

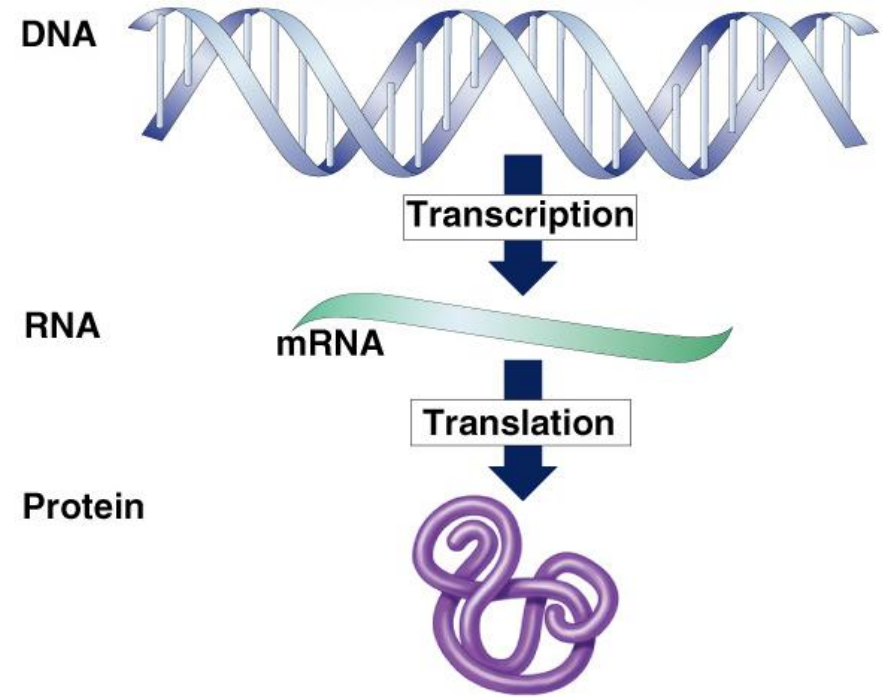
Chapter 17.



10 μ m

Val	His	Leu	Thr	Pro	Val	Glu	...
1	2	3	4	5	6	7	

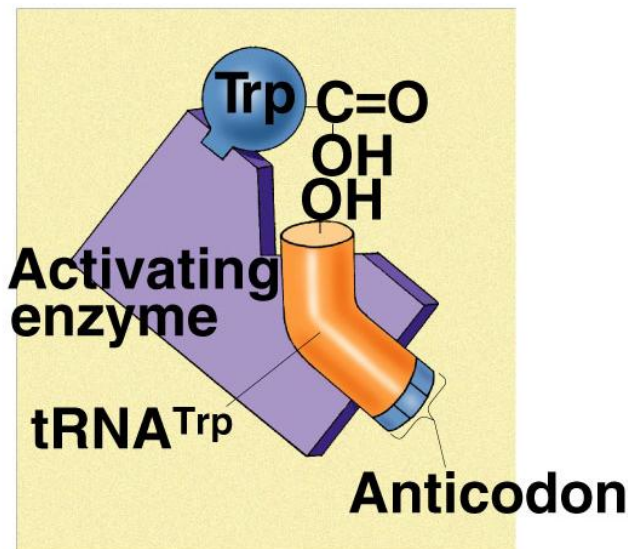
(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin



Mutations

Universal code

- Code is redundant
 - ◆ several codons for each amino acid
 - ◆ “wobble” in the tRNA
 - ◆ “wobble” in the aminoacyl-tRNA synthetase enzyme that loads the tRNA



		Second base				
		U	C	A	G	
First base (5' end)	U	UUU	UCU	UAU	UGU	U
		UUC	UCC	UAC	UGC	C
		UUA	UCA	UAA Stop	UGA Stop	A
		UUG	UCG	UAG Stop	UGG Trp	G
	C	CUU	CCU	CAU	CGU	U
		CUC	CCC	CAC	CGC	C
		CUA	CCA	CAA	CGA	A
		CUG	CCG	CAG	CGG	G
	A	AUU	ACU	AAU	AGU	U
		AUC	ACC	AAC	AGC	C
		AUA	ACA	AAA	AGA	A
		AUG	ACG	AAG	AGG	G
G	GUU	GCU	GAU	GGU	U	
	GUC	GCC	GAC	GGC	C	
	GUA	GCA	GAA	GGA	A	
	GUG	GCG	GAG	GGG	G	
						Third base (3' end)

