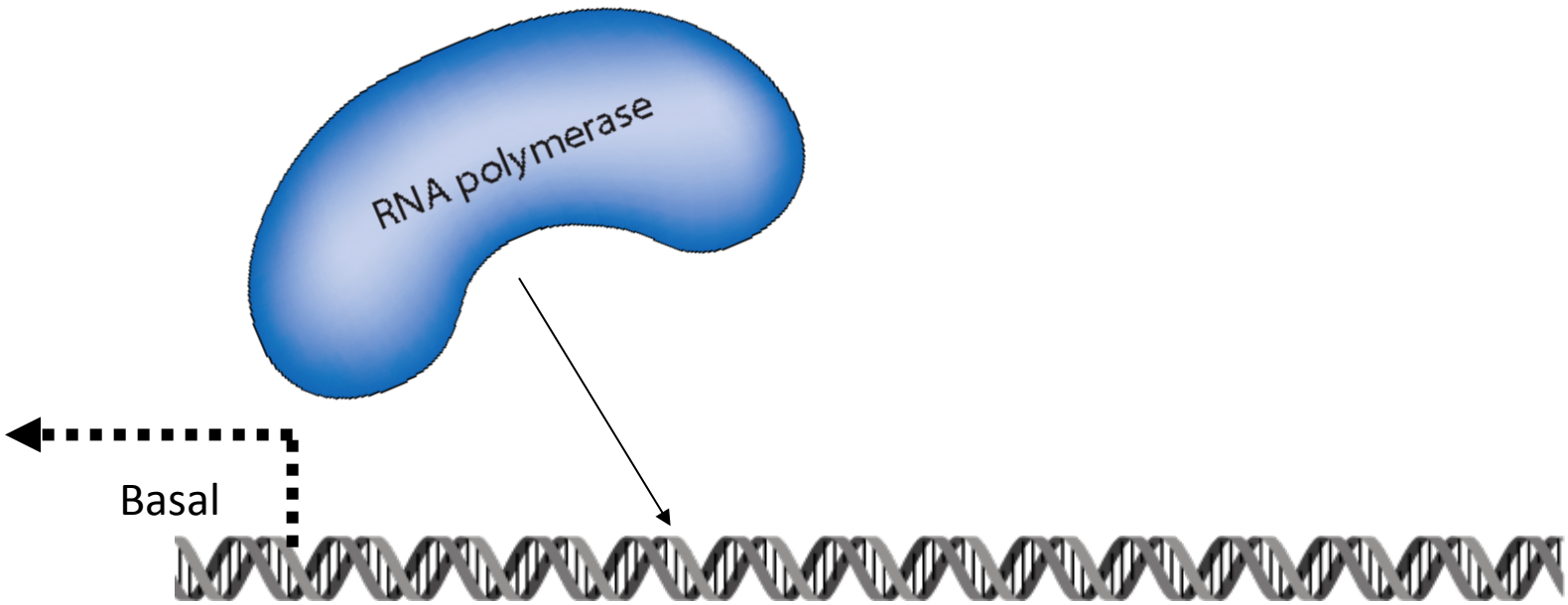
Simon Schama

Think small, talk big.

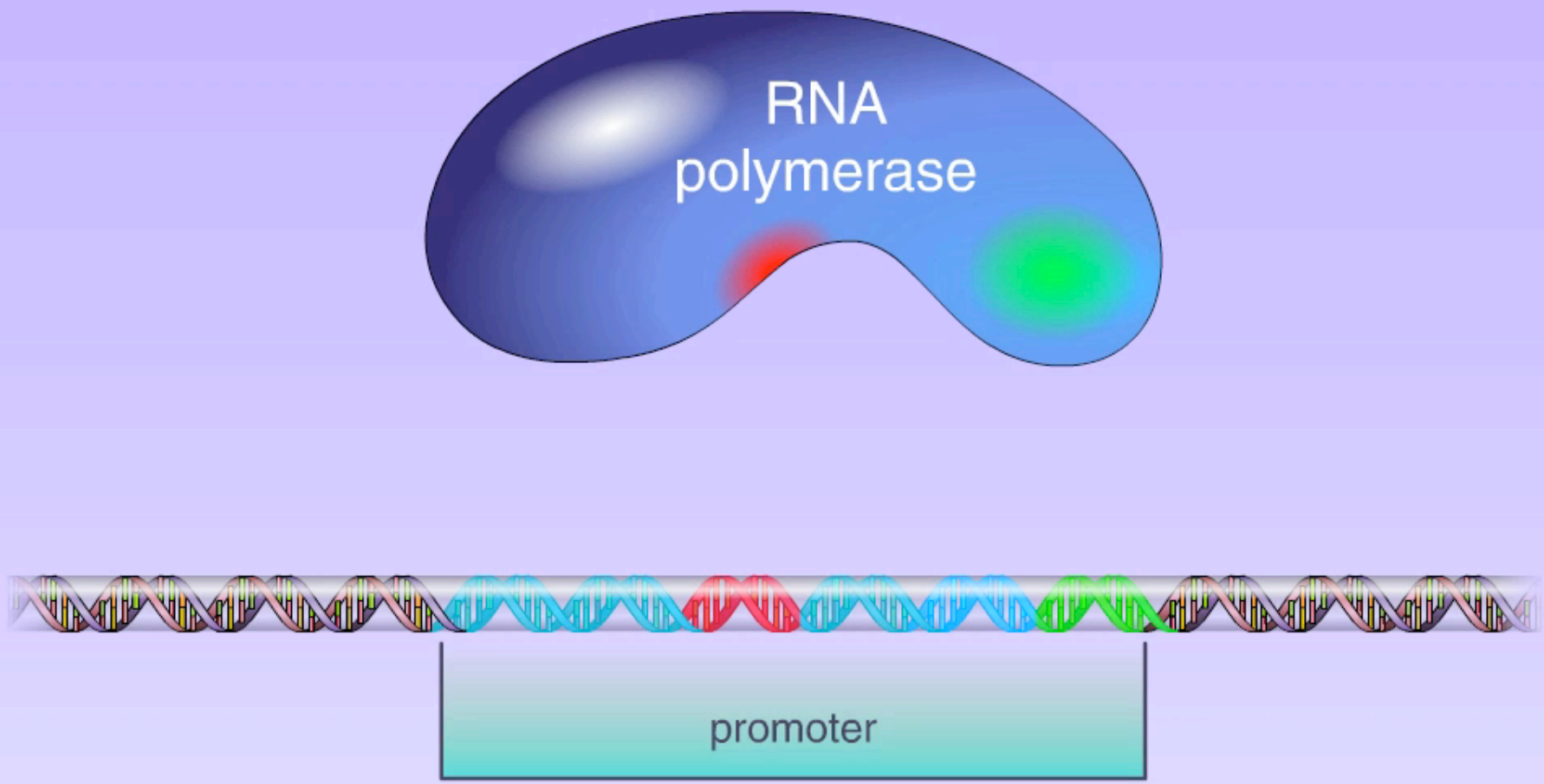
Sydney Brenner

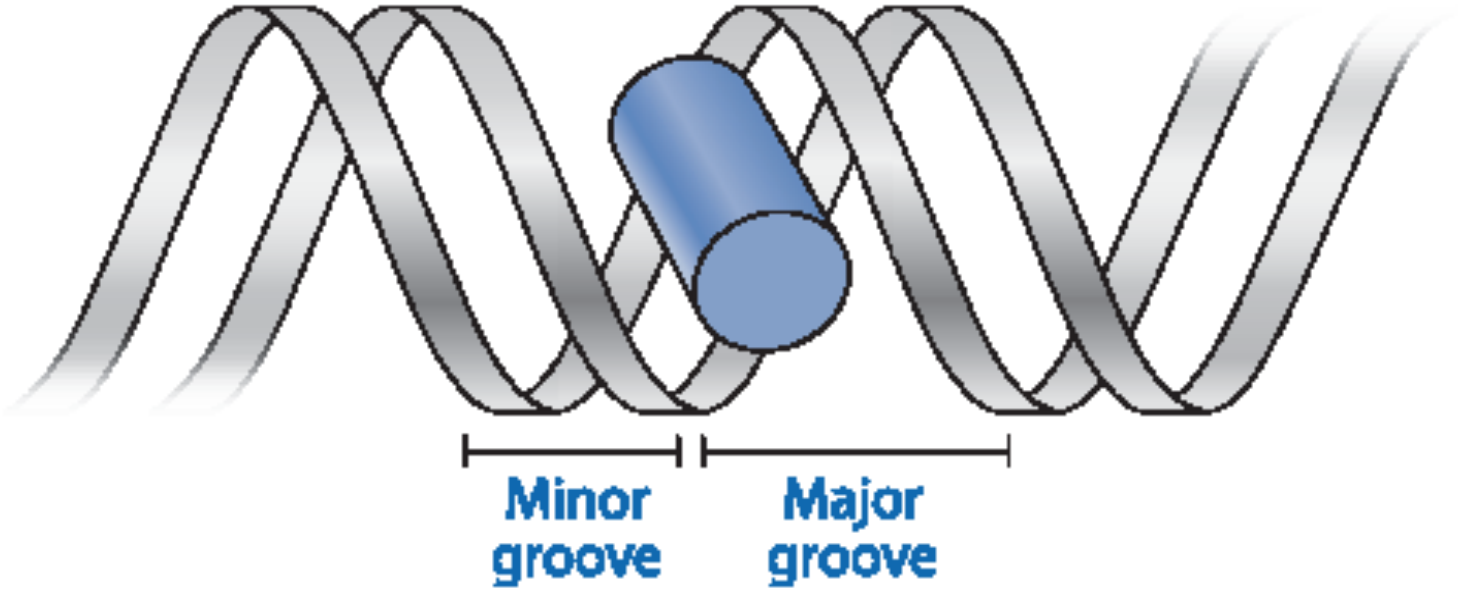
Classical models tell us more than we can at first know.

