

Protein-RNA interactions

As seen by structural biology

THE CELL

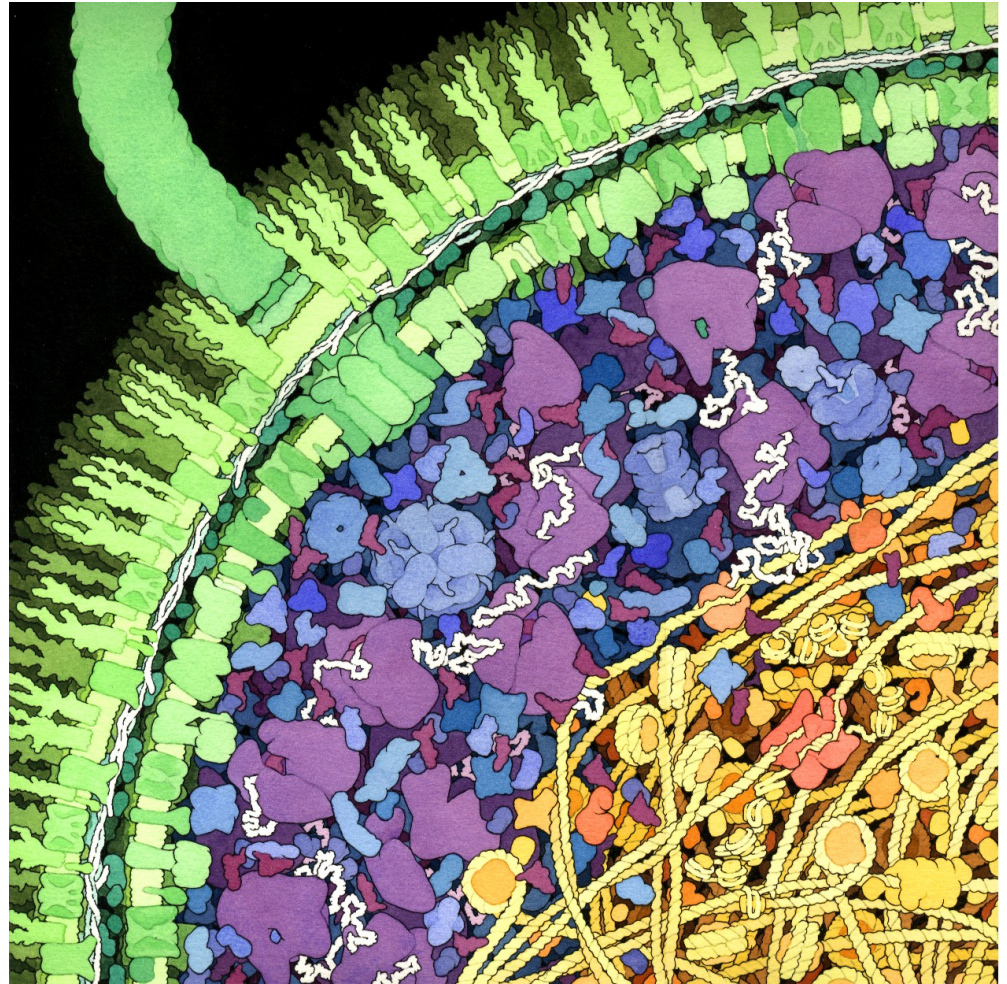
Water

DNA

RNA

Protein

Lipids, sugars and
other small molecules



Molecular Art by David S. Goodsell

Structural biology techniques

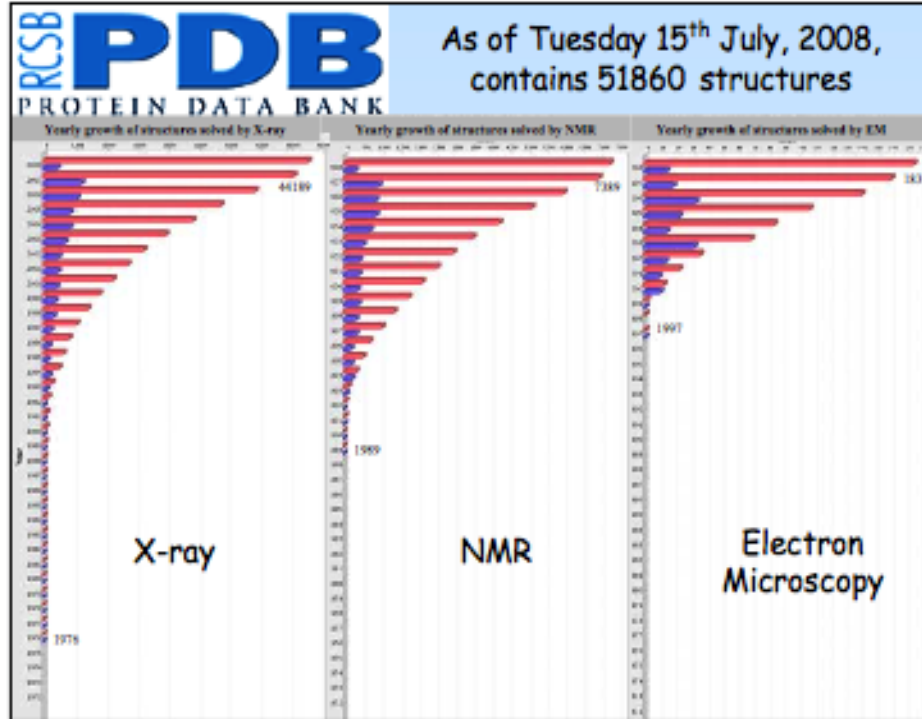
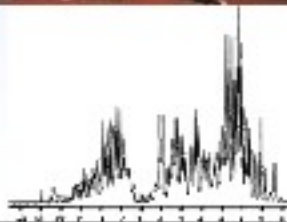
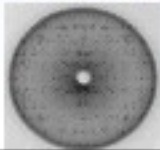
Current situation