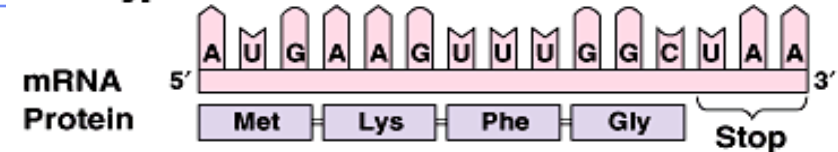
Mutations

■ Point mutations

- ◆ single base change
- ◆ base-pair substitution
 - silent mutation
 - ◆ no amino acid change
 - ◆ redundancy in code
 - missense
 - ◆ change amino acid
 - nonsense
 - ◆ change to stop codon

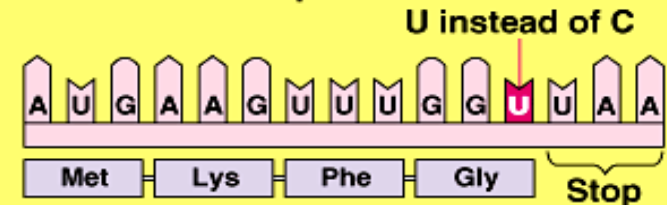
When do mutations affect the next generation?

Wild type



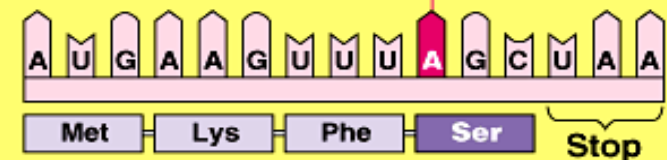
Base-pair substitution

No effect on amino acid sequence



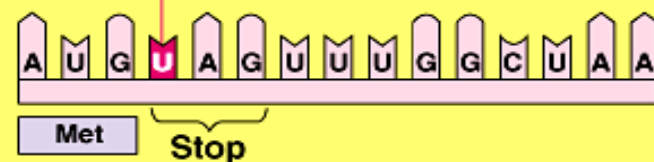
Missense

A instead of G



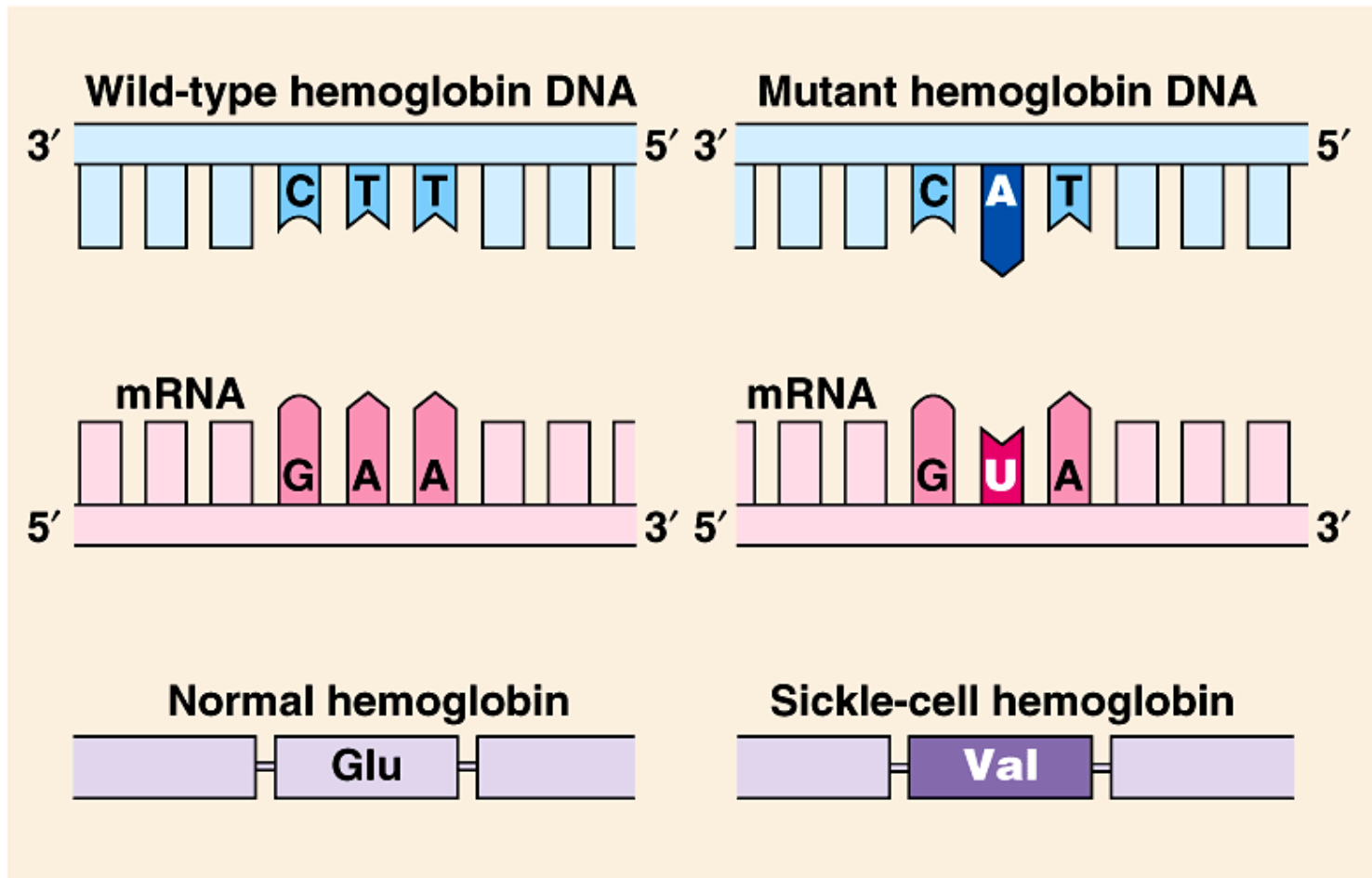
Nonsense