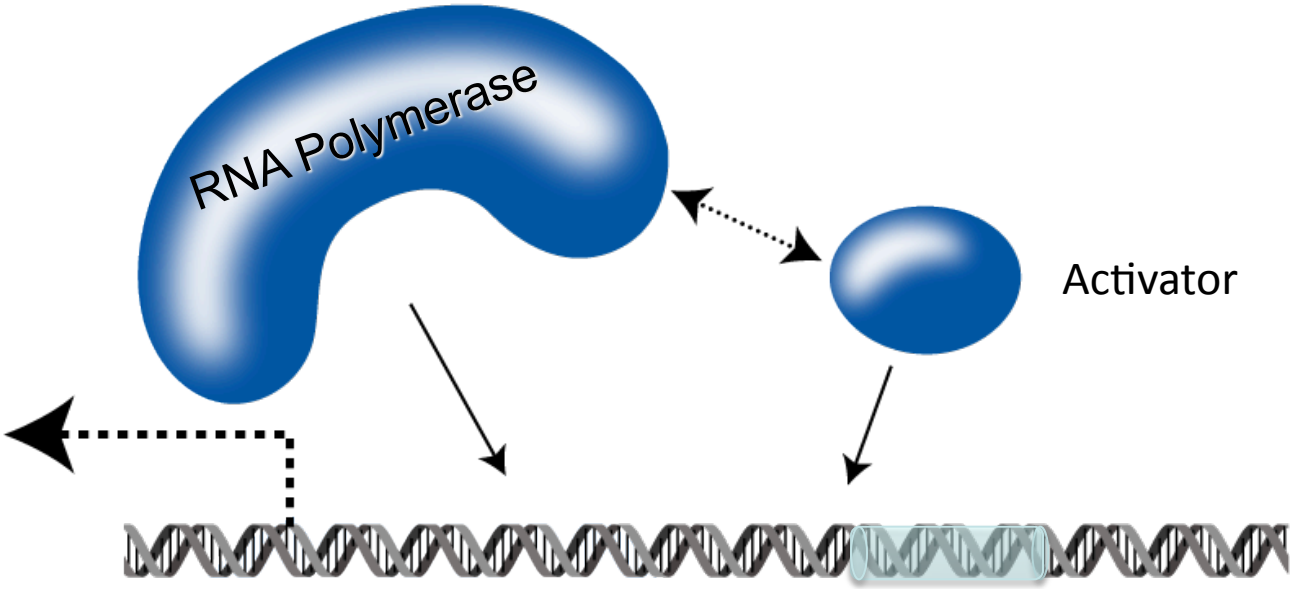
Karl Popper



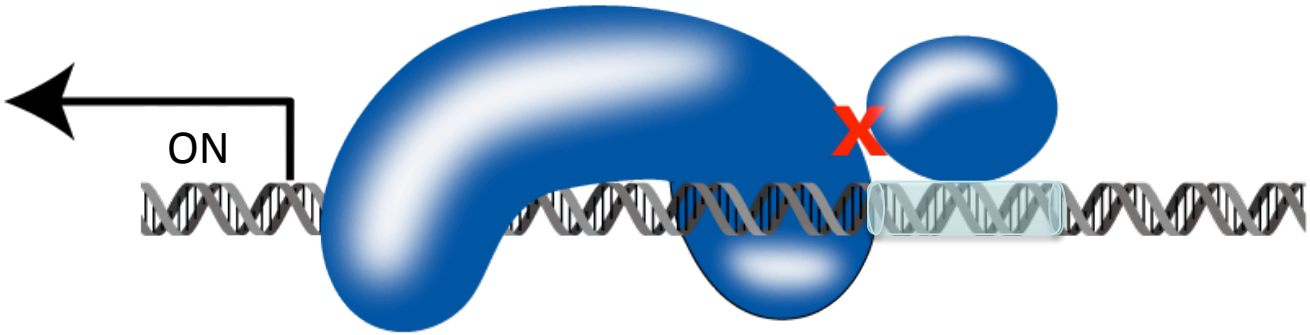
Promoter

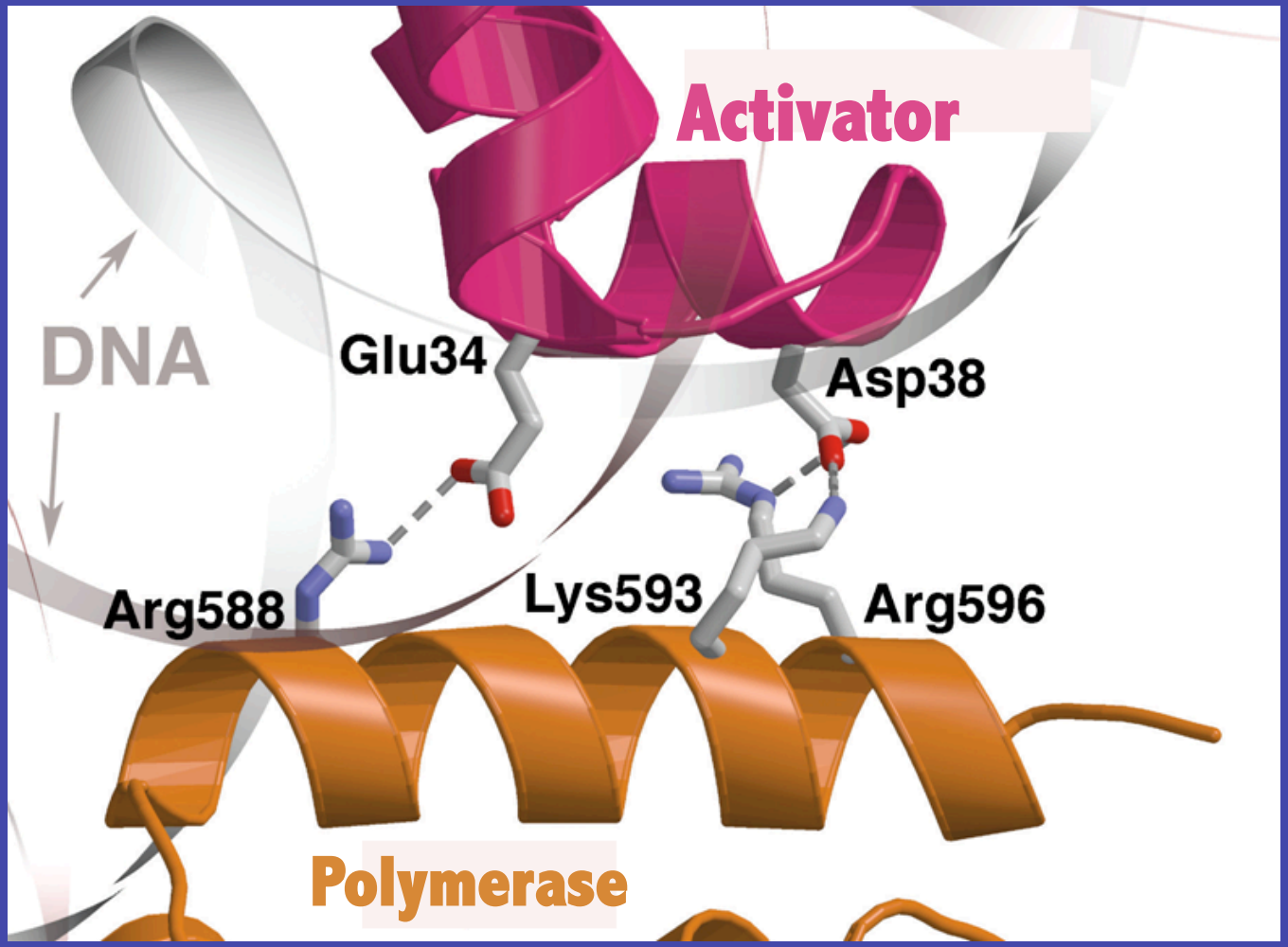

RNA
polymerase
promoter


Minor
groove
Major
groove

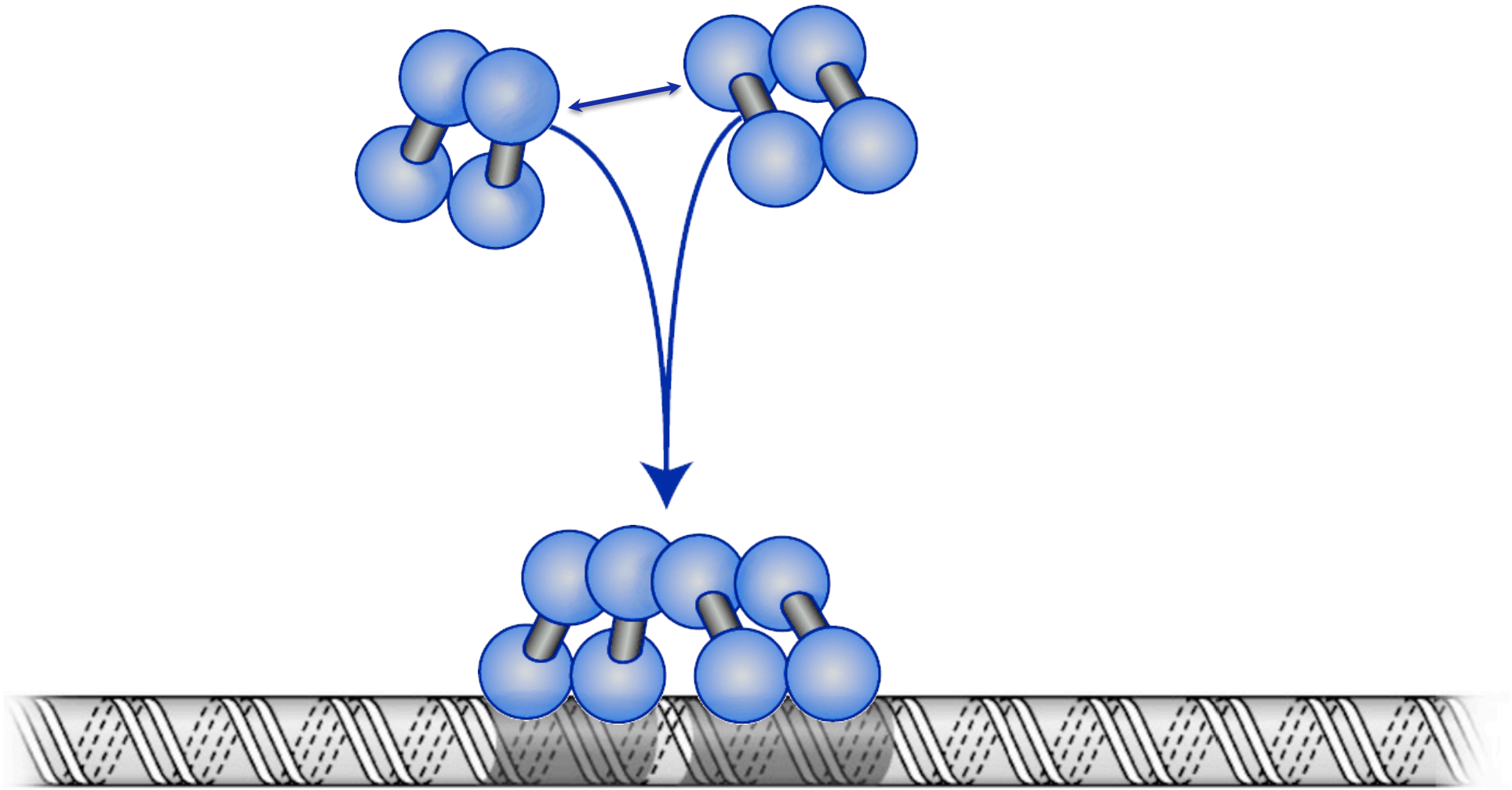


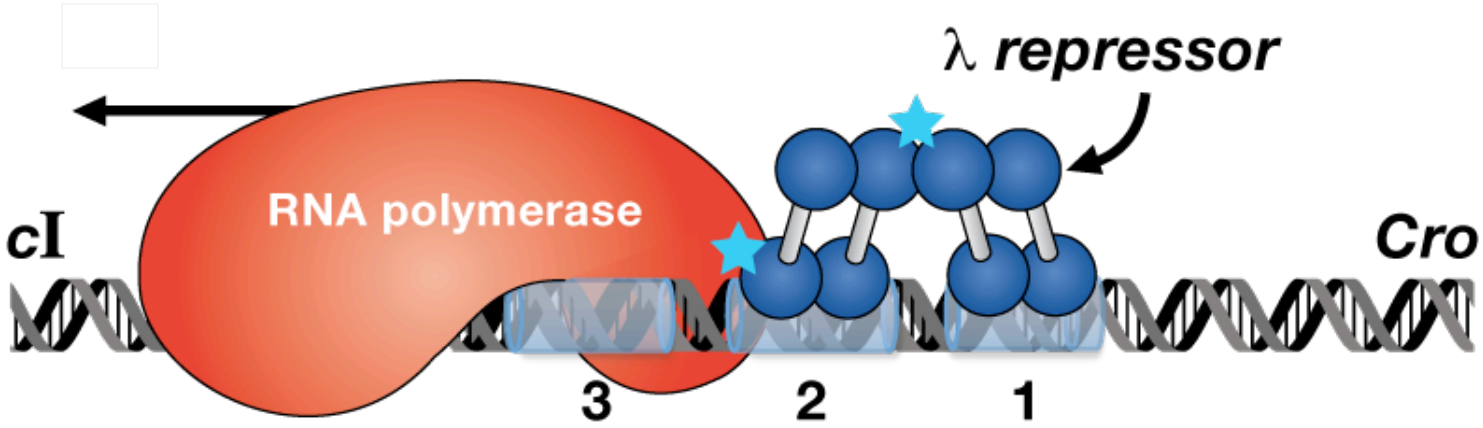
PROMOTER

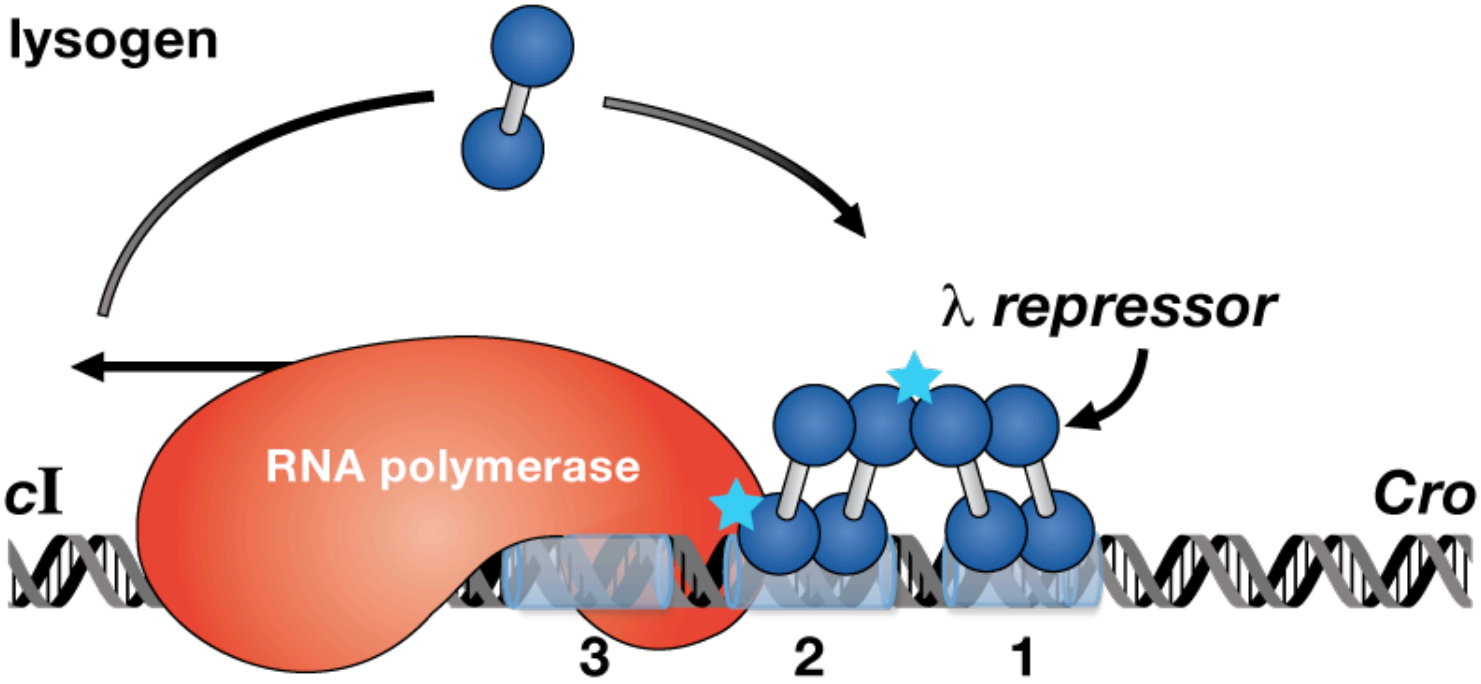




Jain et. al. 2004 Mol. Cell
(Bell and Lewis 2001 J. Mol.Biol.)




λ repressor
RNA polymerase
cI
Cro
3
2
1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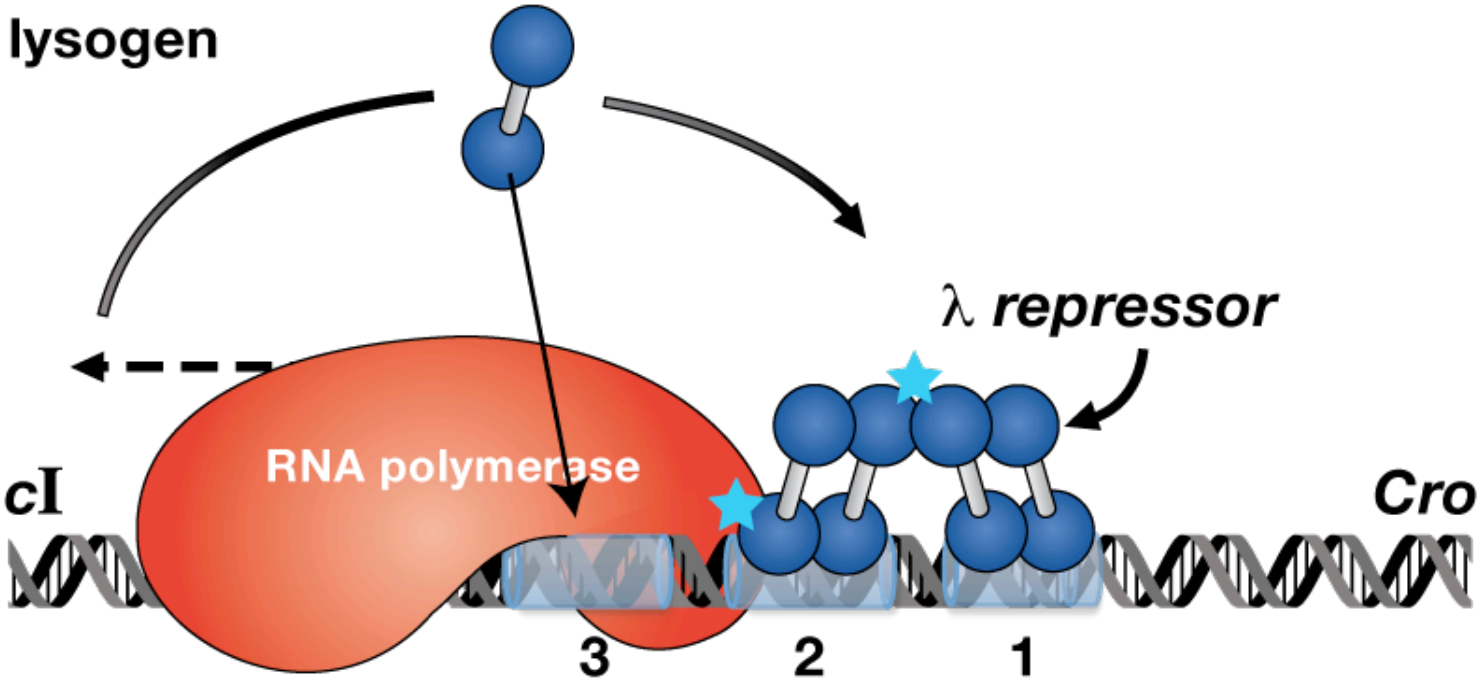
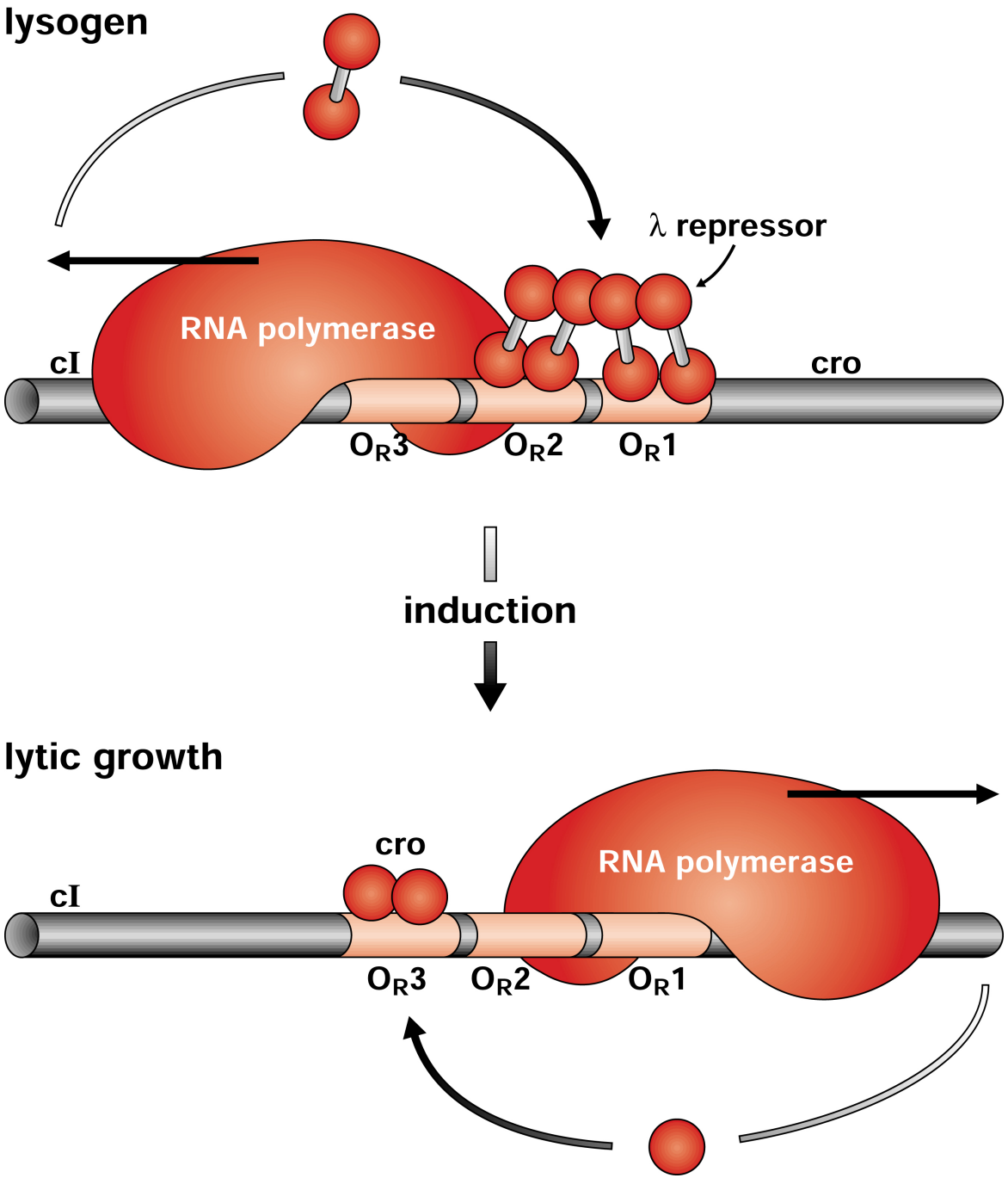
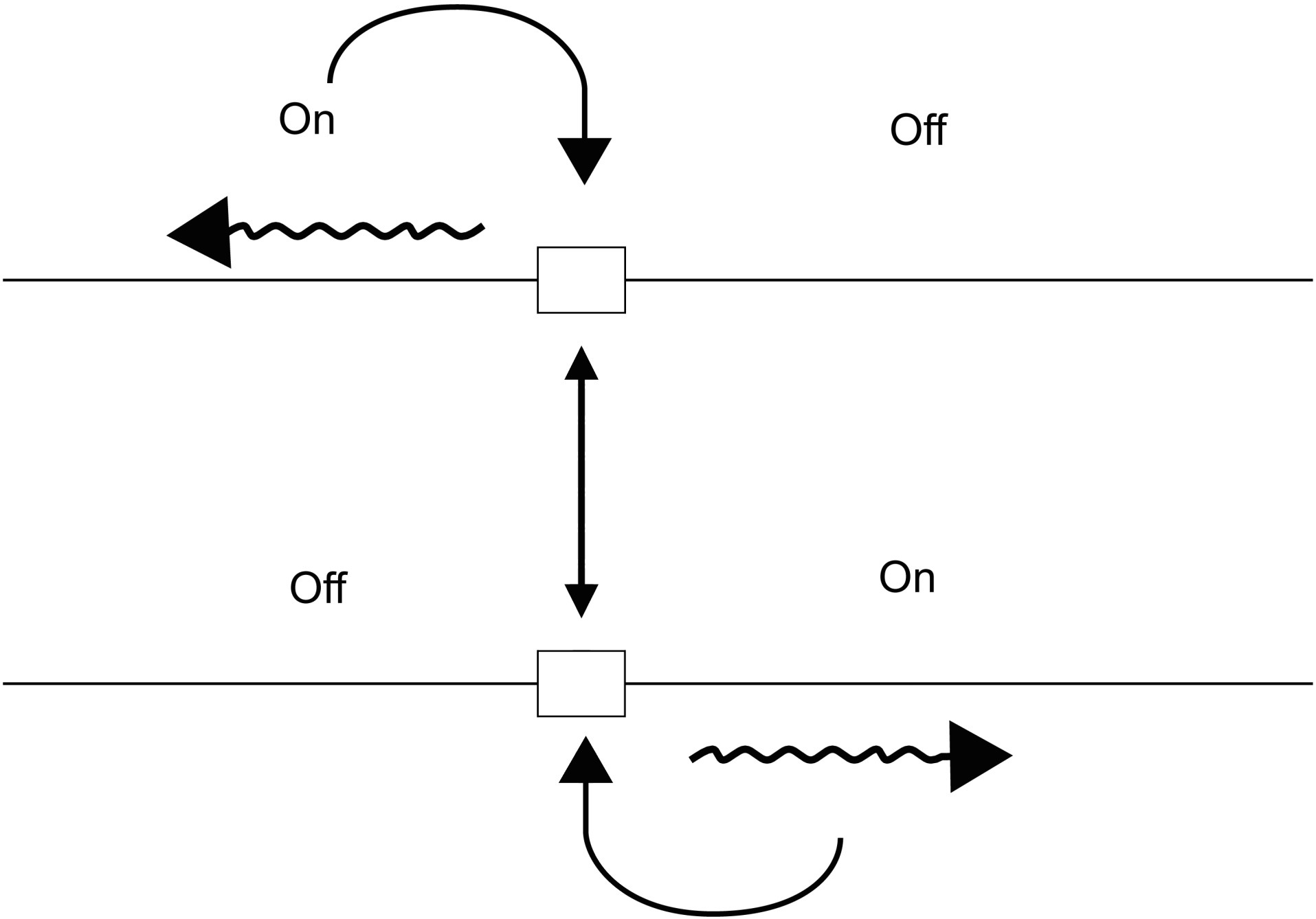
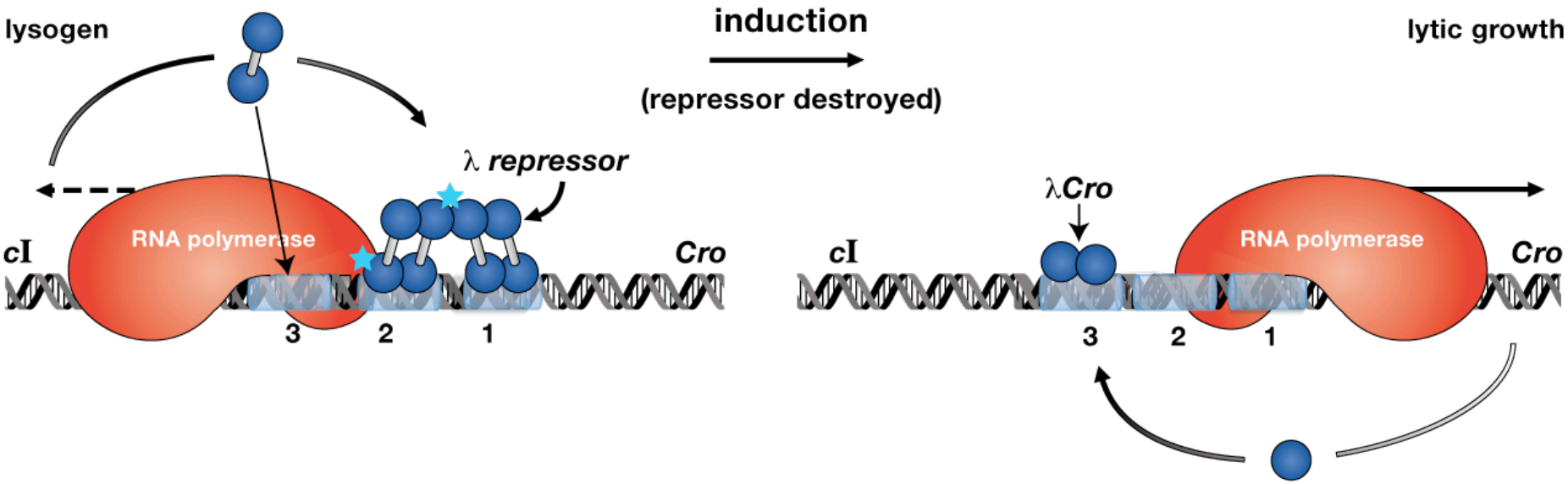
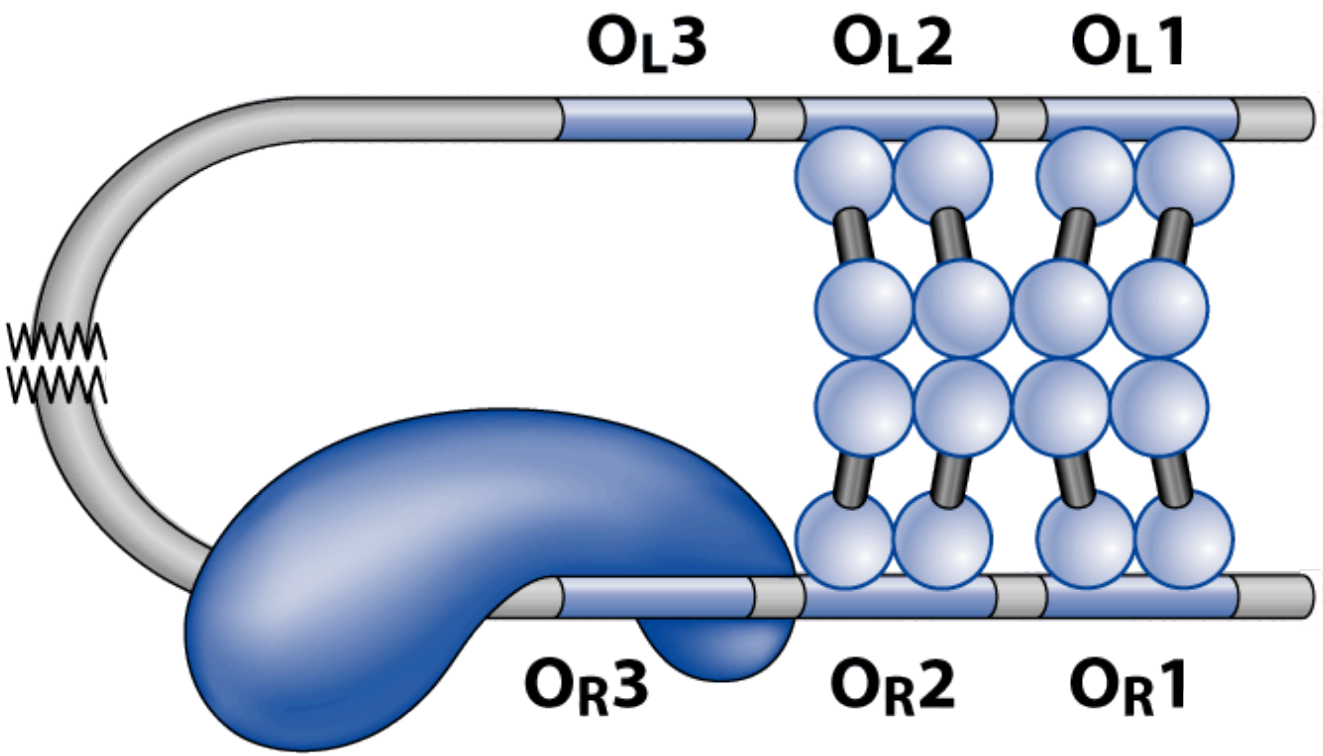
λ repressor
RNA polymerase
cI
Cro
3
2
1