High resolution (<1nm) structural tools:

X-ray diffraction

electron
microscopy

nuclear magnetic
resonance



Gene expression program

DNA



Transcription

RNA Pol I

RNA Pol II

RNA Pol III

RNA (rRNA,mRNA,tRNA)



Translation

Protein

RNA biogenesis

RNA packaging, stability

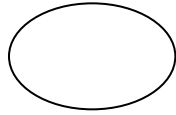
5' capping, RNA editing

splicing, alternative splicing

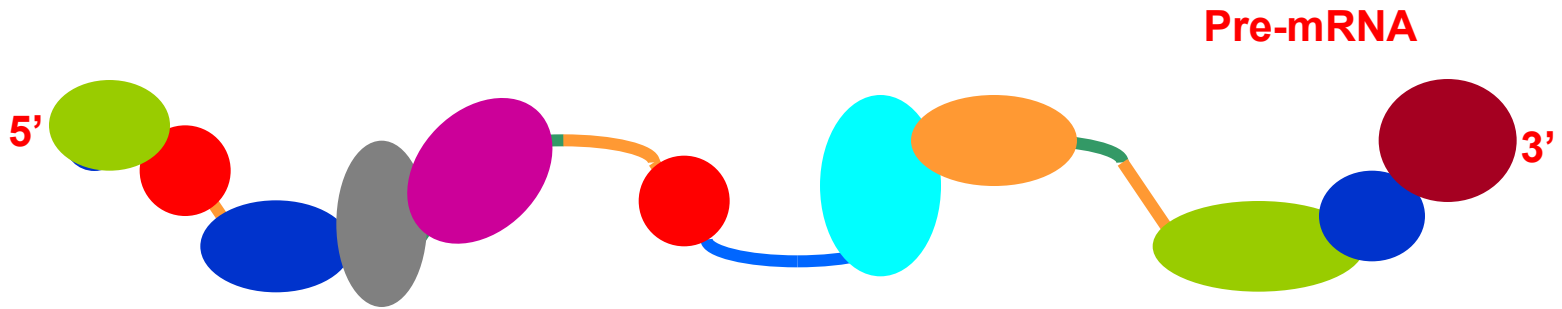
3' end processing

(cleavage and polyadenylation)

export



RNA binding proteins

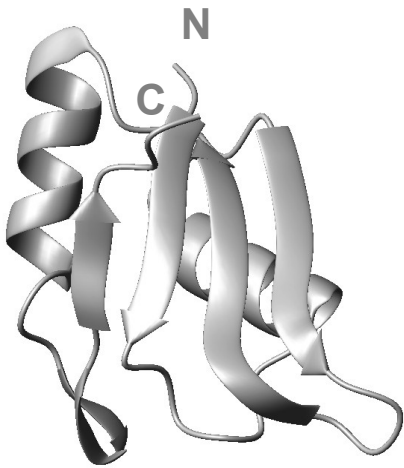


RNA binding proteins control the fate of the pre-mRNA

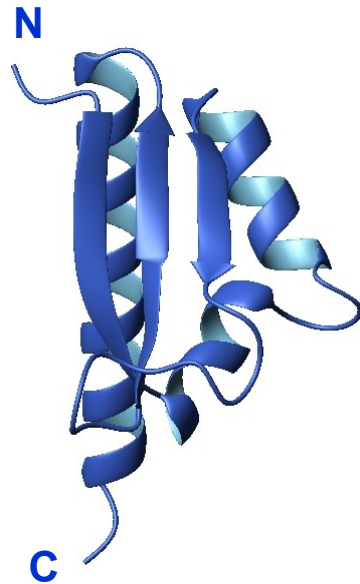
RNA binding proteins



RNA Binding Domain



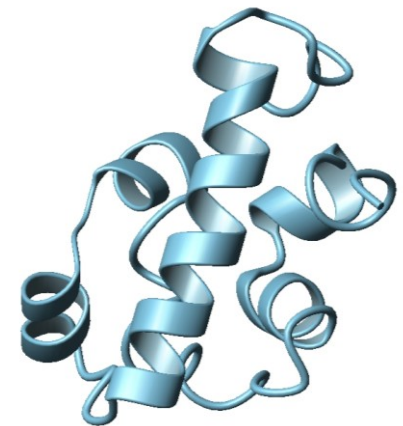
RRM/RBD/RNP



KH domain



dsRBM



SAM domain

RNA binding proteins of two types:

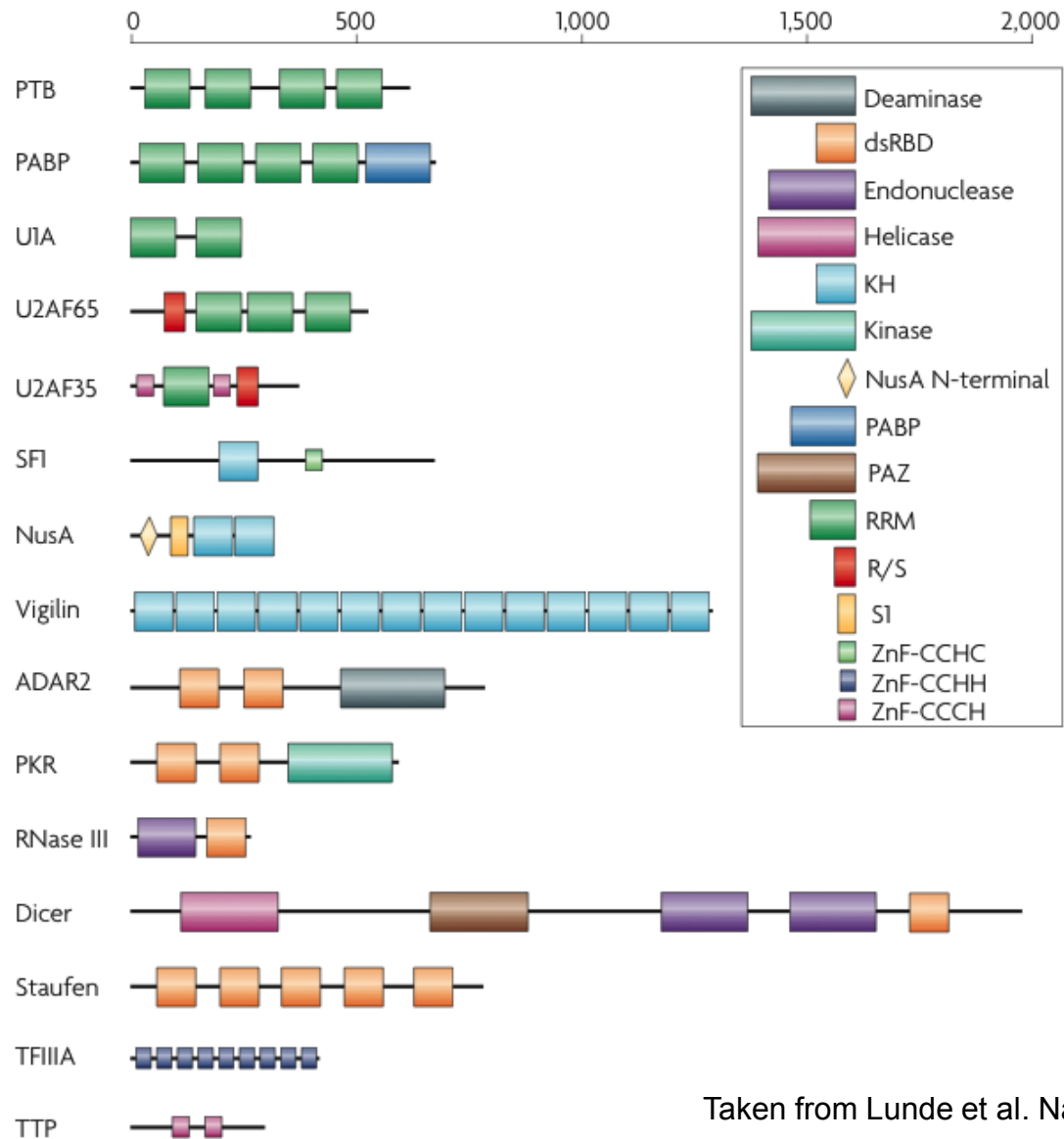
- **enzymes**

polymerase, nuclease, modifying enzymes

- **binding proteins**

protection, folding (chaperone), gene regulation

Modular architecture of RNA-binding proteins



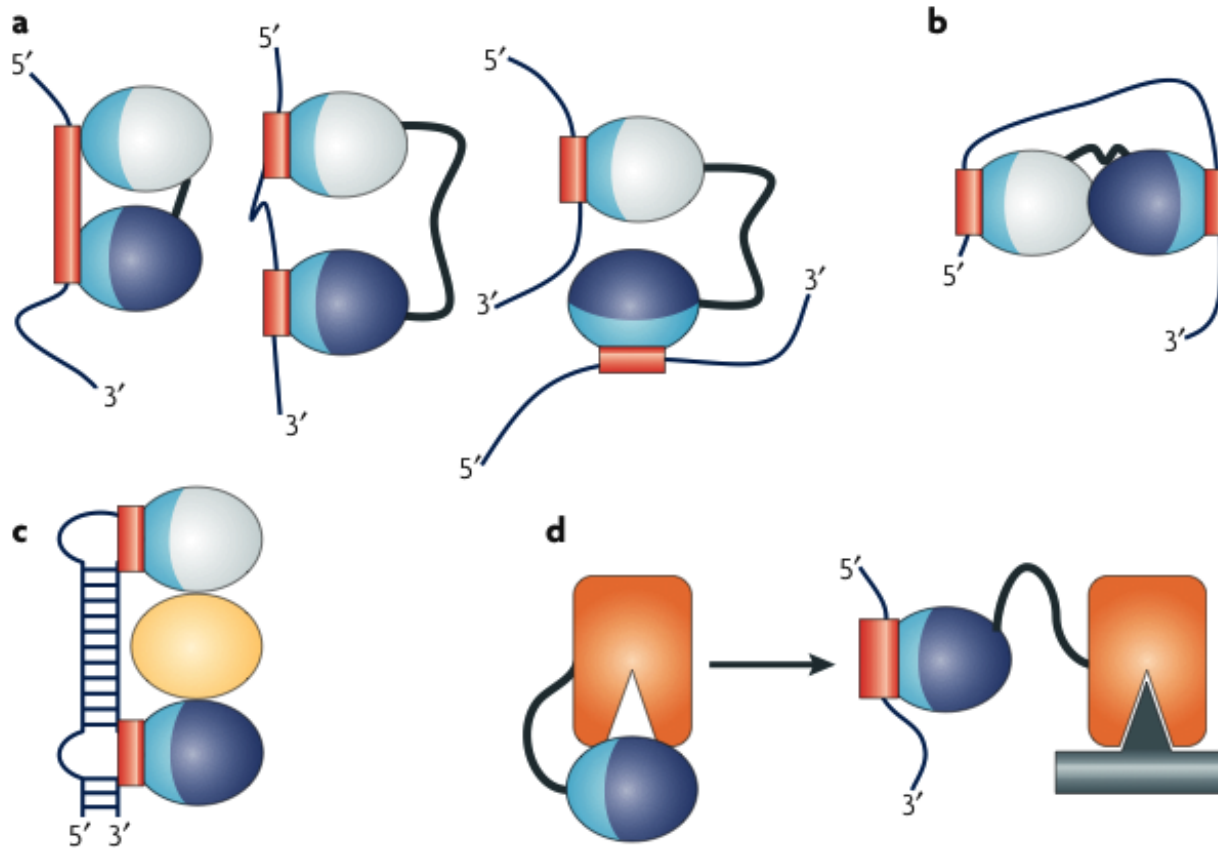
Taken from Lunde et al. Nat. Rev Mol. Cell Biol 2007