U instead of A

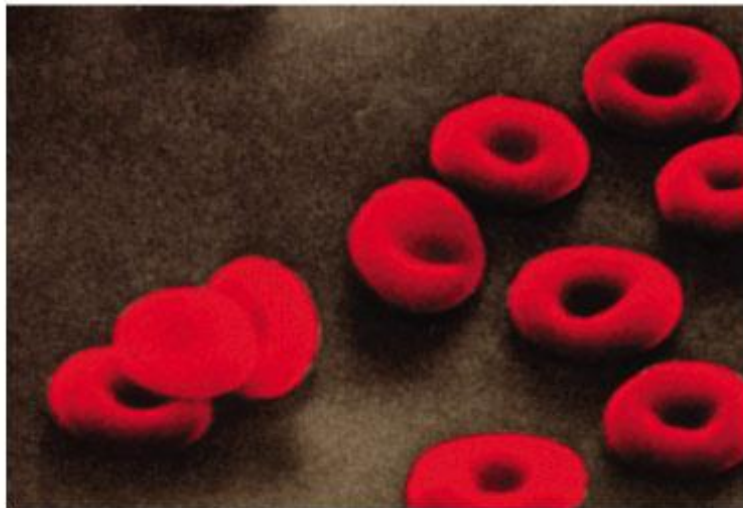


Point mutation leads to Sickle cell anemia

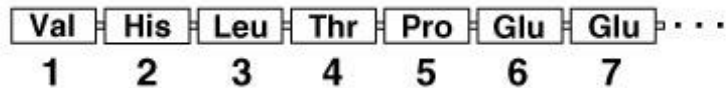
What kind of mutation?



Sickle cell anemia



10 μ m



(a) Normal red blood cells and the primary structure of normal hemoglobin



10 μ m



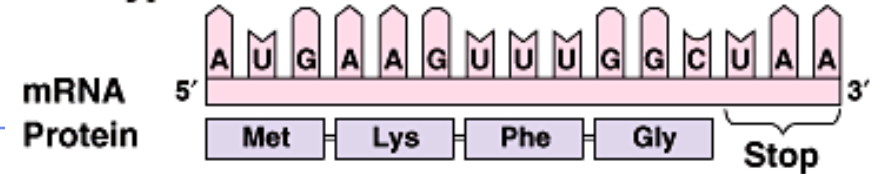
(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

Mutations

■ Frameshift

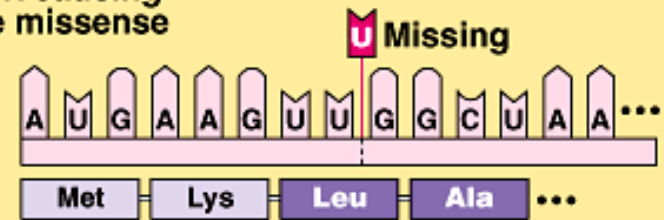
- ◆ shift in the reading frame
 - changes everything “downstream”
- ◆ insertions
 - adding base(s)
- ◆ deletions
 - losing base(s)