lysogen
λ repressor
RNA polymerase
cI
Cro
3
2
1

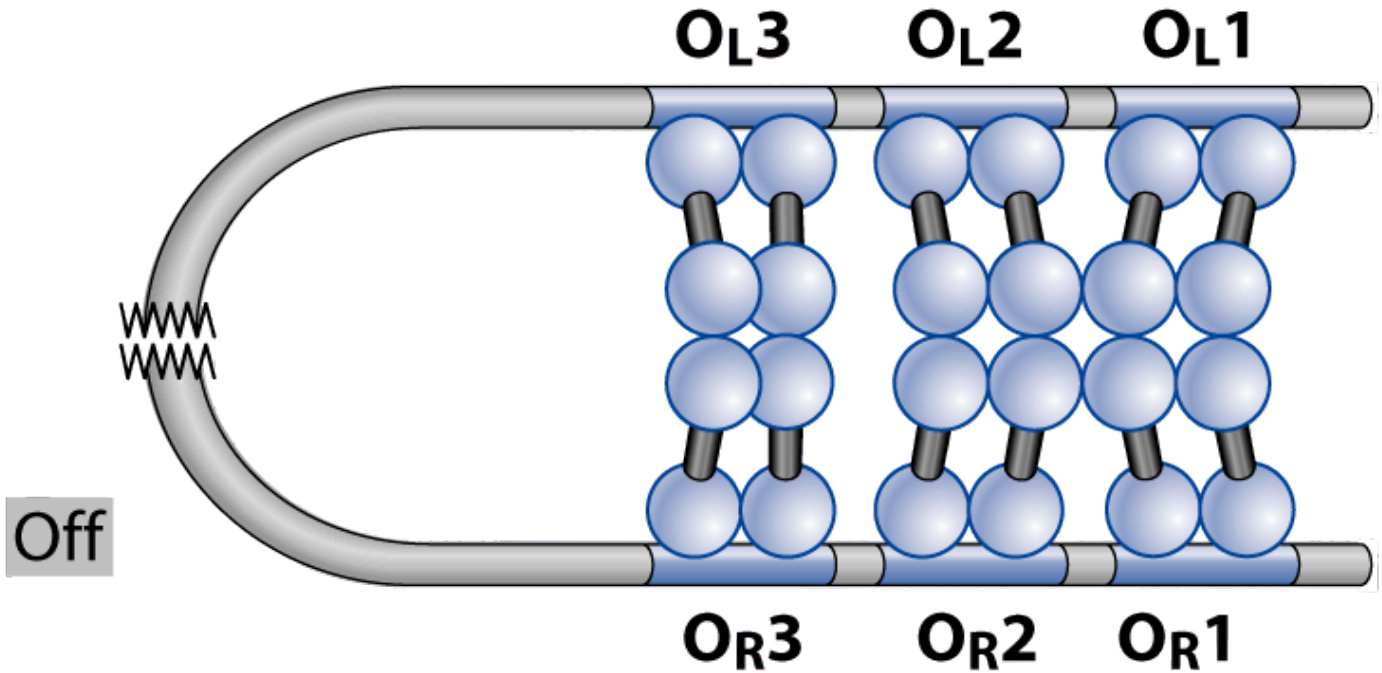

lysogen
λ repressor
RNA polymerase
cI
cro
O_R3
O_R2
O_R1
induction
lytic growth
cro
RNA polymerase
cI
O_R3
O_R2
O_R1

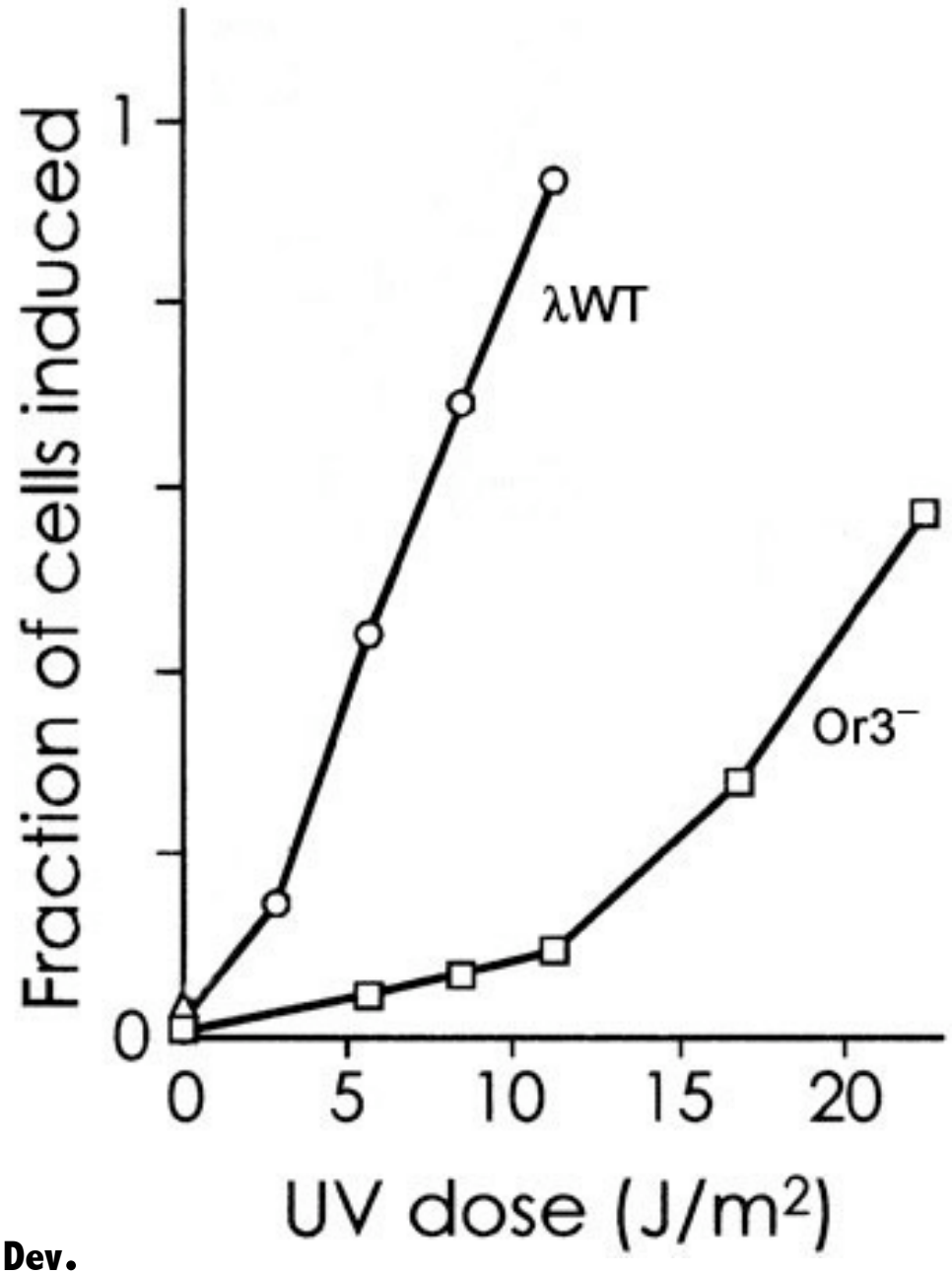

On
Off
Off
On


lysogen
induction
(repressor destroyed)
lytic growth
λ repressor
λCro
cI
RNA polymerase
Cro
3
2
1

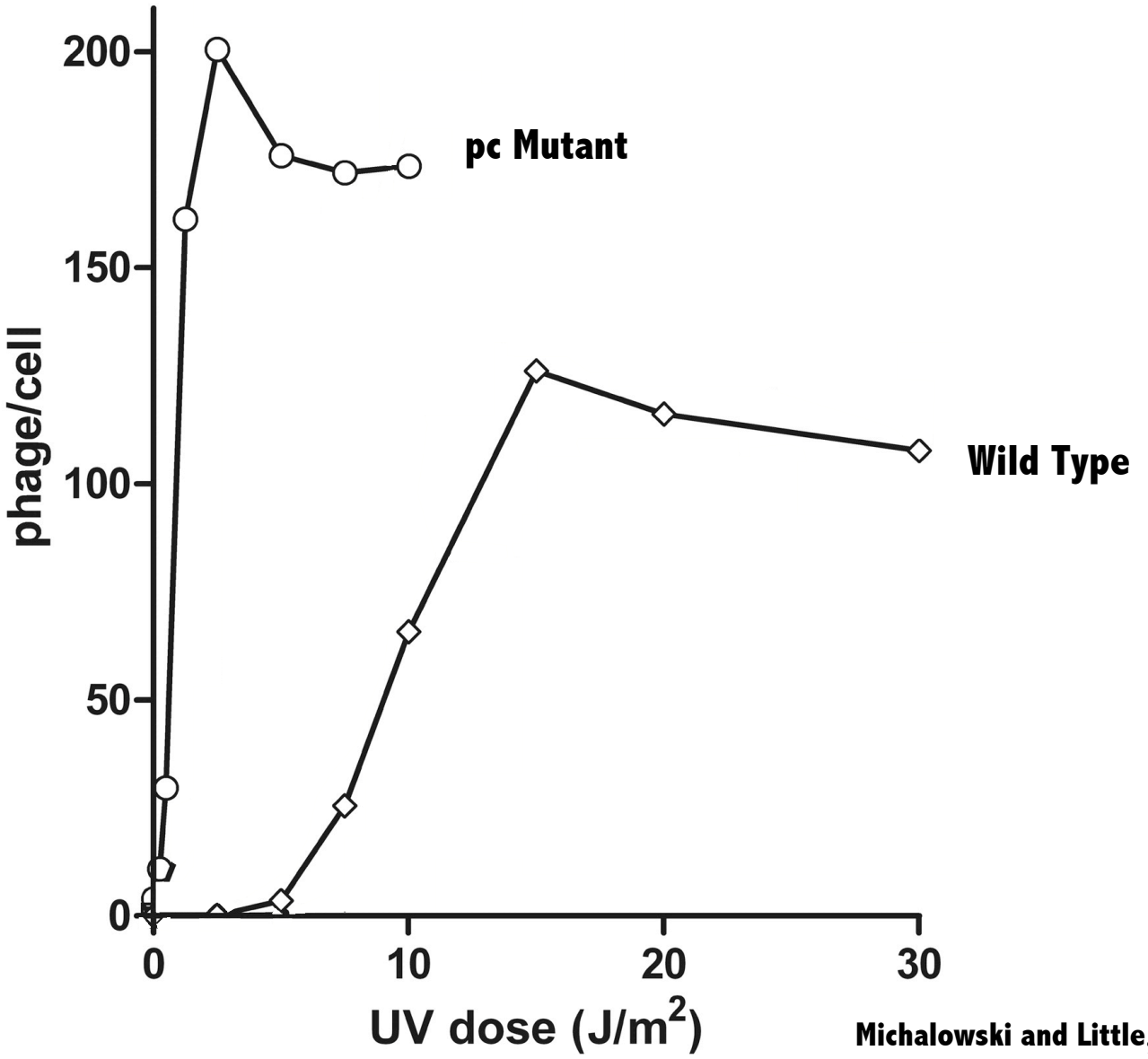


Dodd et al 2001 Genes Dev.