Protein-RNA interactions

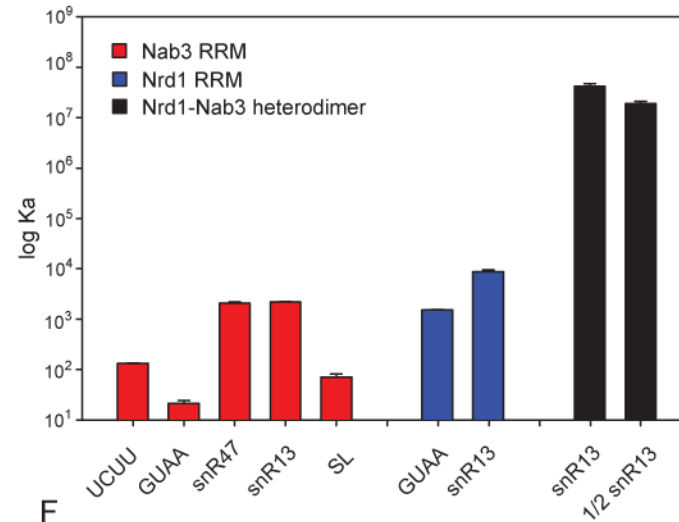
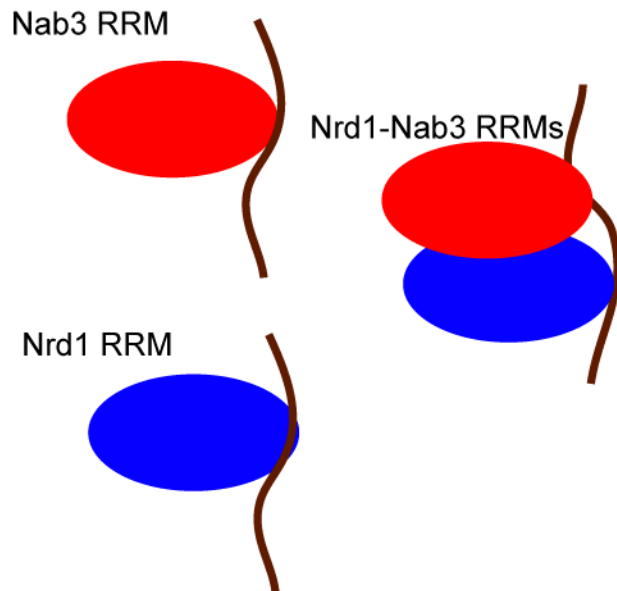
As seen by structural biology

- Basic description
- **Basic principles & Binding modes**
- Thermodynamics

RNA-binding modules are often combined to perform multiple functional roles



Positive cooperativity in RNA-binding



snR47: UUU**UCU**UUUUU**UCU**UAU**UCU**UAUU

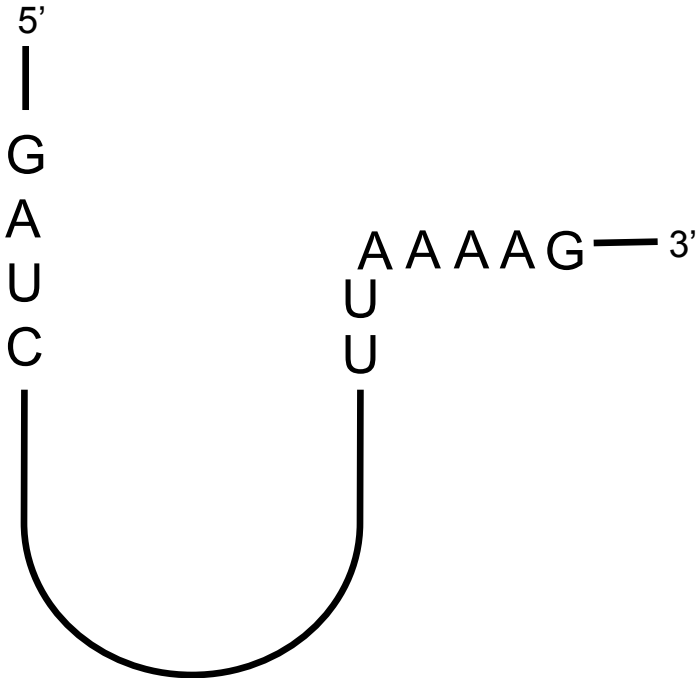
snR13: CCCC**GUAG**AAAA**UCU**U**AGUA**AUCCCU**UCU**UACAUUG