Wild type

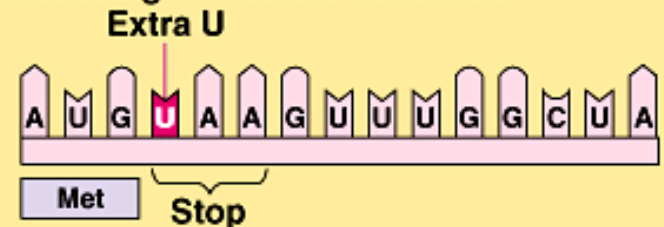


Base-pair insertion or deletion

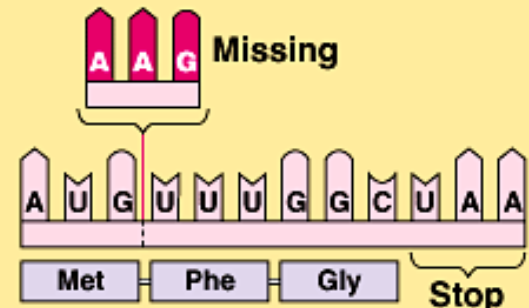
Frameshift causing extensive missense



Frameshift causing immediate nonsense

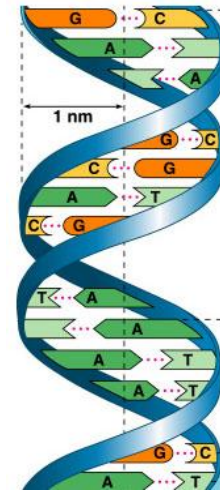


Insertion or deletion of 3 nucleotides: no frameshift; extra or missing amino acid



Chapter 17.

RNA Processing



Transcription -- another look

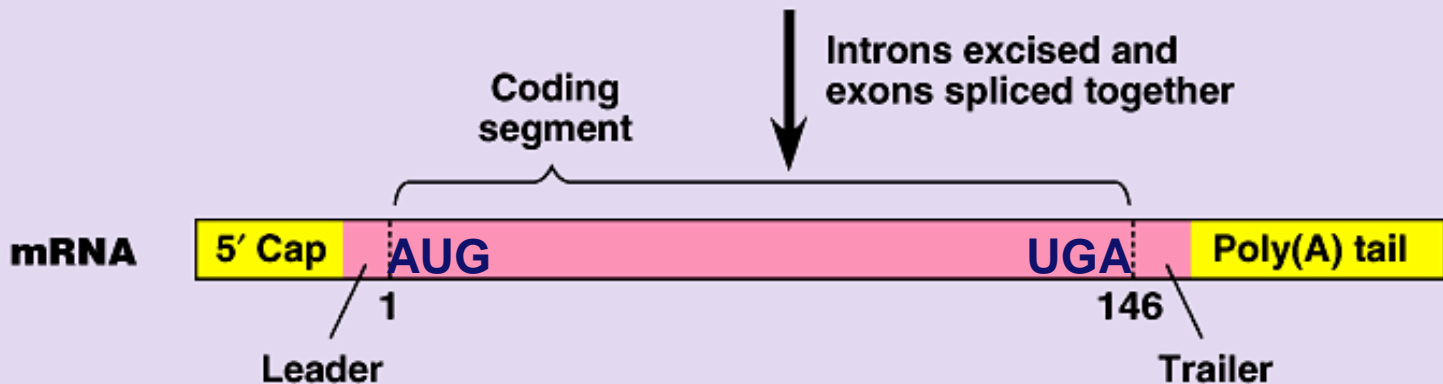
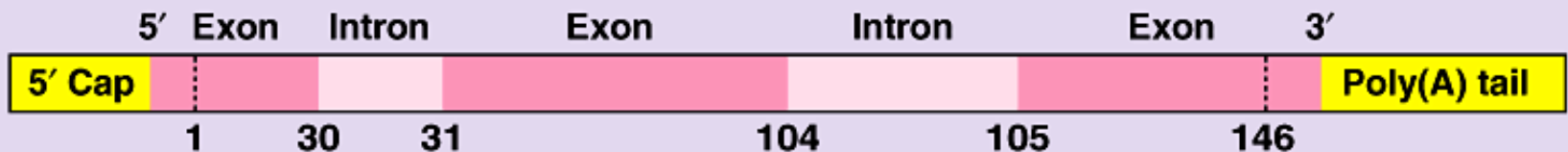
- **The process of transcription includes many points of control**
 - ◆ **when to start reading DNA**
 - ◆ **where to start reading DNA**
 - ◆ **where to stop reading DNA**
 - ◆ **editing the mRNA**
 - ◆ **protecting mRNA as it travels through cell**