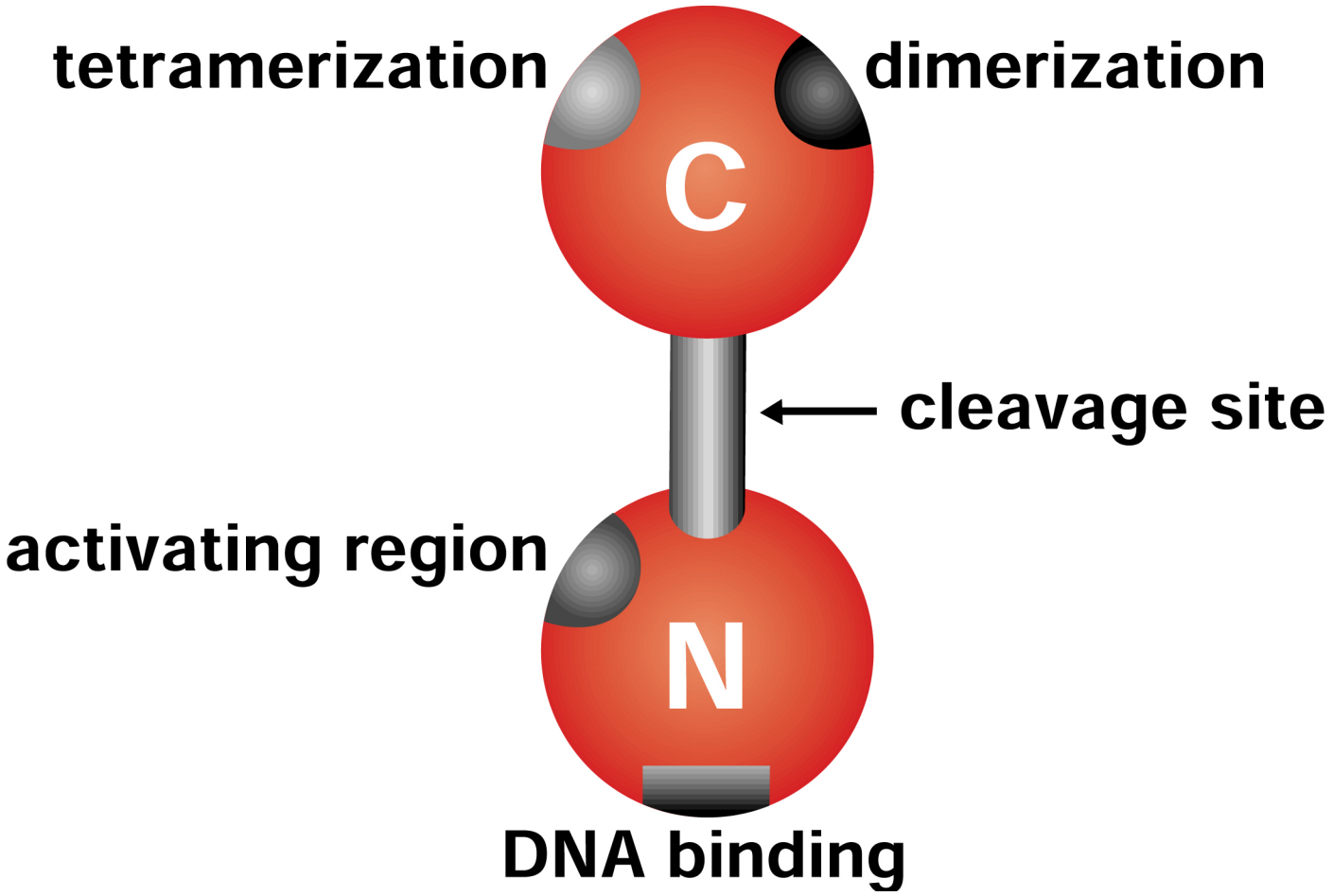

O_L3
O_L2
O_L1
Off
O_R3
O_R2
O_R1

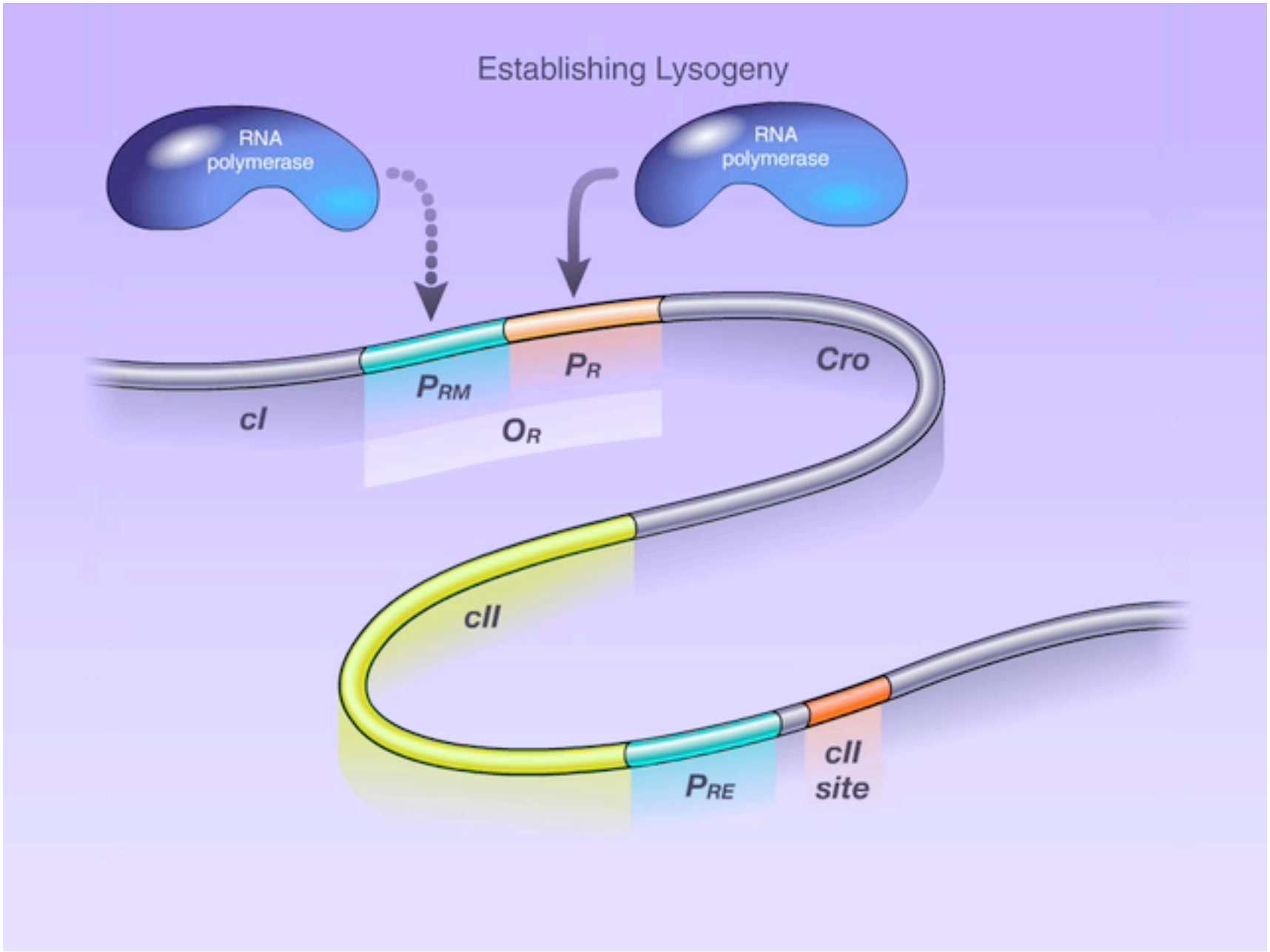


Dodd et al, 2001, Genes and Dev.



Michalowski and Little, J Bact 2005
Hochschild, Irwin, Ptashne, Cell 1983


tetramerization
dimerization
C
cleavage site
activating region
N
DNA binding


Establishing Lysogeny
RNA polymerase
RNA polymerase
cI
P_{RM}
P_R
Cro
O_R
cII
P_{RE}
cII site

Lessons From Lambda

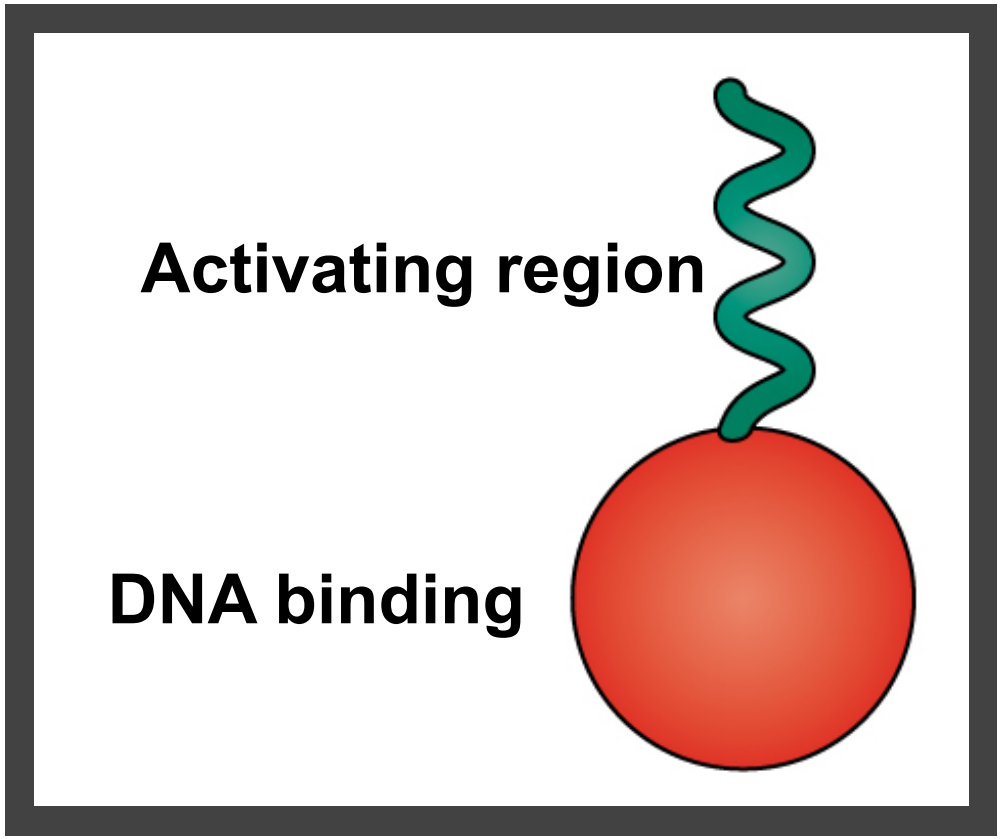
Gene transcription:
basal/activated/repressed

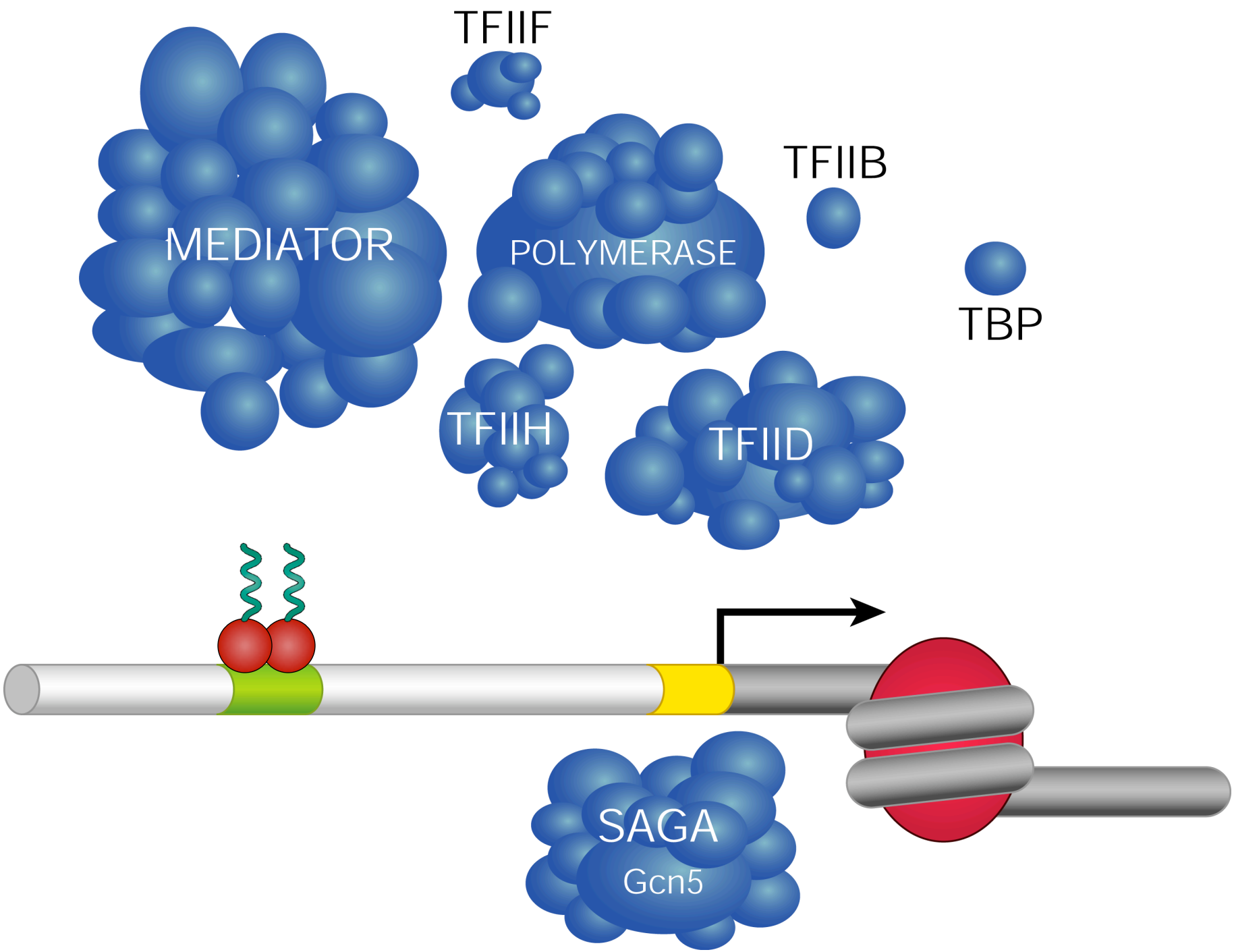
Specificity

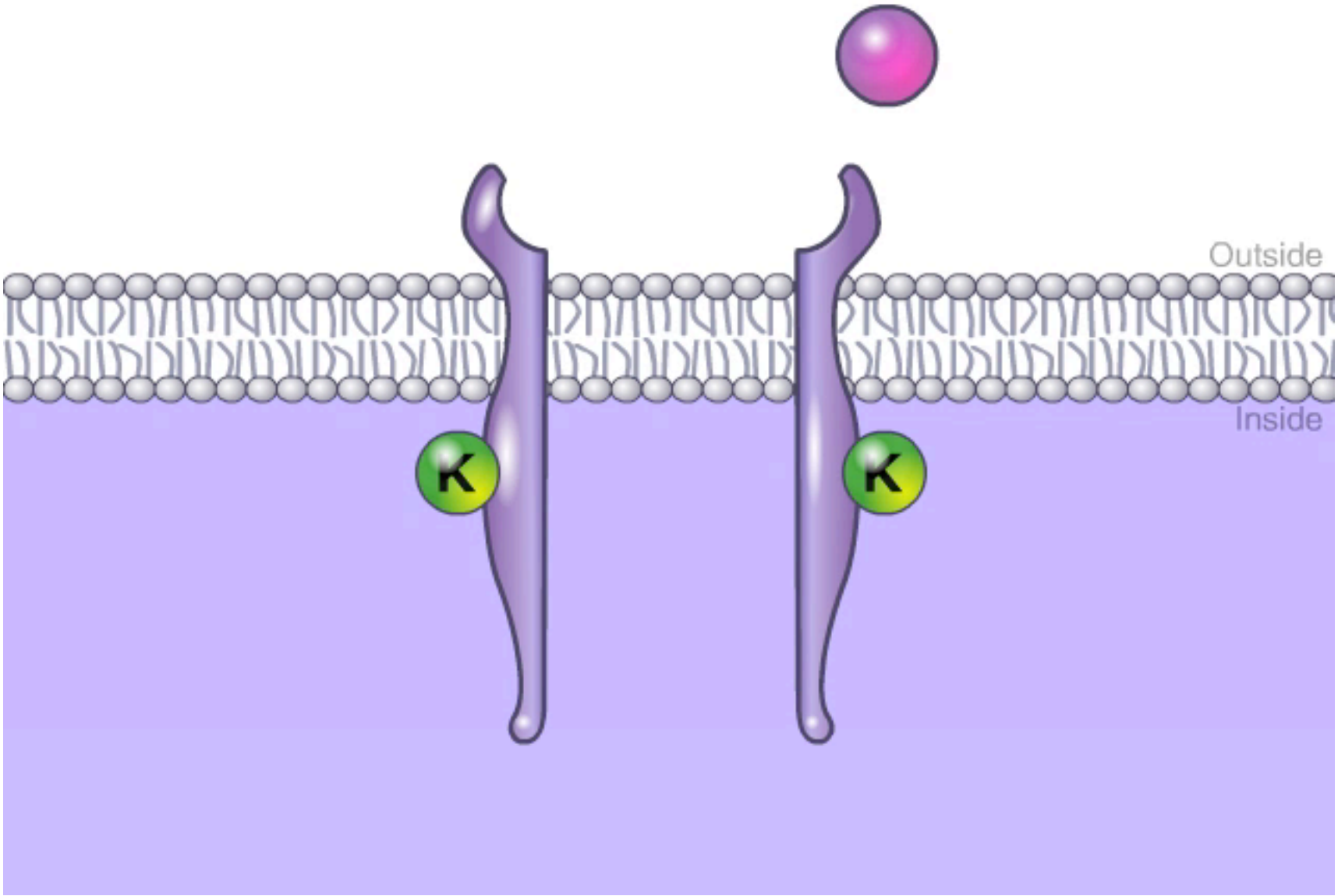
An epigenetic switch (feedback)