SL: GUAUAUAACAUAUCCGUGUUGUUUAUAGUACC

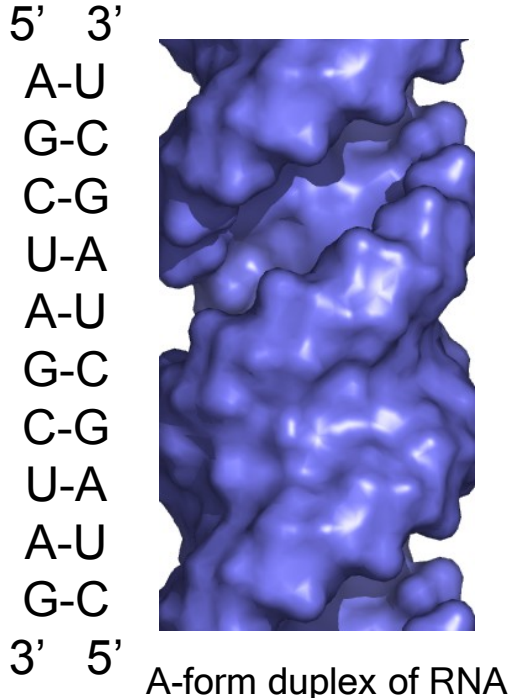
1/2 snR13: AA**UCU**U**AGUA**AUC

What information is recognized by proteins:

Recognition of RNA sequence

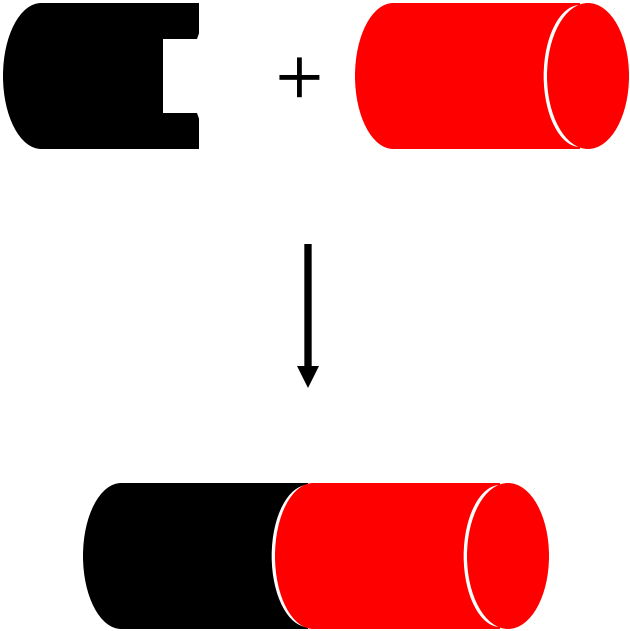


Recognition of RNA shape

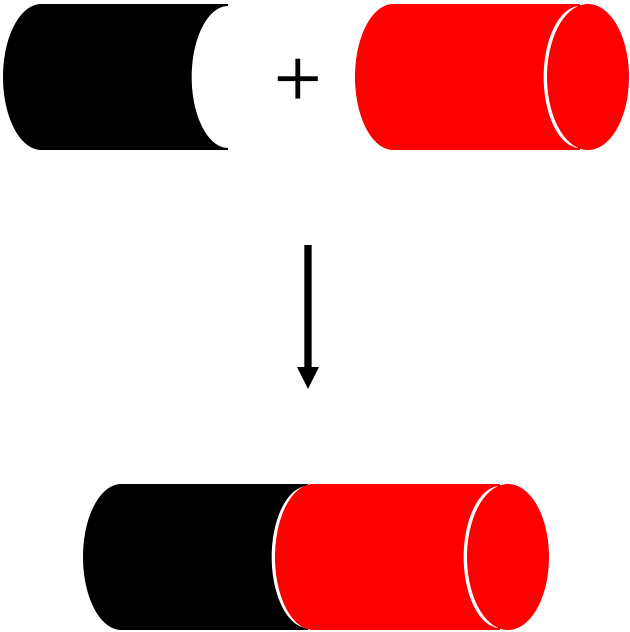


What recognition mode is used by proteins:

Induced fit



Rigid-body docking

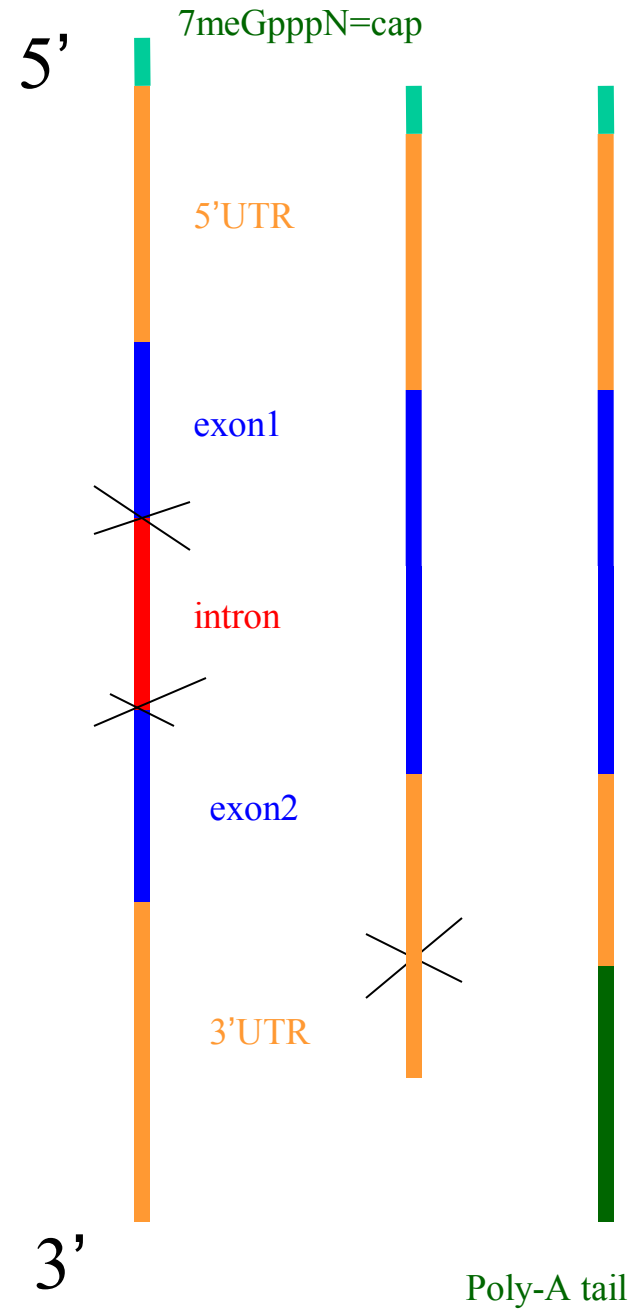
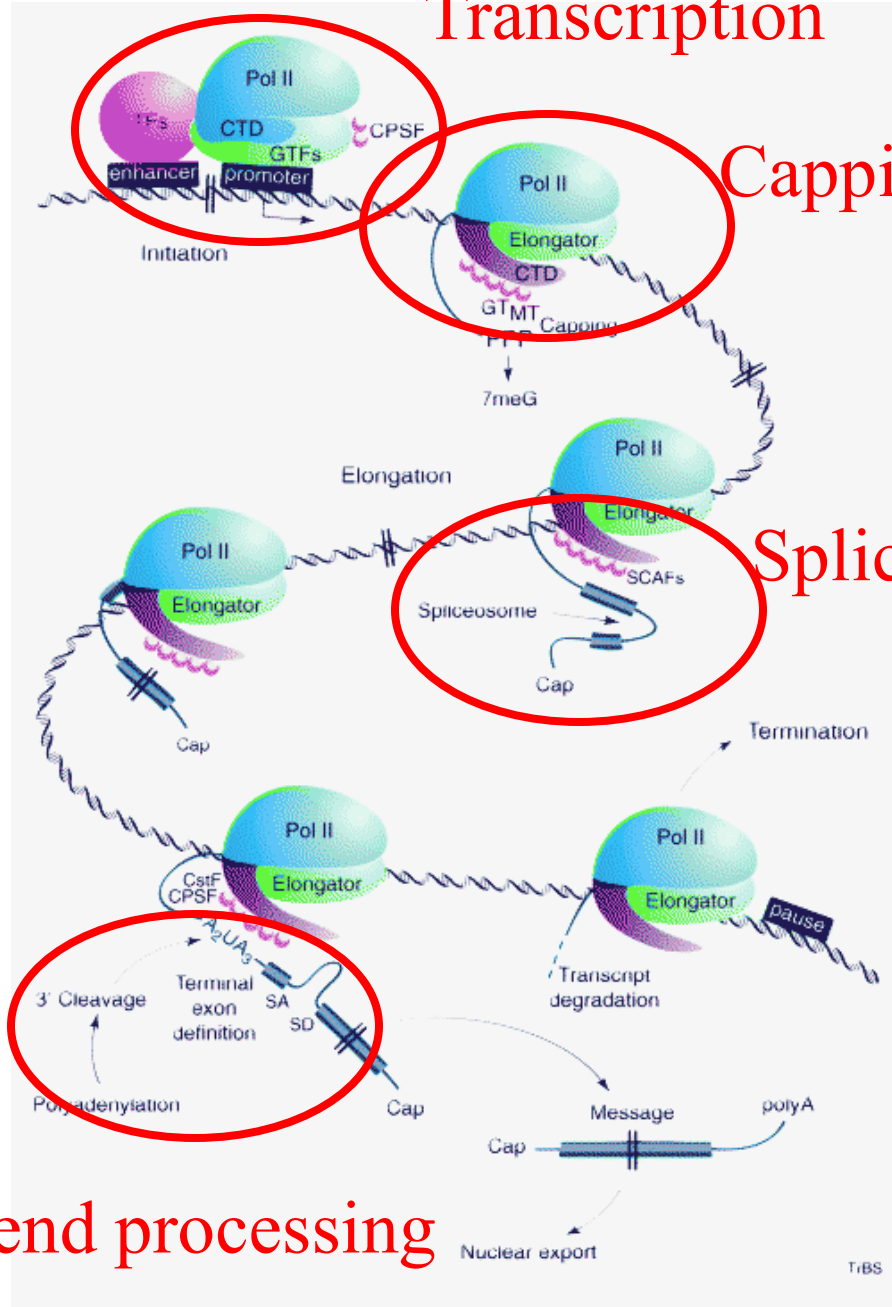