Primary transcript

■ Processing mRNA

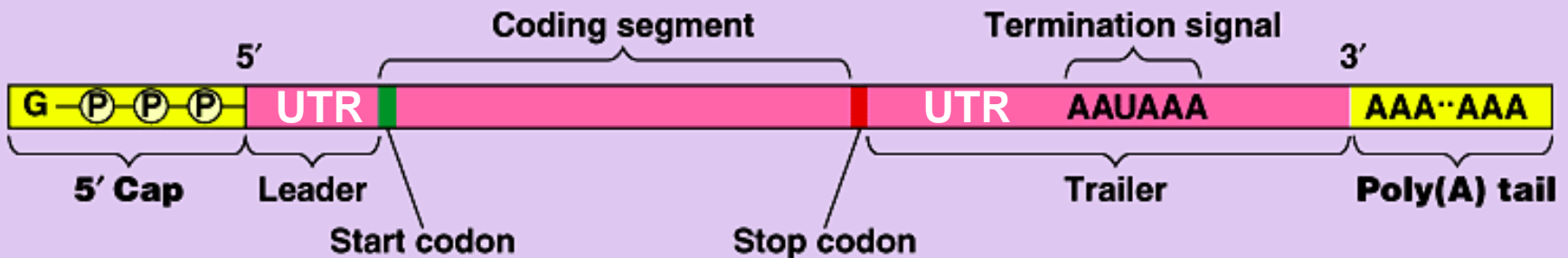
- ◆ protecting RNA from RNase in cytoplasm
 - add 5' cap
 - add polyA tail
- ◆ remove introns

Pre-mRNA



Protecting RNA

- **5' cap added**
 - ◆ G trinucleoside (G-P-P-P)
 - ◆ protects mRNA
 - from RNase (hydrolytic enzymes)
- **3' poly-A tail added**
 - ◆ 50-250 A's
 - ◆ protects mRNA
 - from RNase (hydrolytic enzymes)
 - ◆ helps export of RNA from nucleus



Dicing & splicing mRNA

■ Pre-mRNA → mRNA

◆ edit out introns

- intervening sequences

◆ splice together exons

- expressed sequences

◆ In higher eukaryotes

- 90% or more of gene can be intron
- no one knows why...yet
 - ◆ **there's a Nobel prize waiting...**