Add-ons

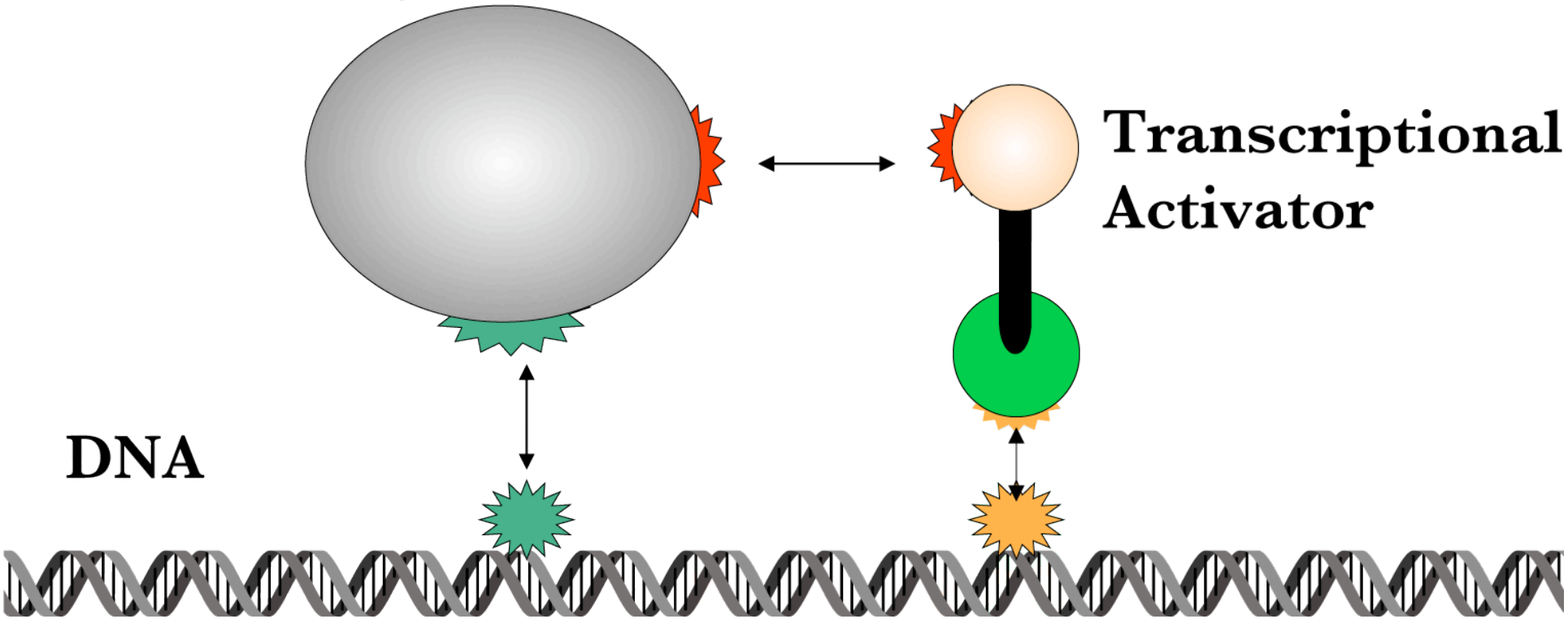
BINDING REACTIONS!