Transcription

Capping

Splicing

3' end processing



Induced fit recognition

Examples

Induced fit binding

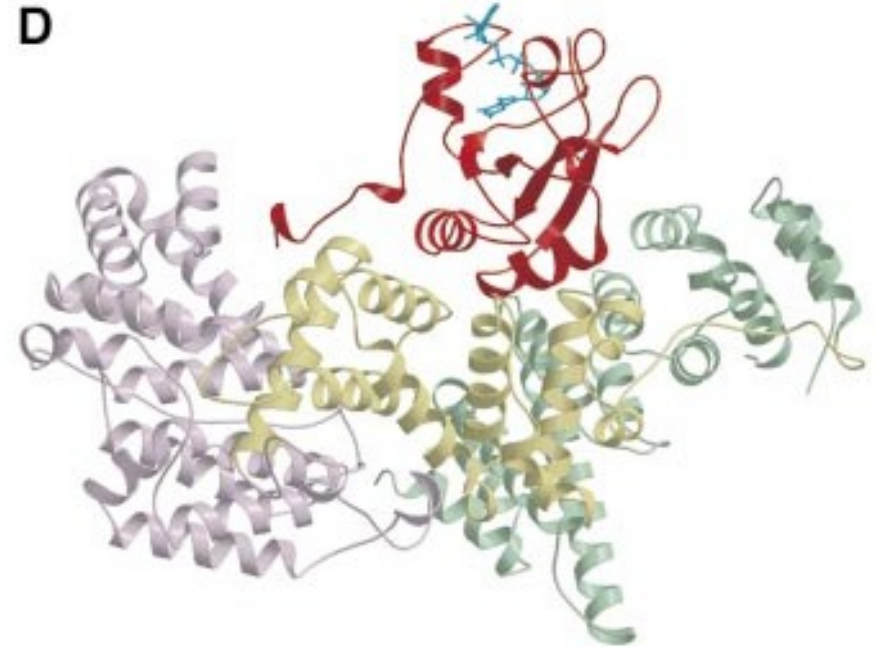
5' cap binding protein, **CBP20**-CBP80

C



CBP20-CBP80

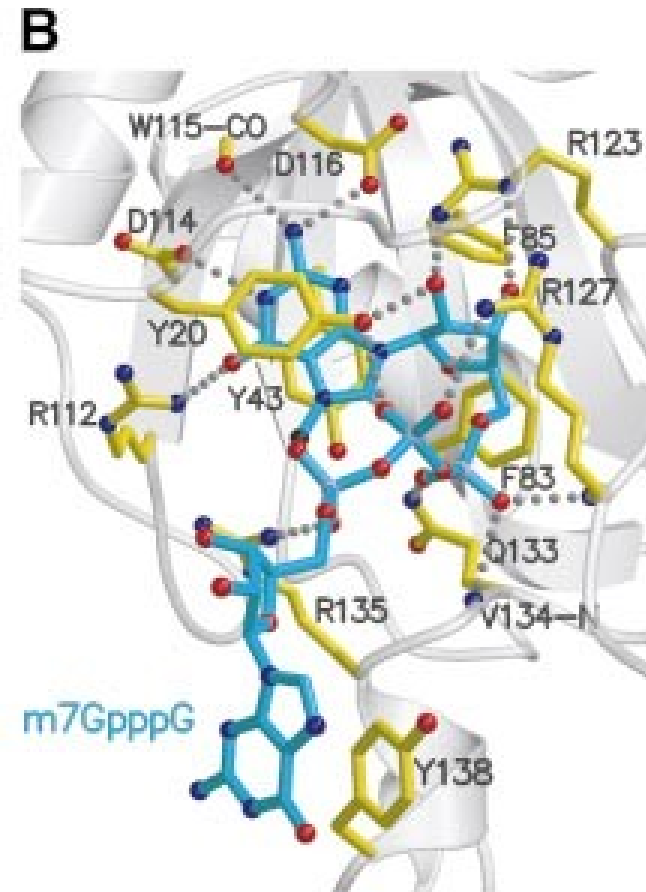
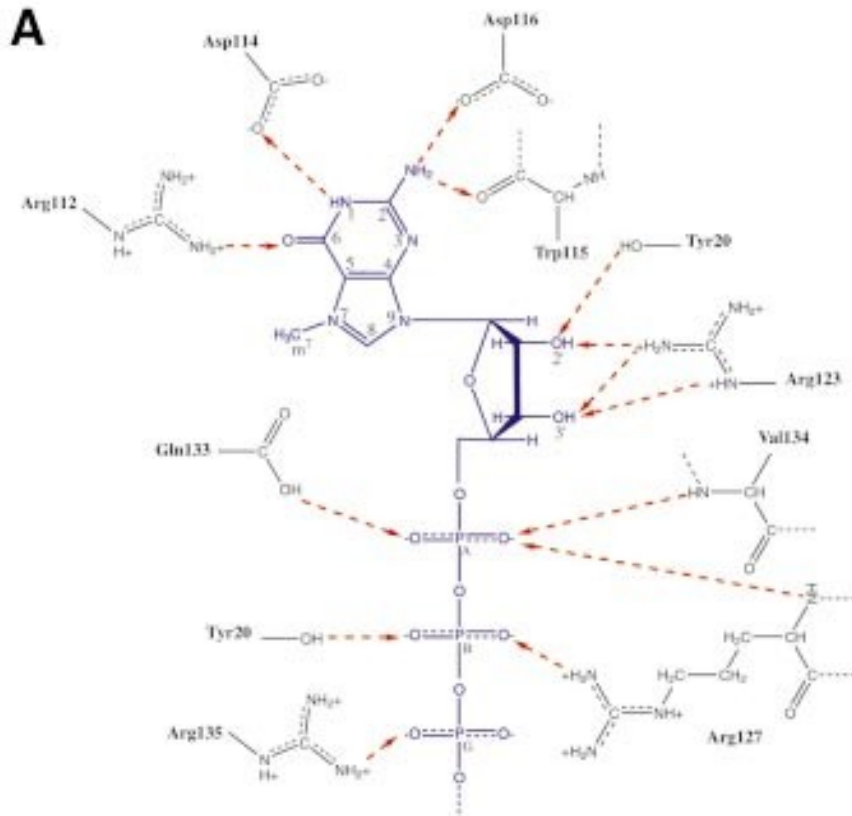
D



Mazza et al, EMBO J (2002)