1977 | 1993

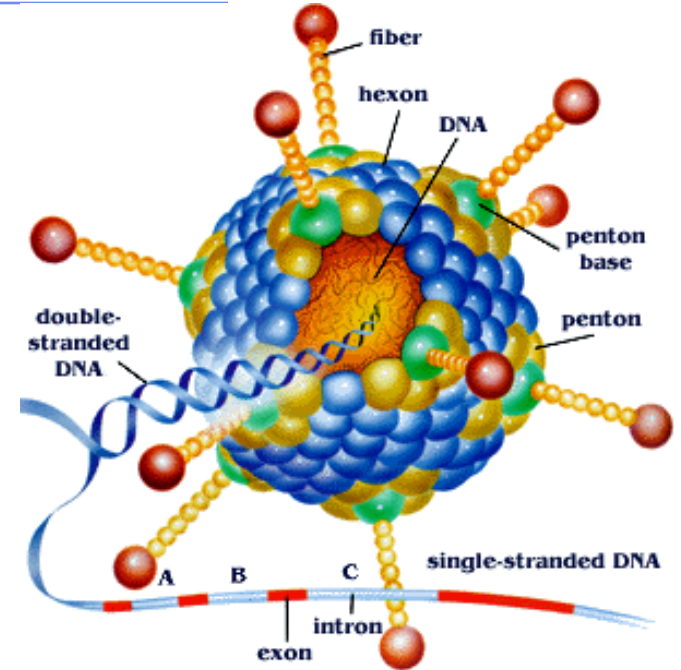
Discovery of Split genes



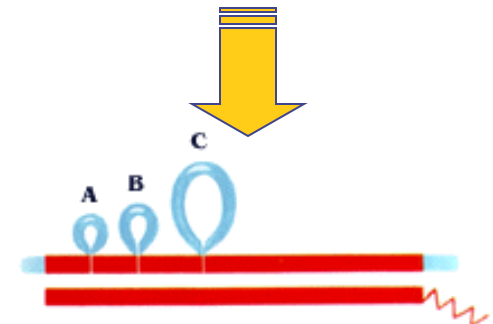
Richard Roberts
NE BioLabs



Philip Sharp
MIT



adenovirus
common cold



Splicing enzymes

■ snRNPs

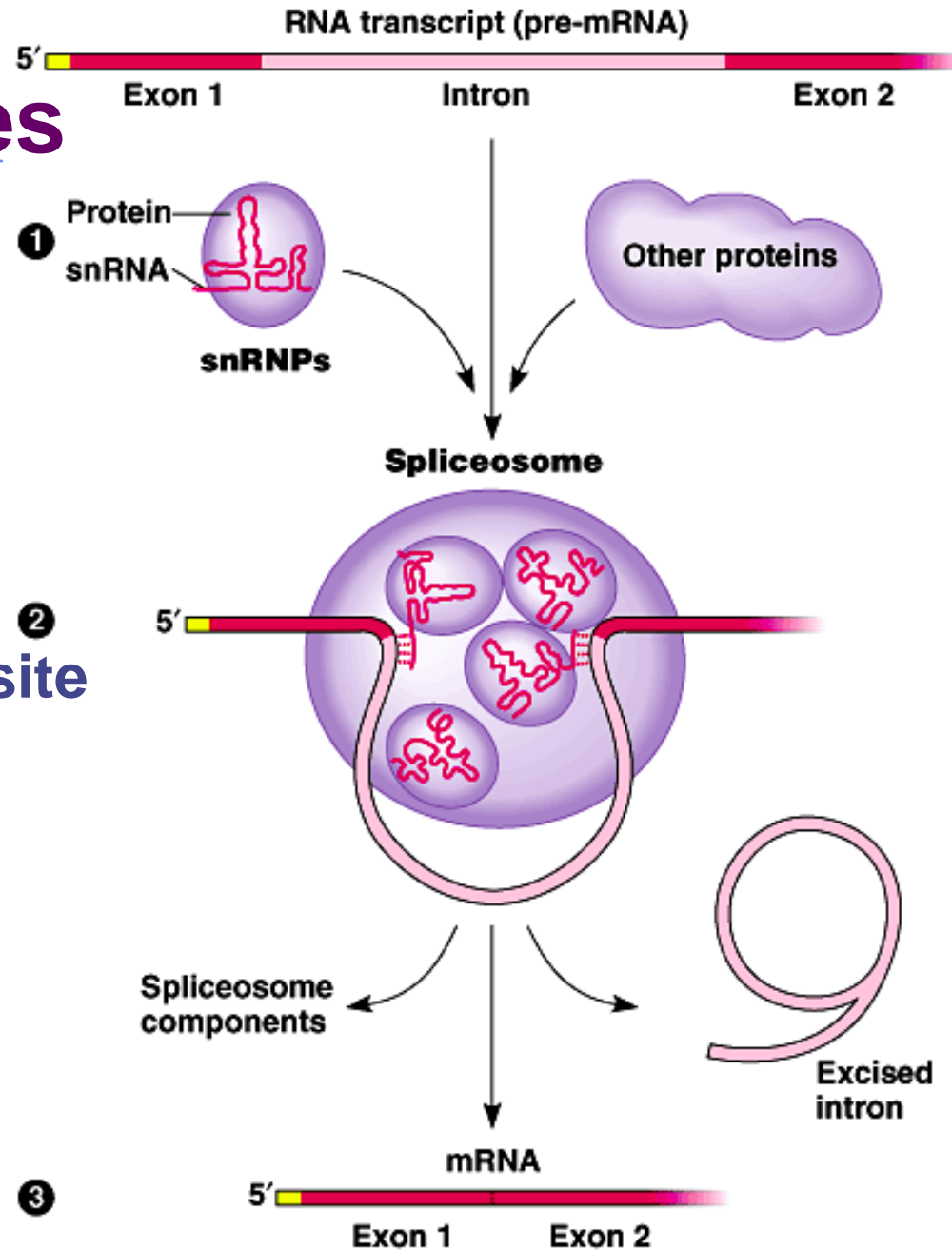
- ◆ small nuclear RNA
- ◆ RNA + proteins