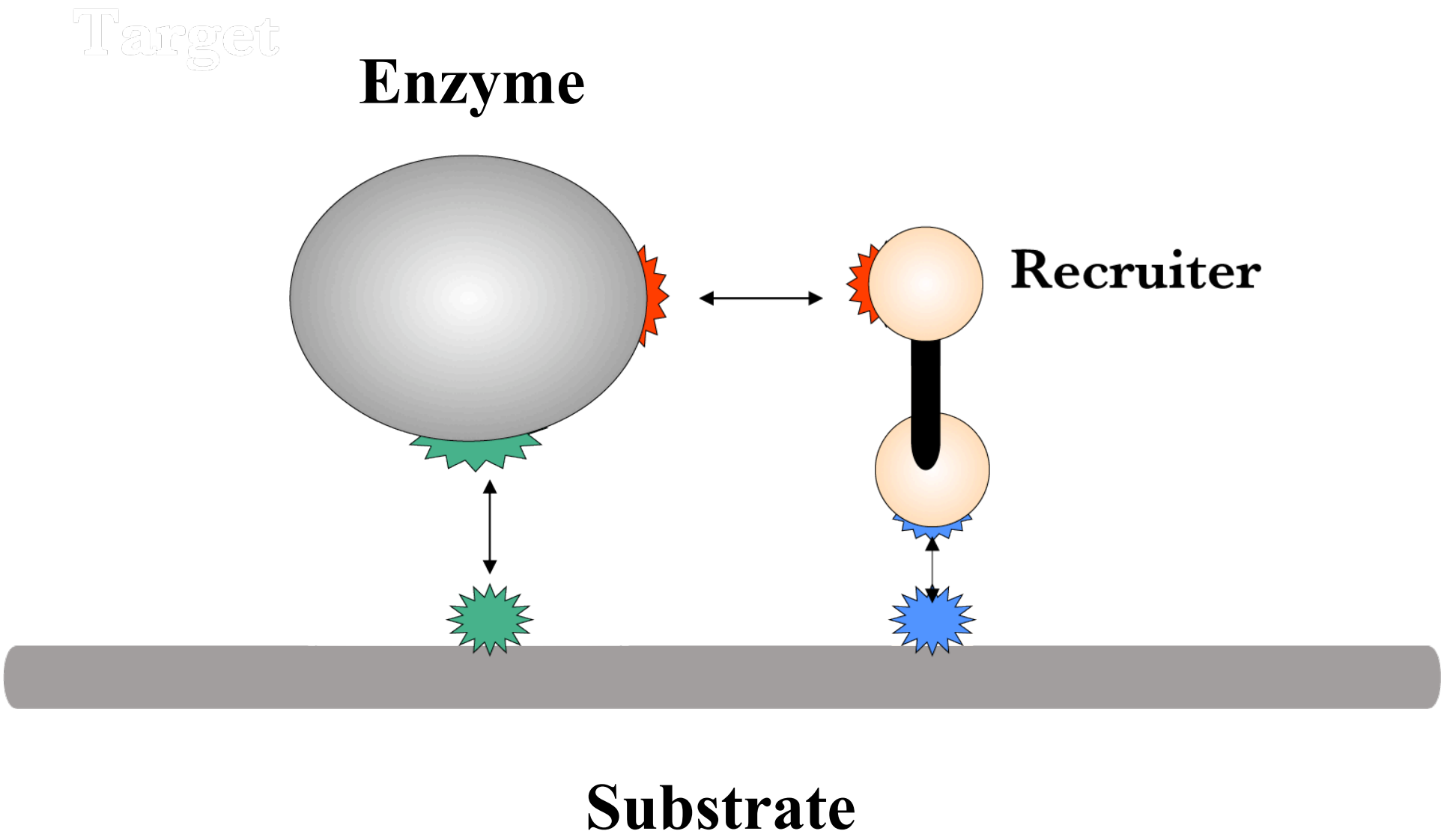

Activating region
DNA binding

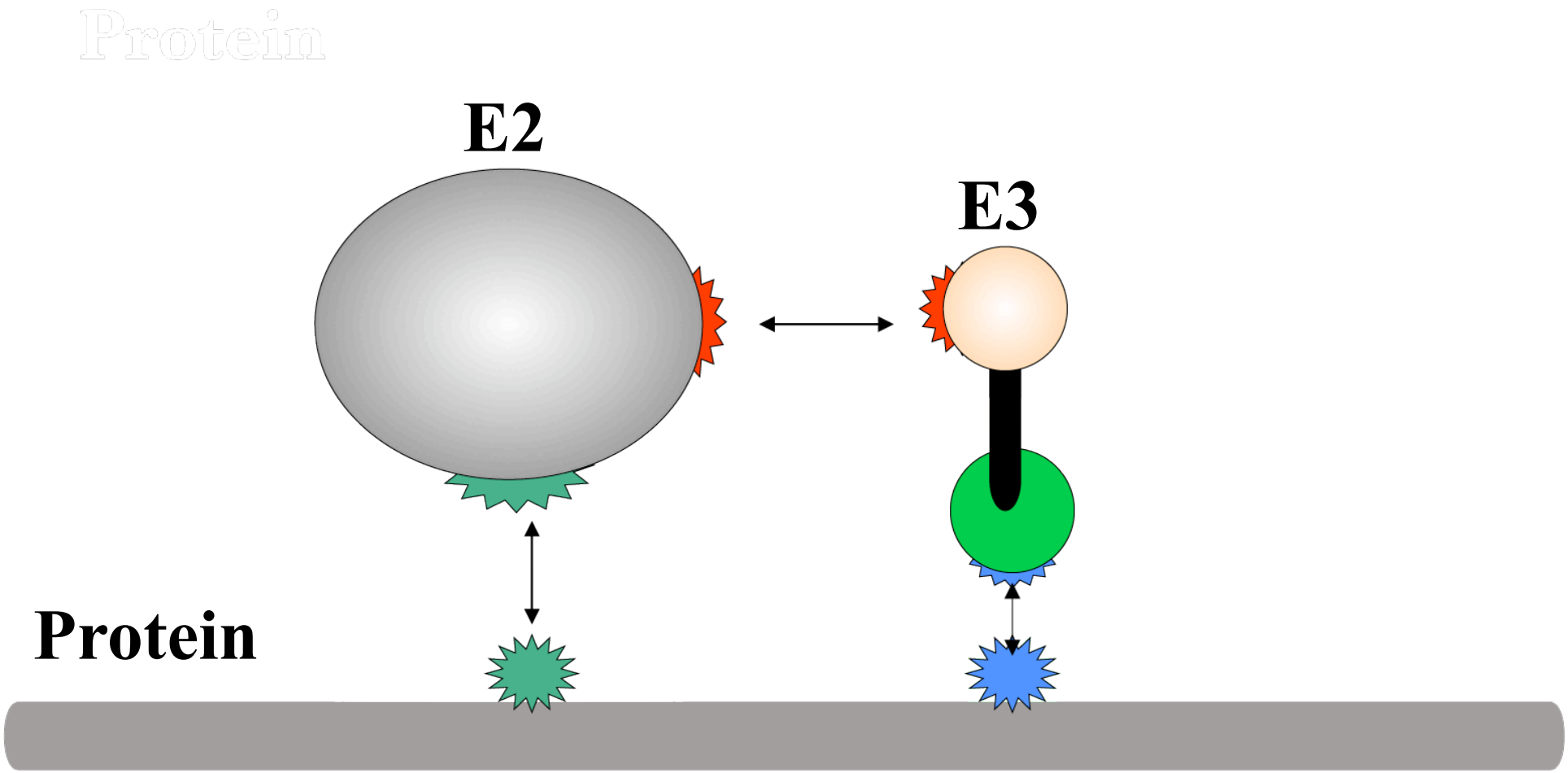

TFIIF
MEDIATOR
POLYMERASE
TFIIB
TBP
TFIIH
TFIID
SAGA
Gcn5


Outside
Inside
K
K

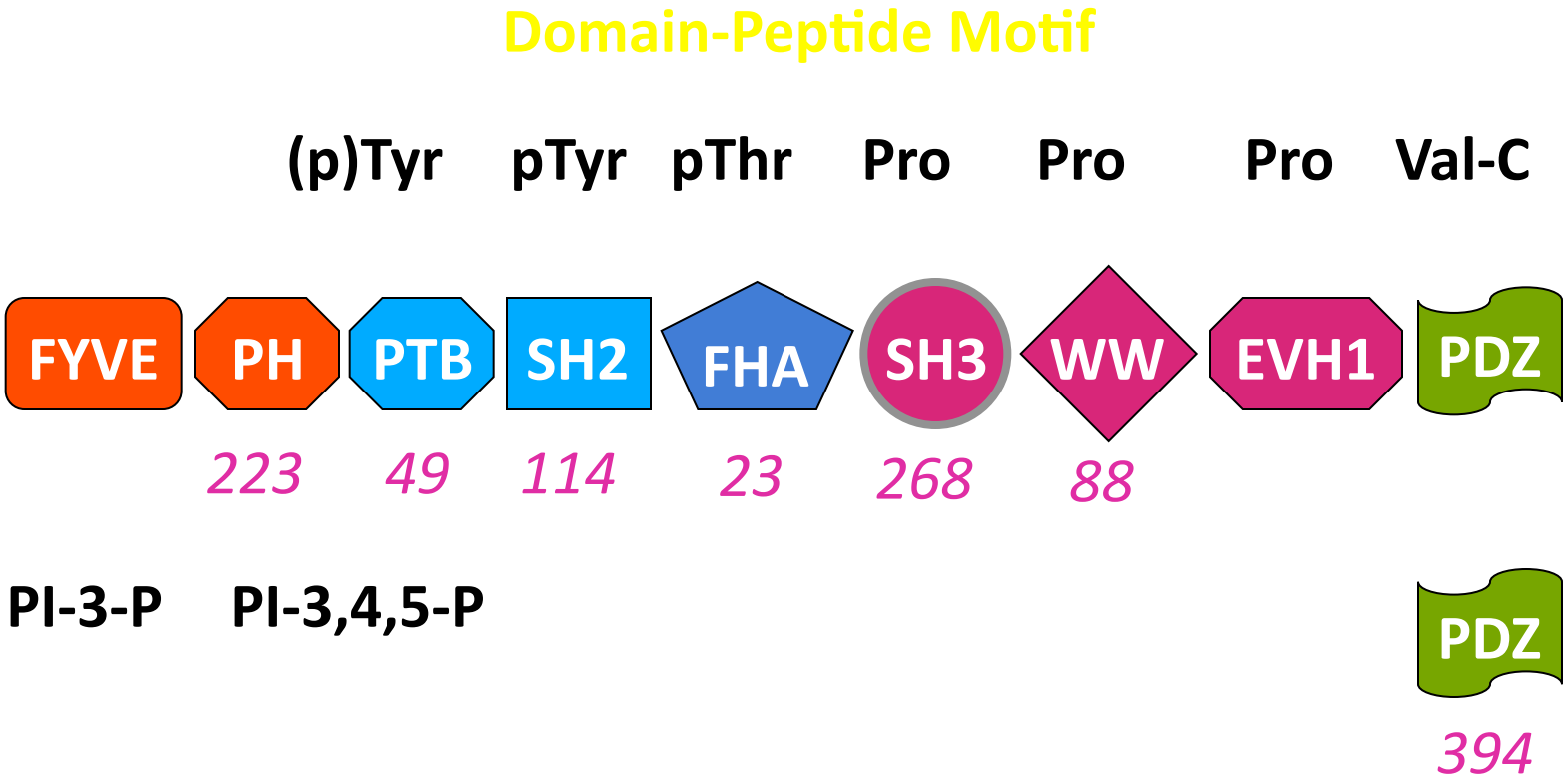
Transcriptional Machinery



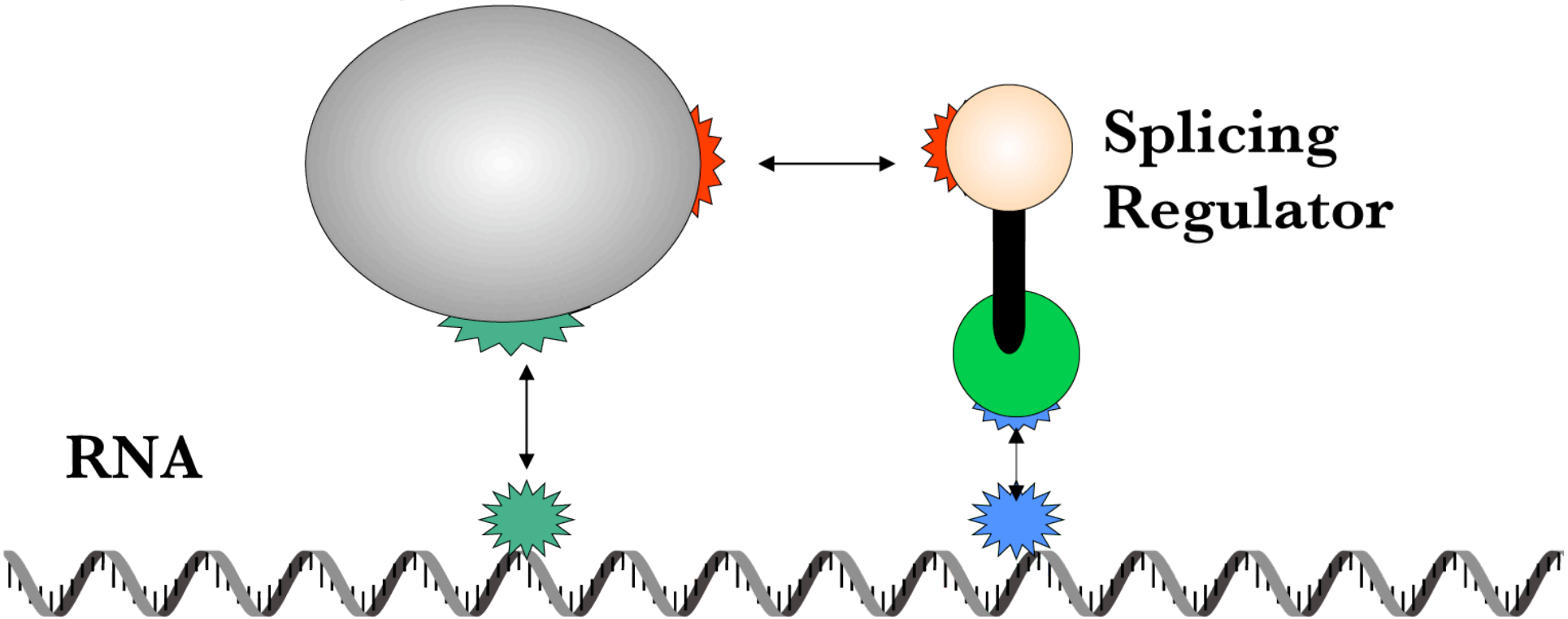

Target
Enzyme
Recruiter
Substrate


Protein
E2
E3
Protein

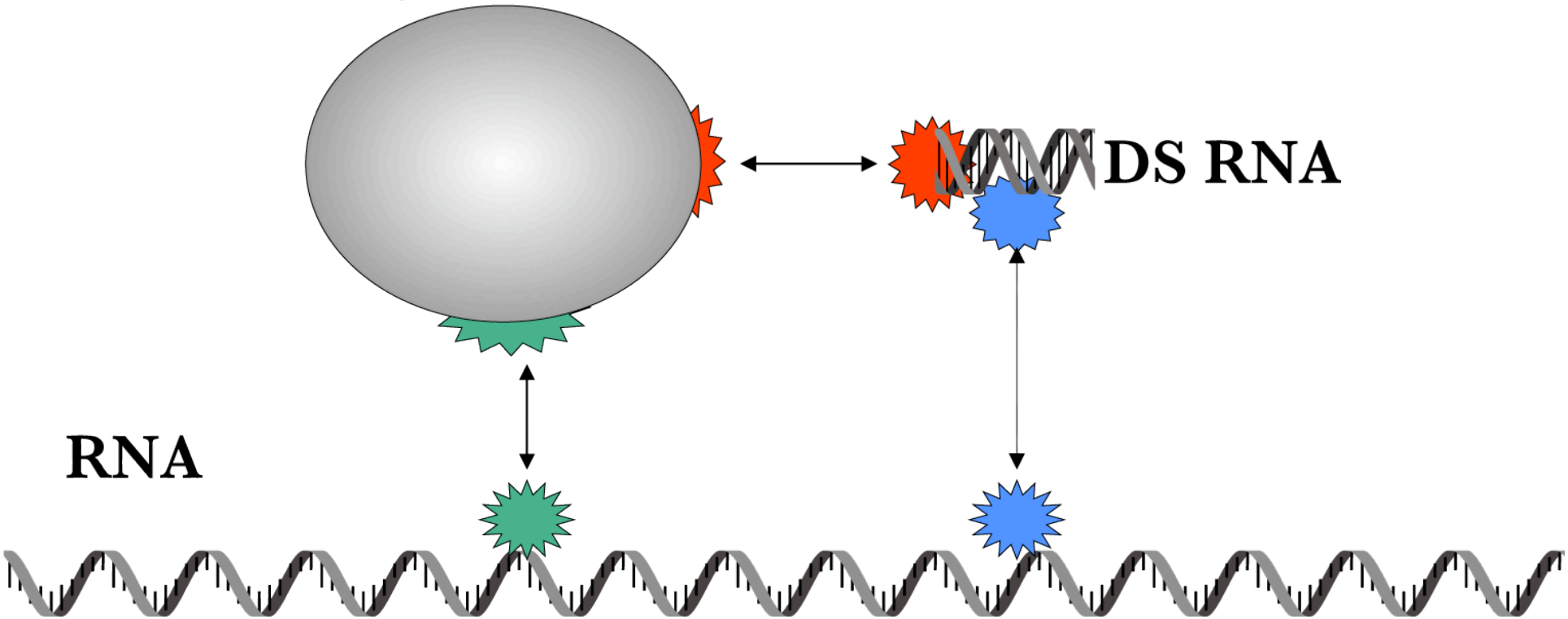
Interaction Domains in Signal Transduction