Induced fit binding

CBP20-m7GpppG contacts

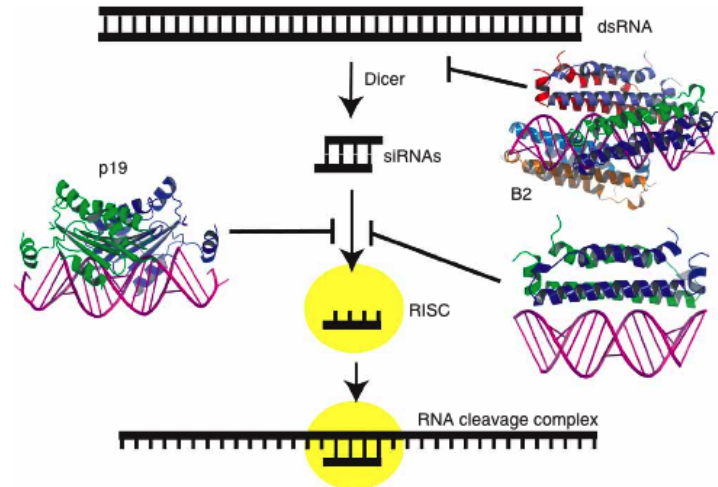
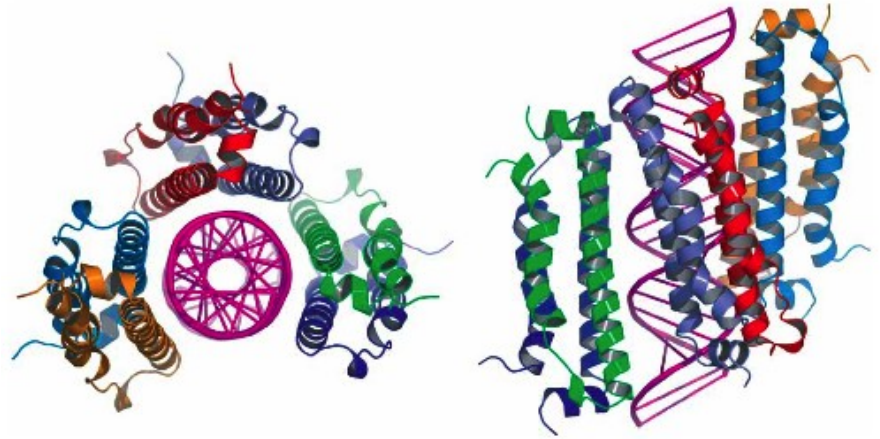
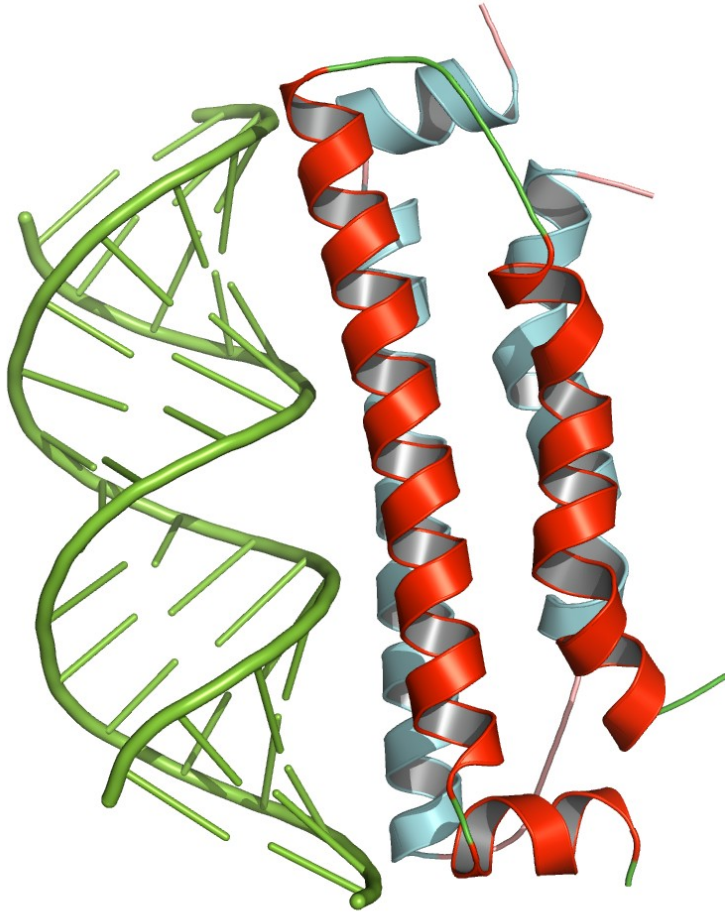


Rigid body docking

Examples

Viral B2 protein supresses RNAi by masking dsRNA or siRNA.

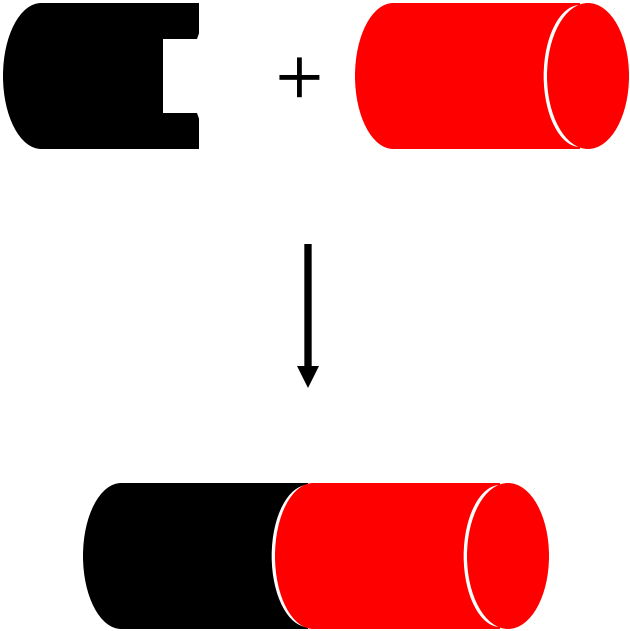
Rigid-body docking



Taken from Chao et al. Nat. Struct. Mol. Biol. 2005

What recognition mode is used by proteins:

Induced fit



Rigid-body docking