■ Spliceosome

- ◆ several snRNPs
- ◆ recognize splice site sequence
 - cut & paste

■ RNA as ribozyme

- ◆ some mRNA can splice itself
- ◆ RNA as enzyme



Ribozyme

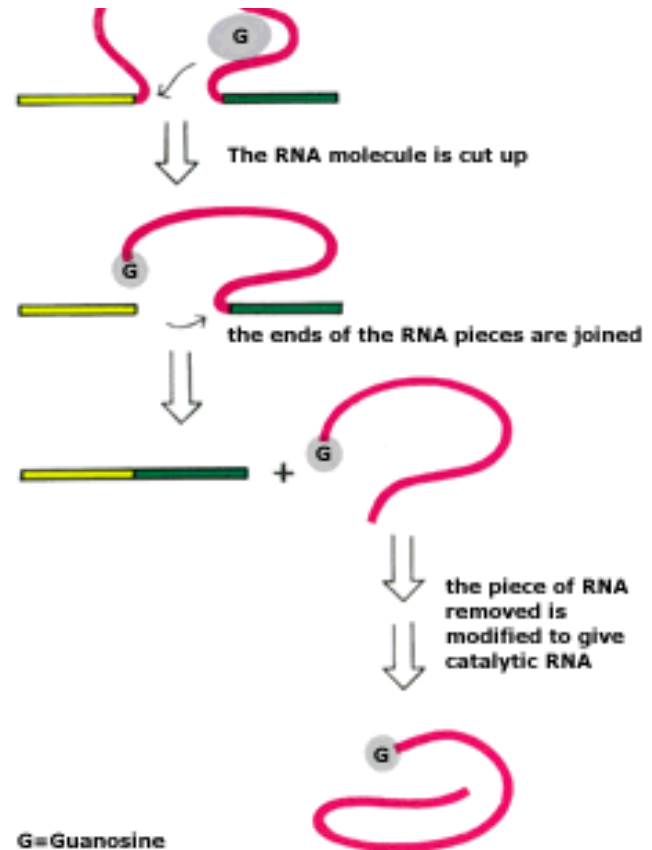
■ RNA as enzyme



Sidney Altman
Yale