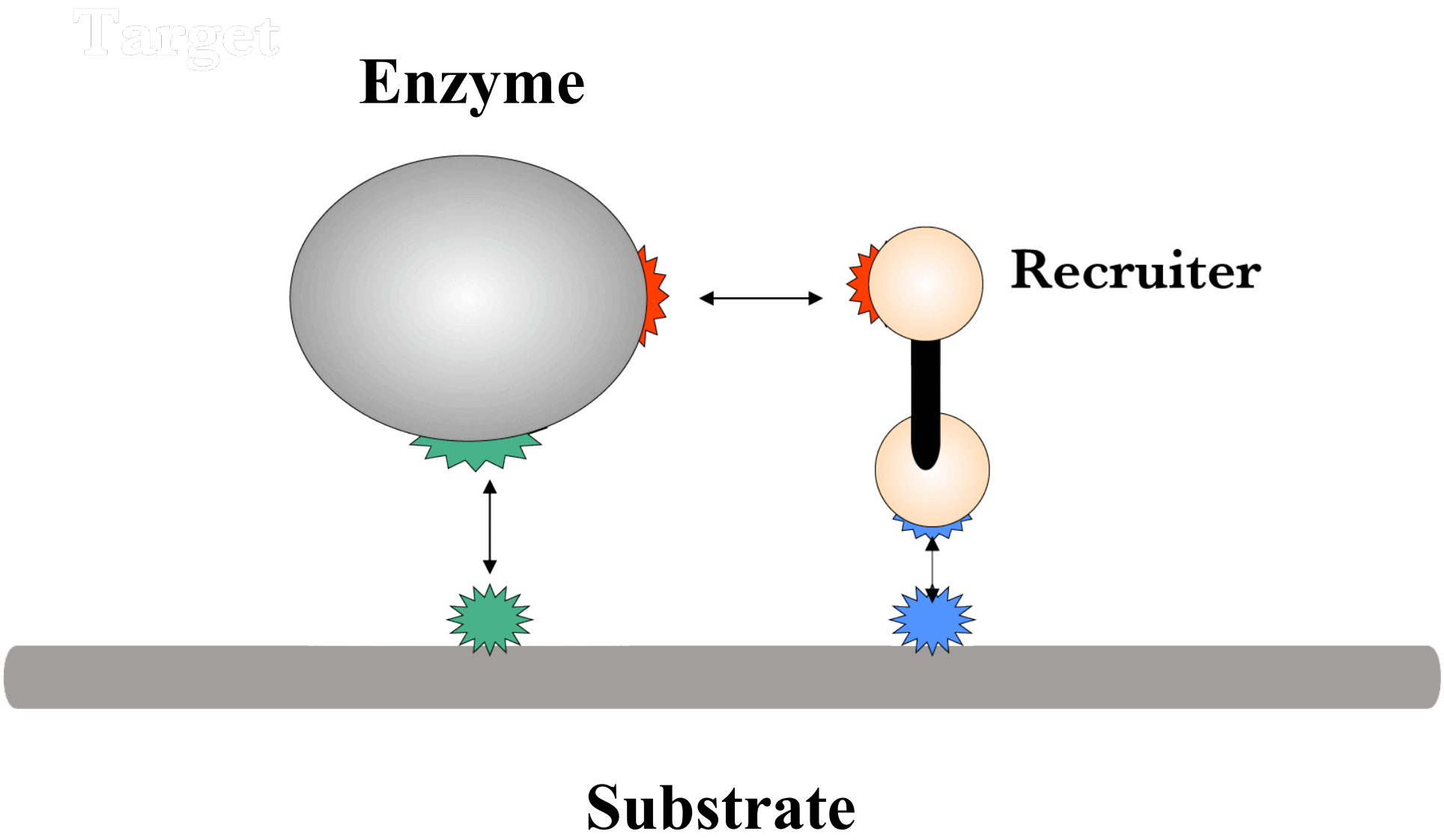


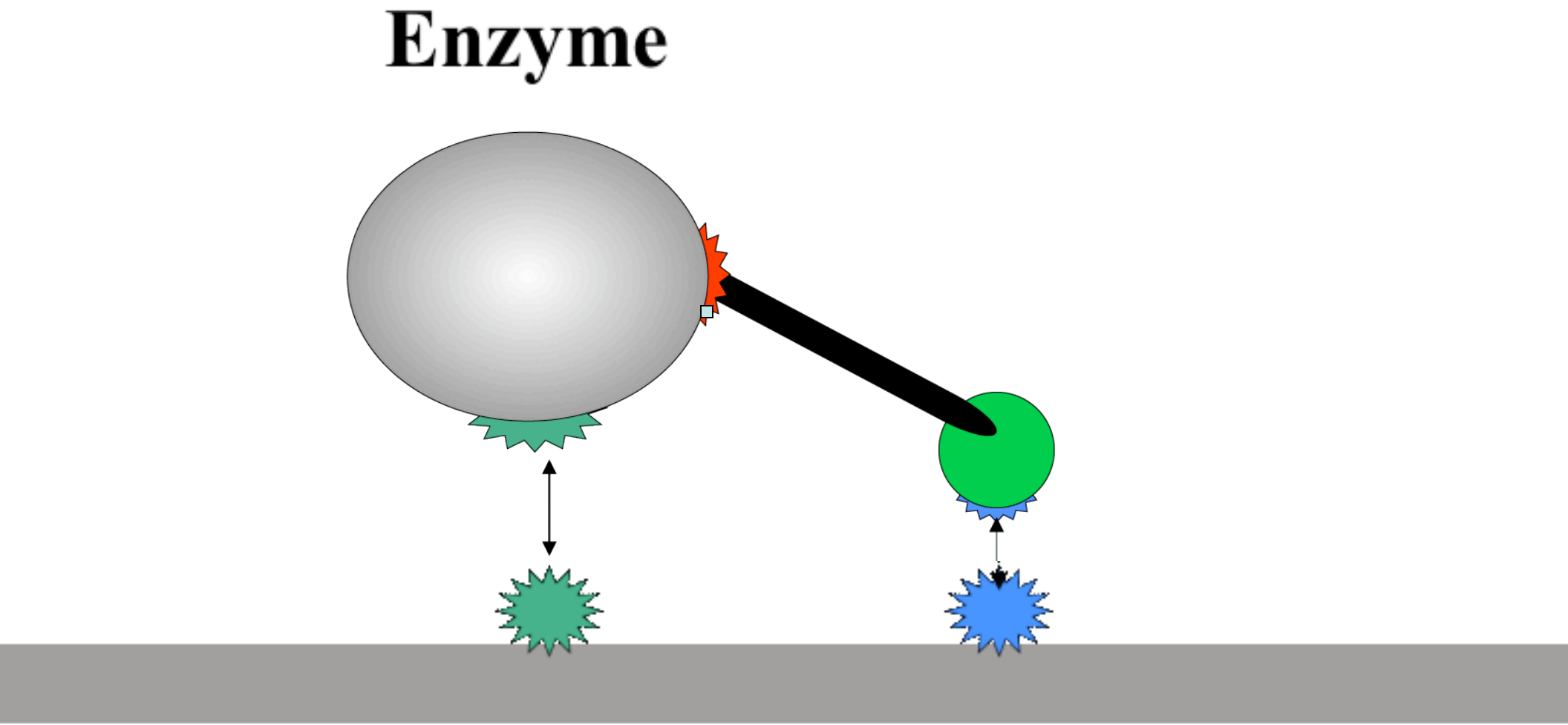
Splicing Machinery



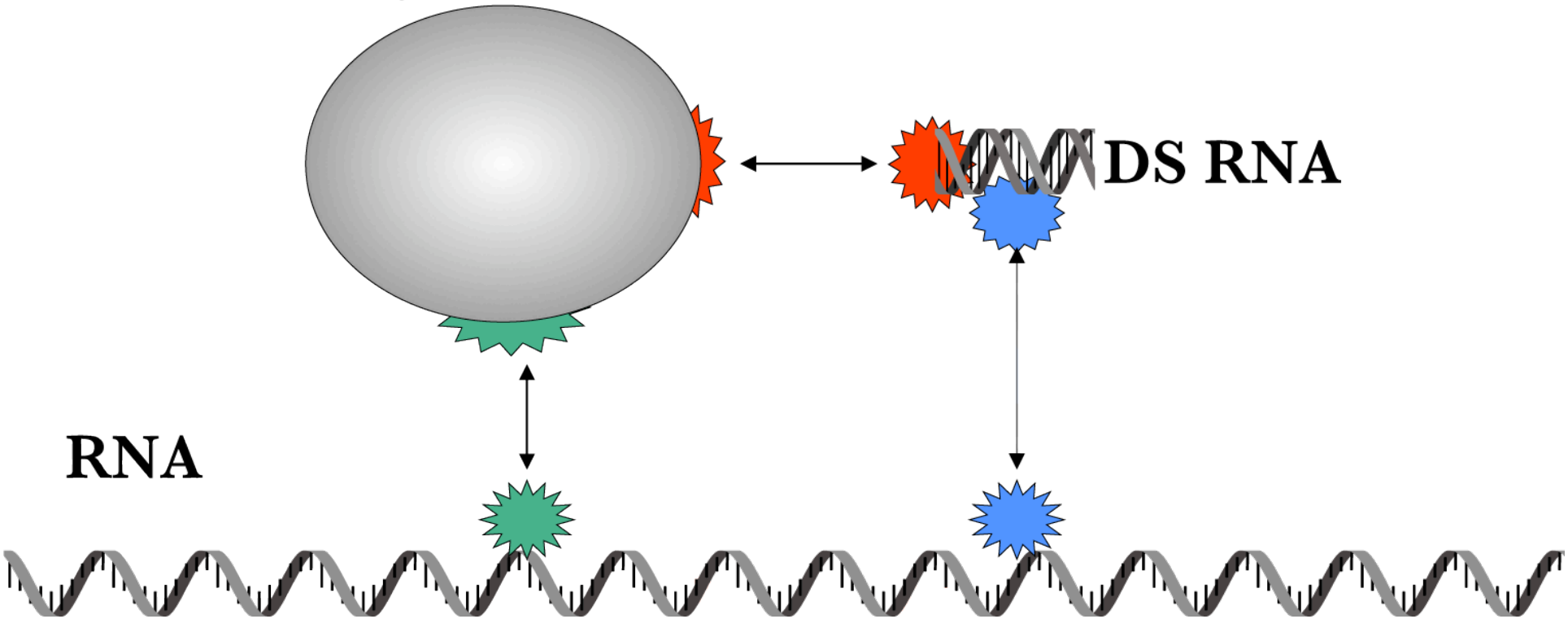
RNAi Machinery

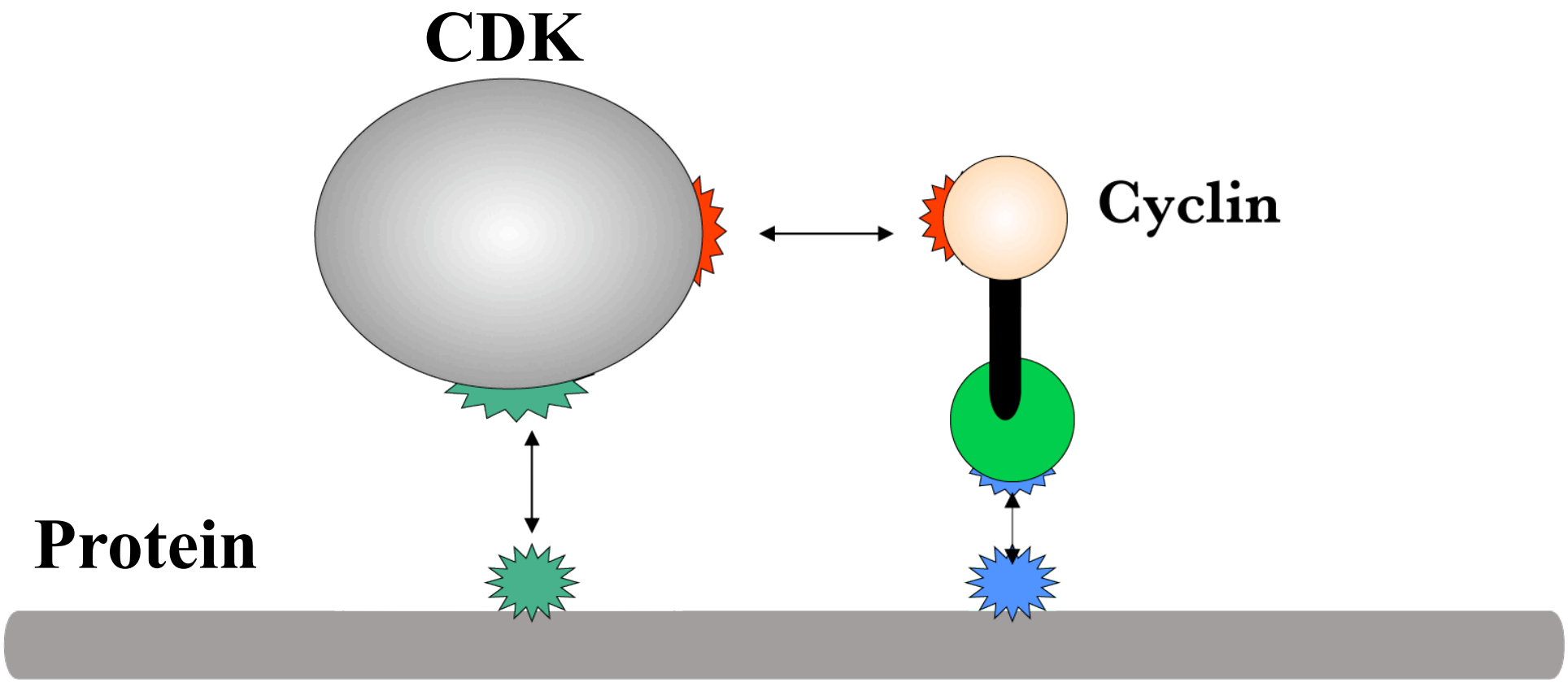


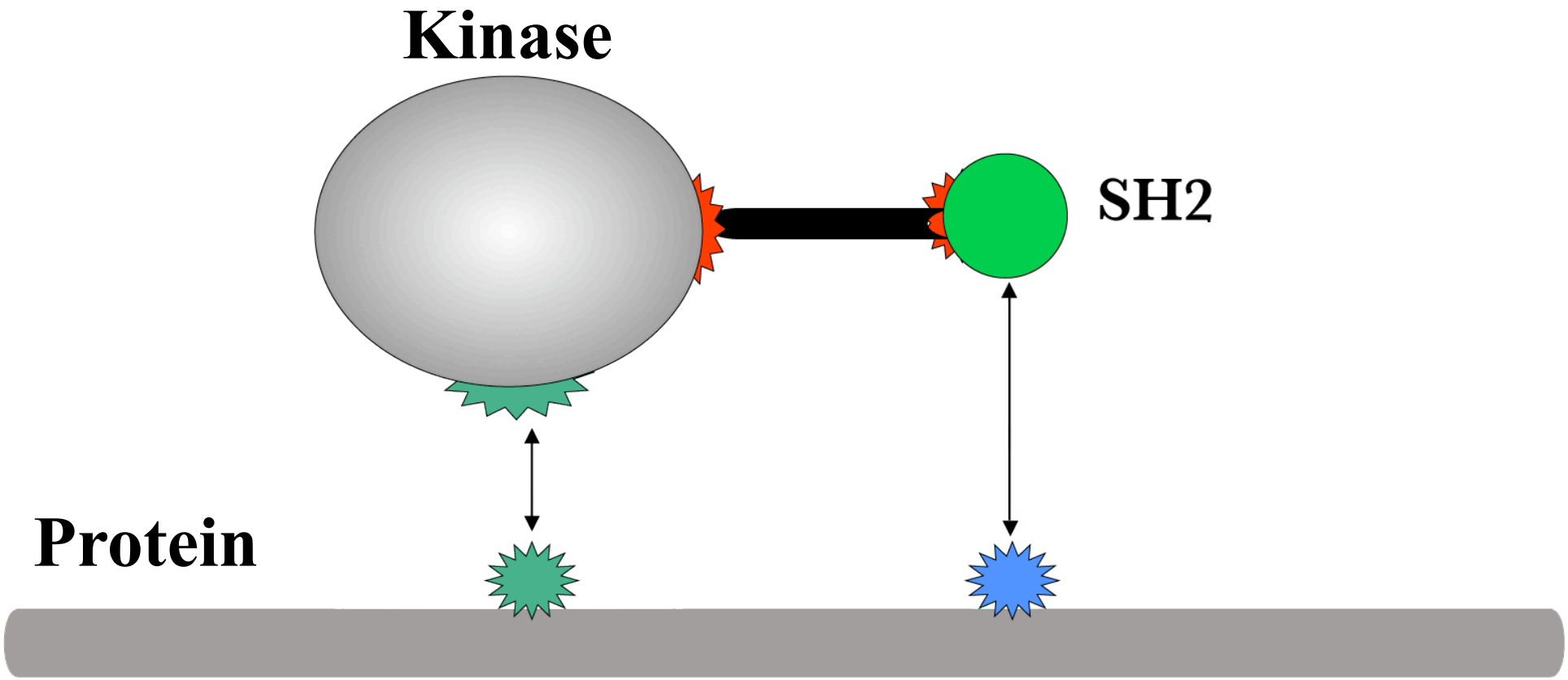

Target
Enzyme
Recruiter
Substrate

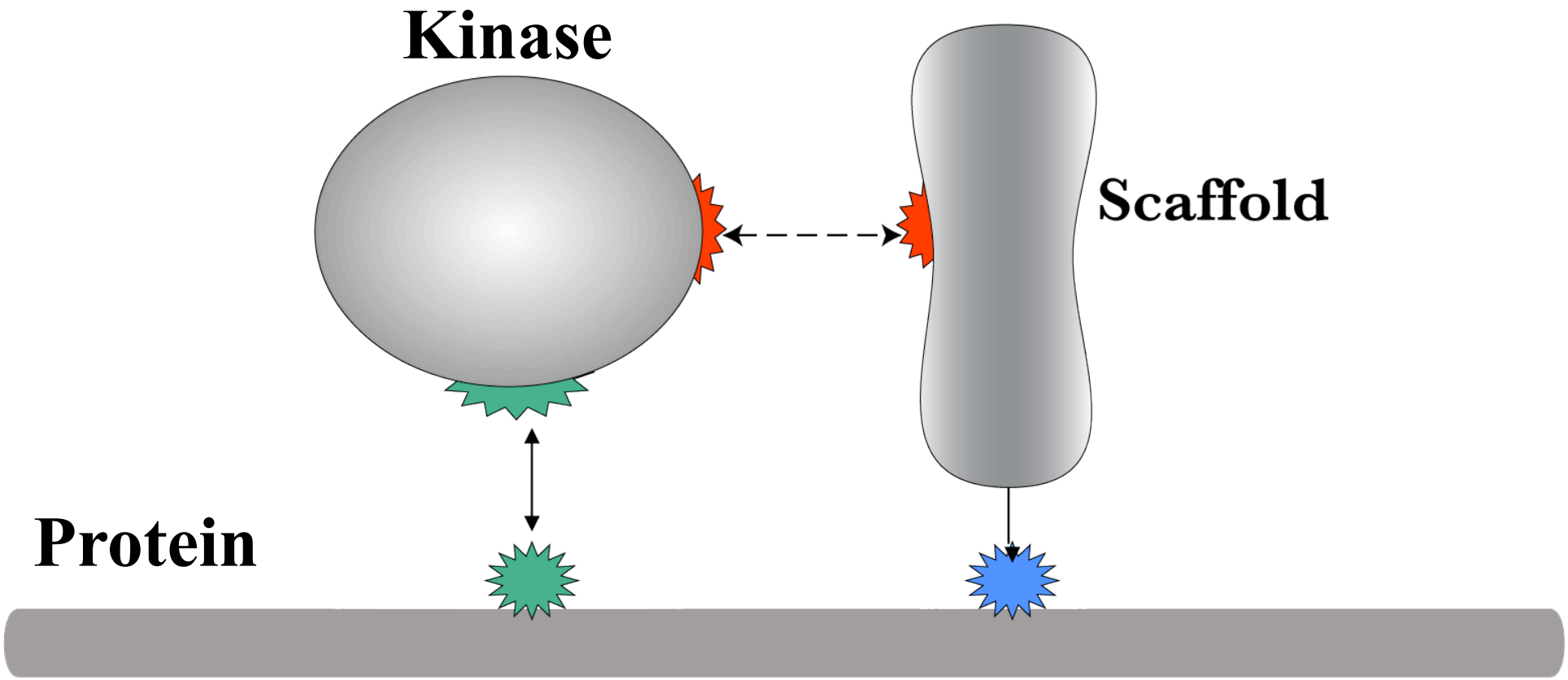

Enzyme
Substrate

RNAi Machinery

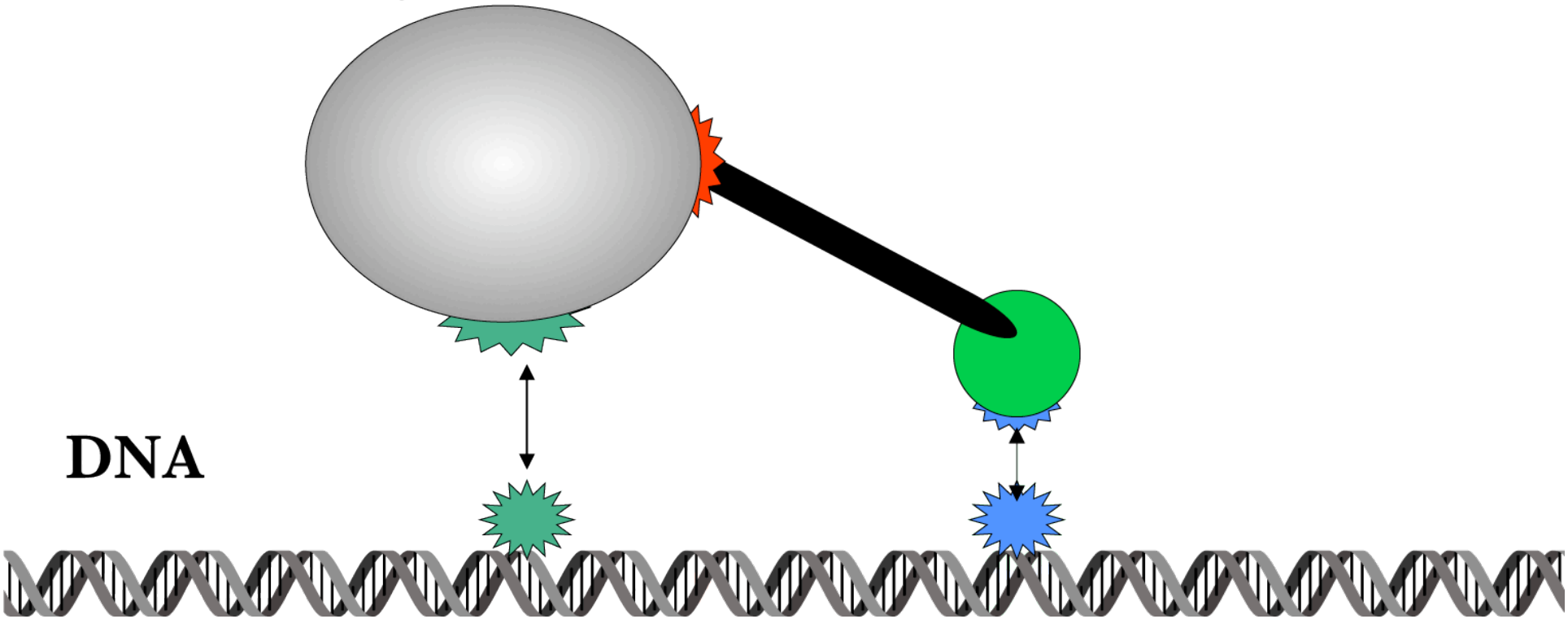



CDK
Cyclin
Protein

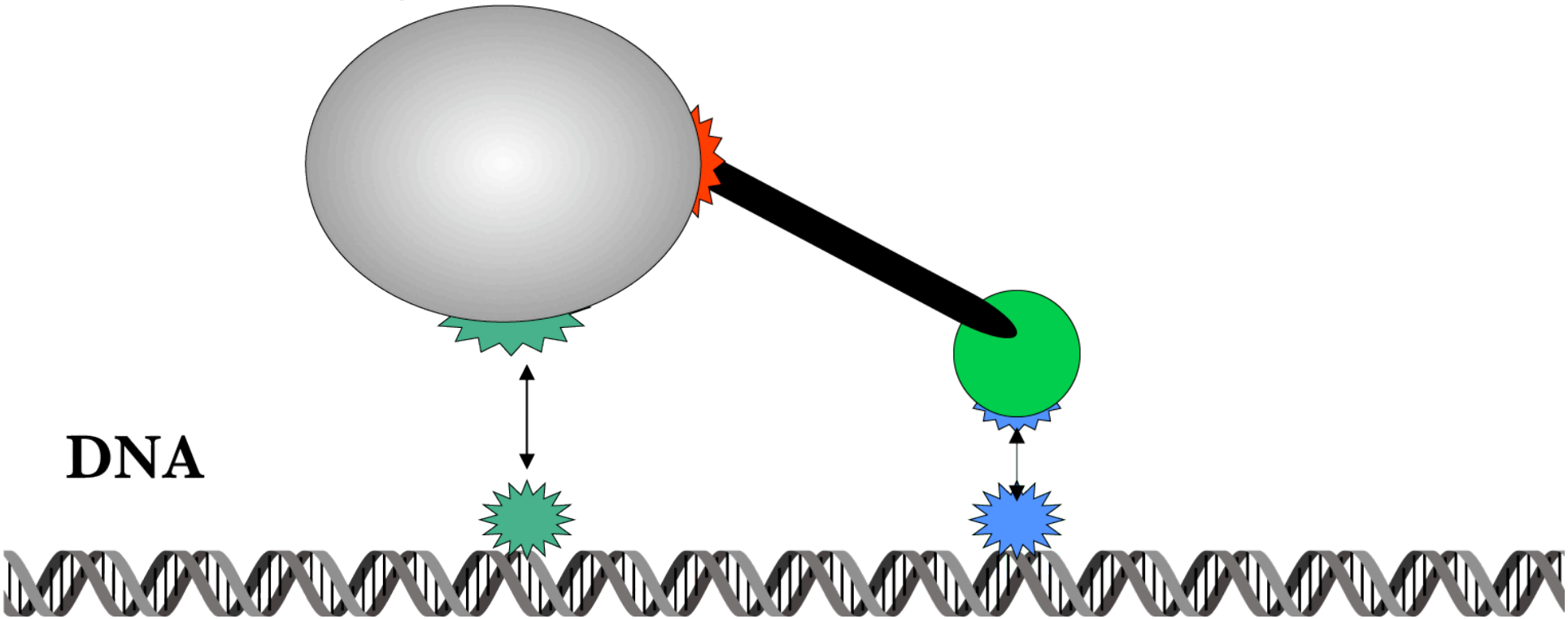

Kinase
SH2
Protein


Kinase
Scaffold
Protein

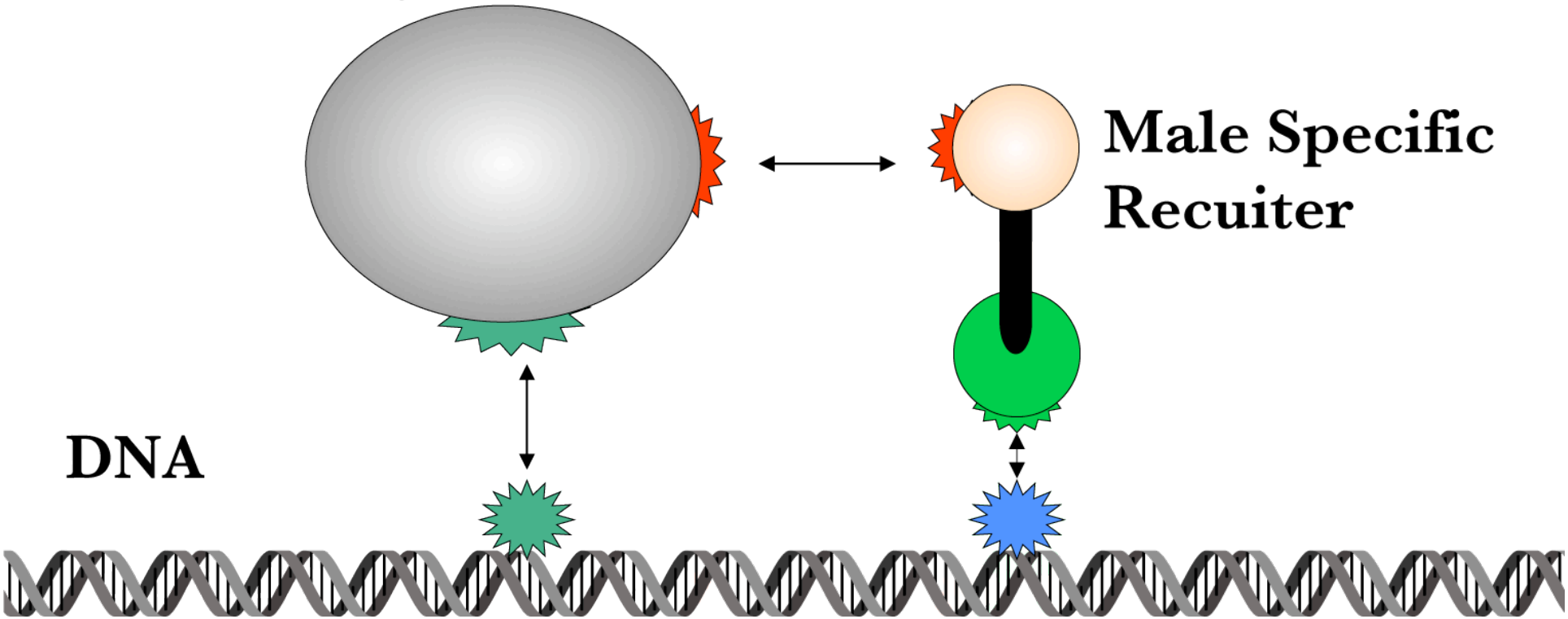
Transcriptional Machinery



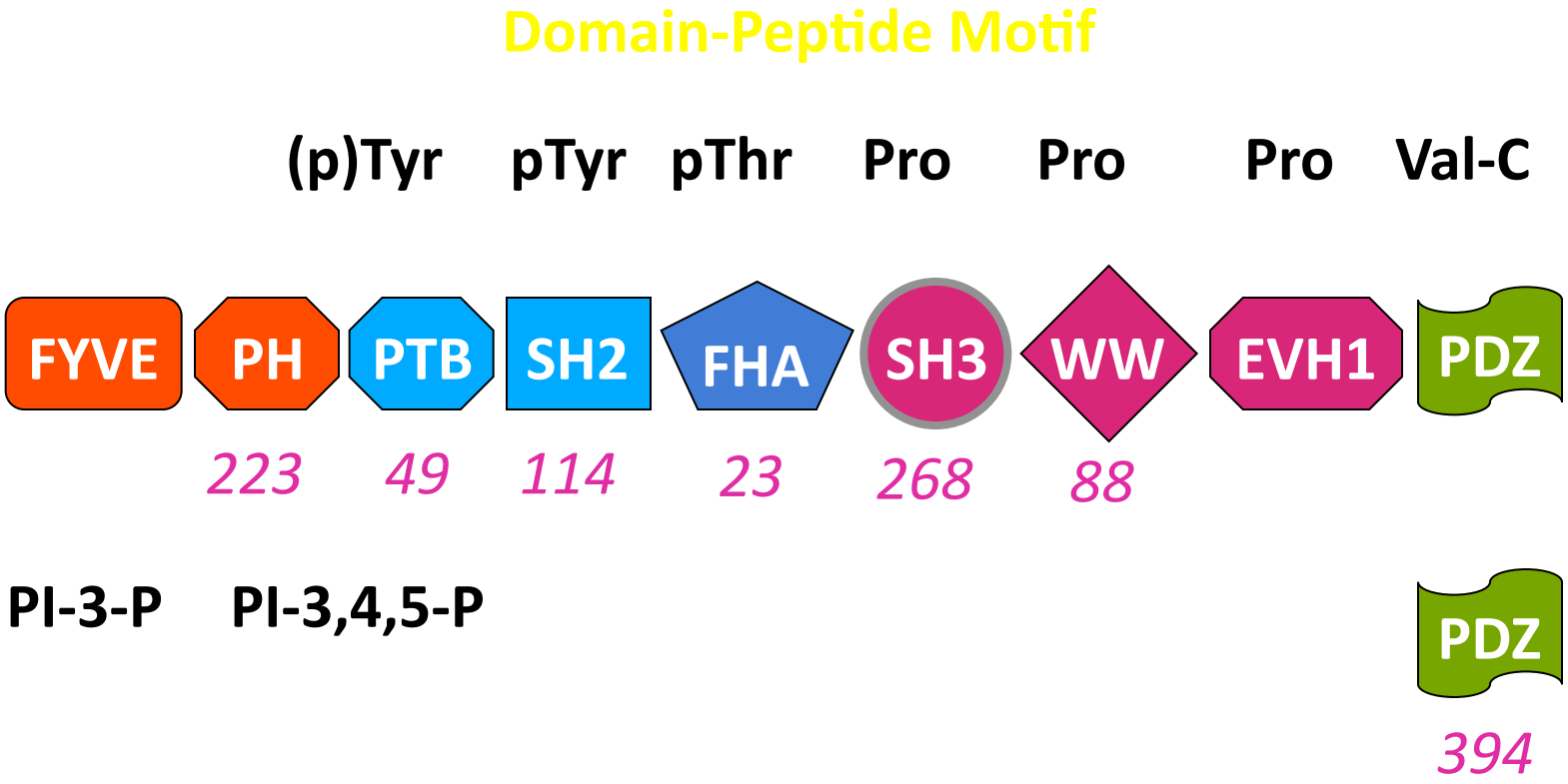
Transcriptional Machinery



Dosage Comp Machinery



Interaction Domains in Signal Transduction



Signal Transduction Pathway

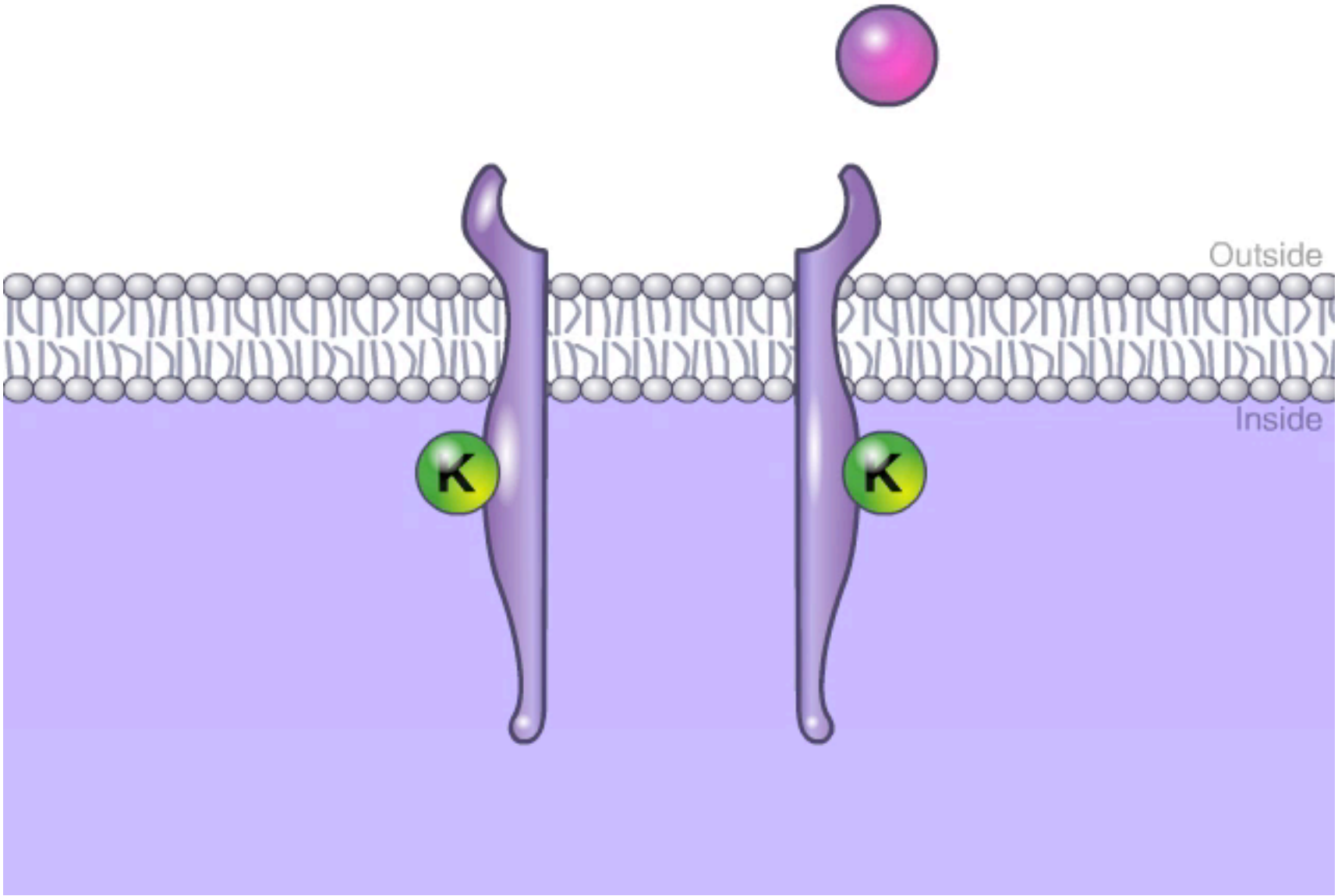
A series of binding/recruiting reactions

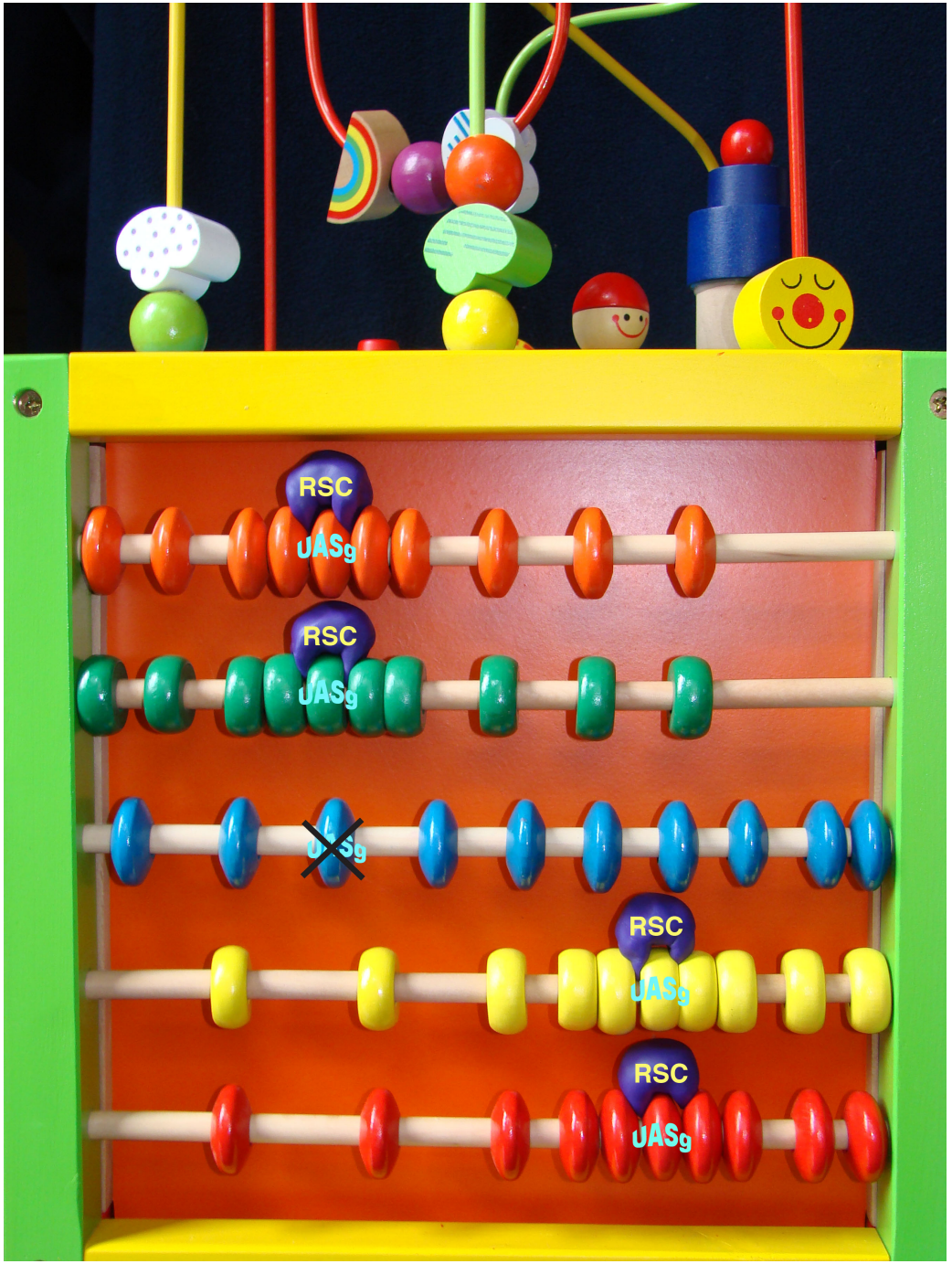
Signal Transduction Pathway

A series of binding/recruiting reactions

Enzymes that make binding sites

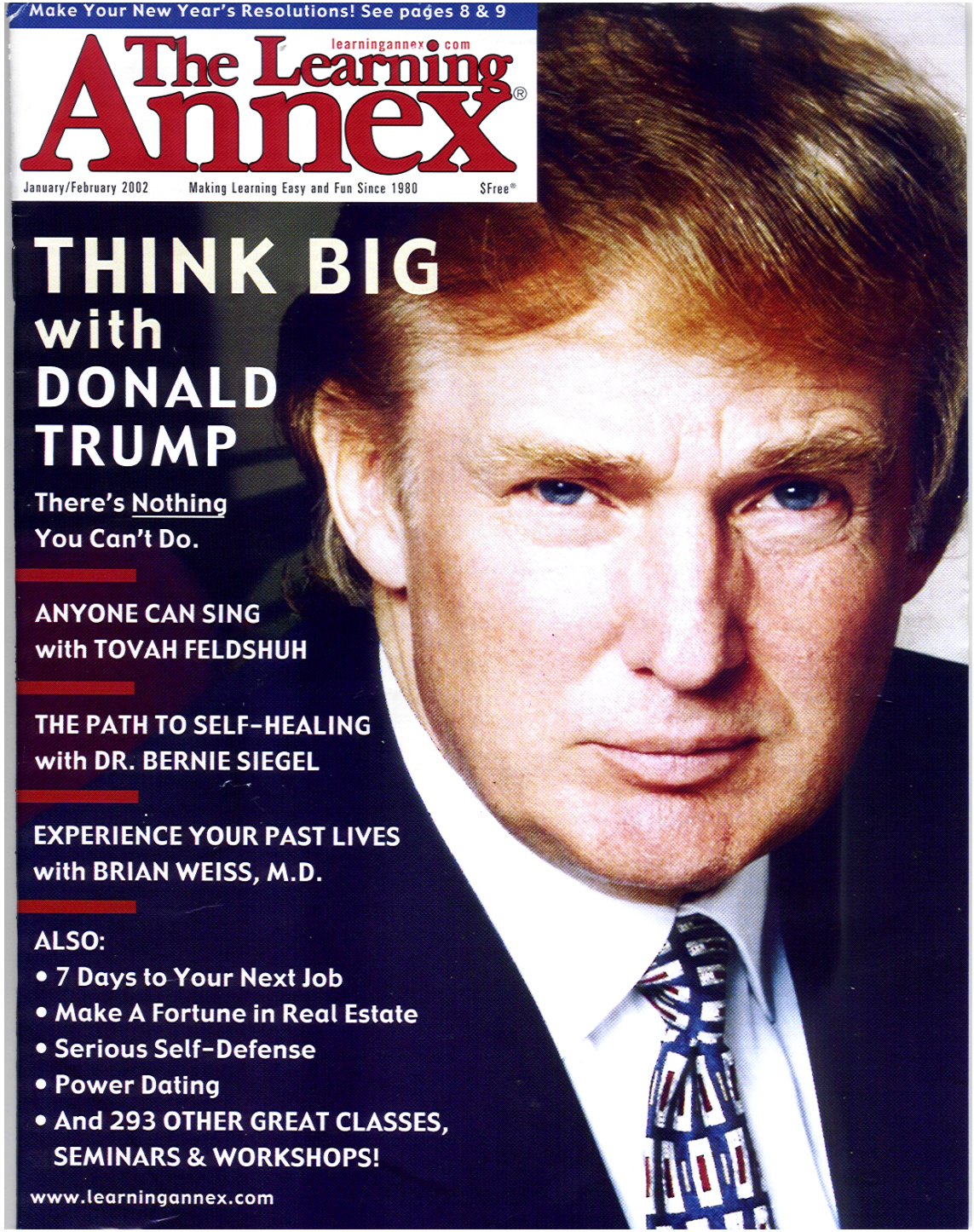
(eg kinases)


Outside
Inside
K
K


RSC
UASg
RSC
UASg
RSC
UASg
RSC
UASg

[He], like the rest of us, had many impressions which saved him the trouble of distinct ideas.

George Elliot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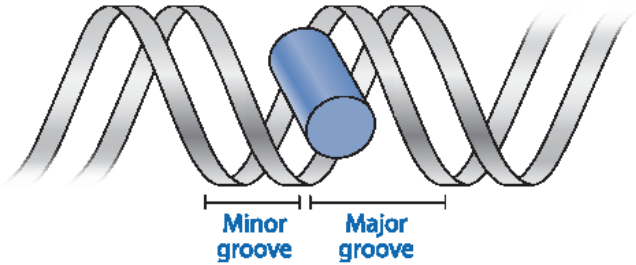
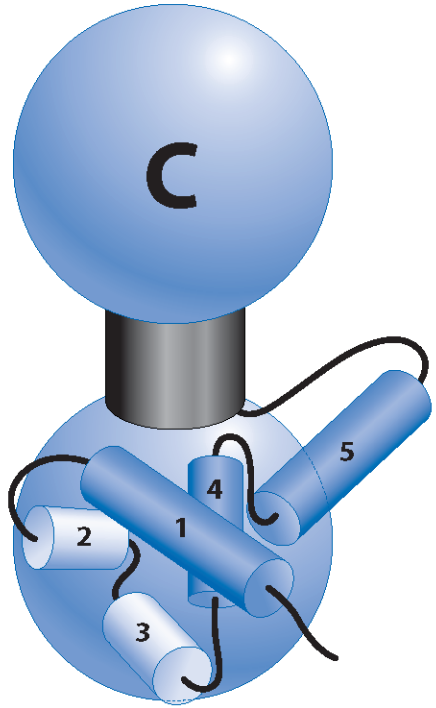
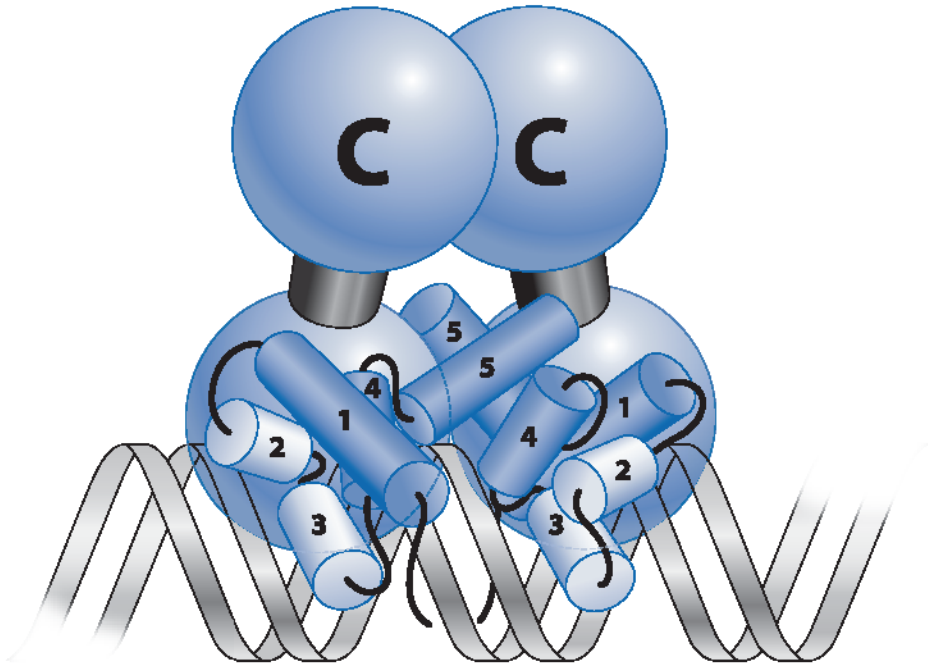

Minor
groove
Major
groove


C
1
2
3
4
5


C
C
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2
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