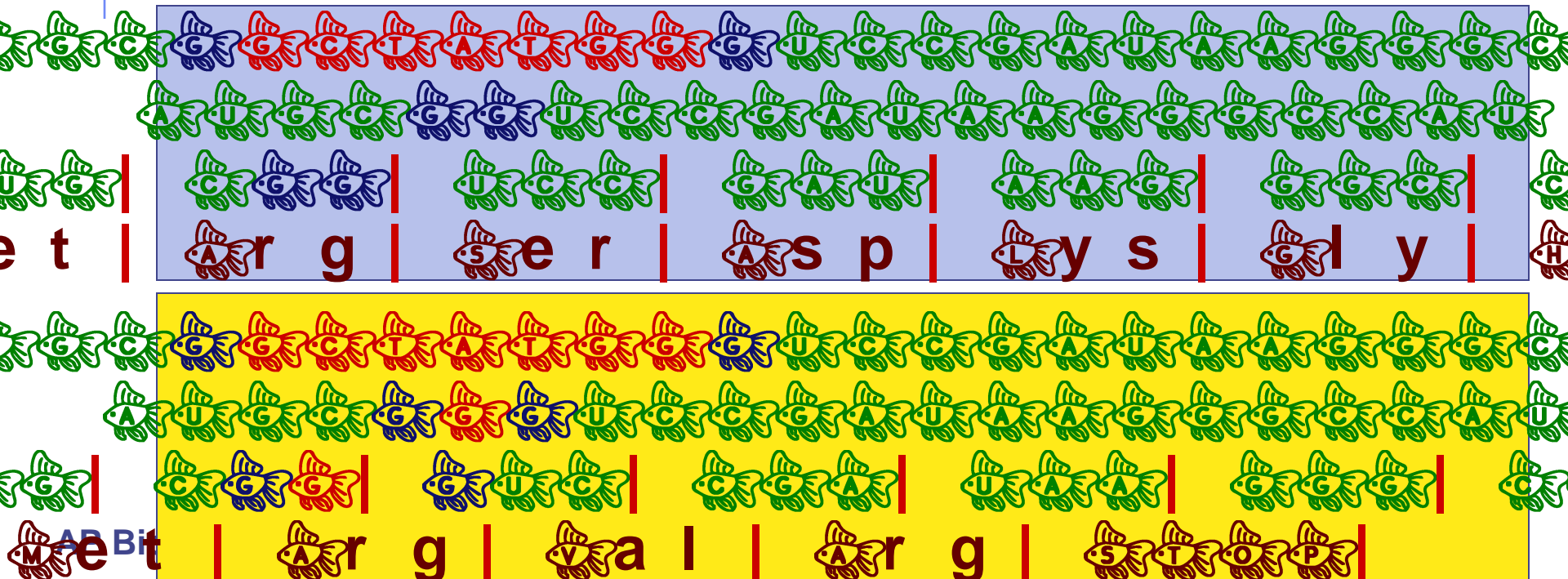
Thomas Cech
U of Colorado



Splicing details

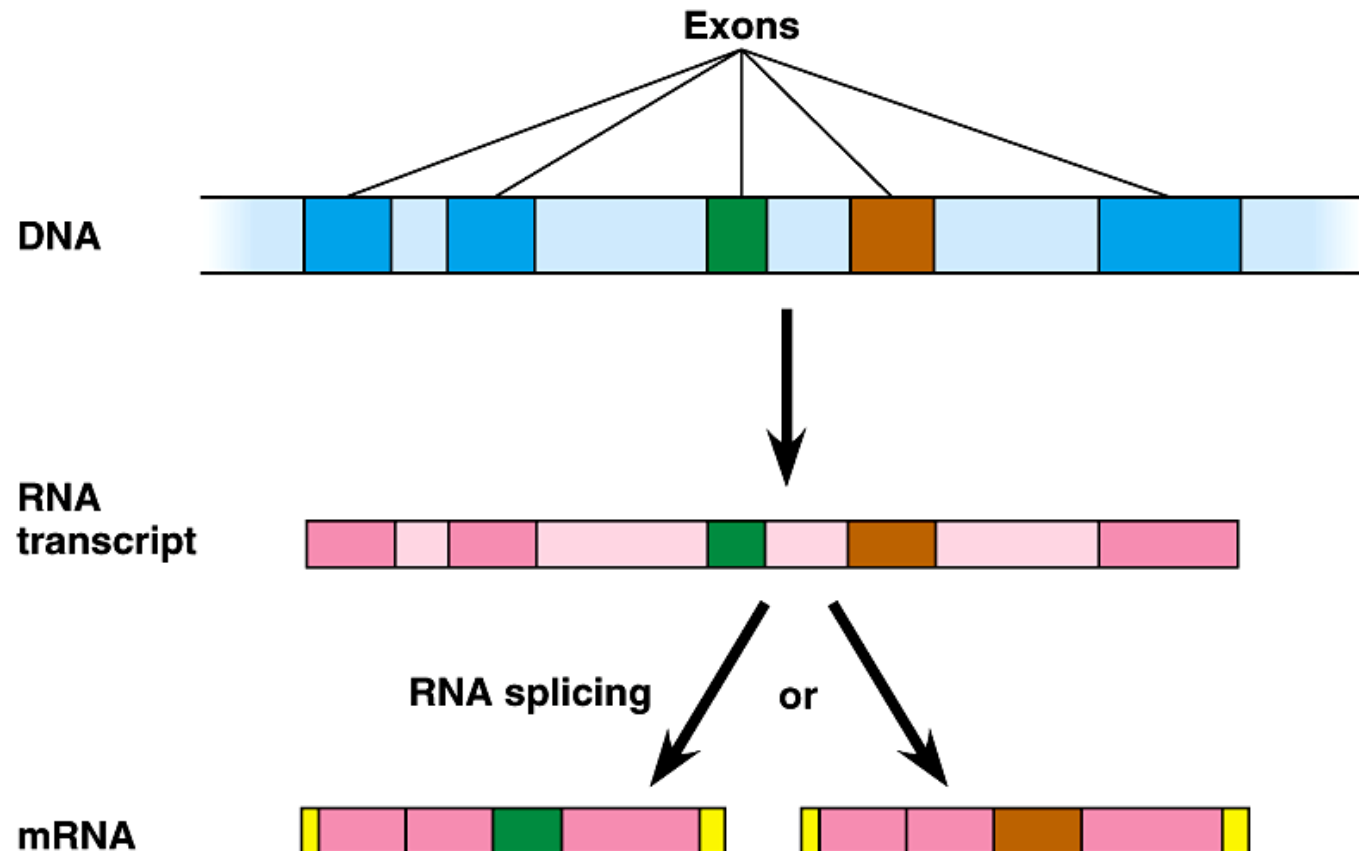
- No room for mistakes!

- ◆ editing & splicing must be exactly accurate
- ◆ a single base added or lost throws off the reading frame



Alternative splicing

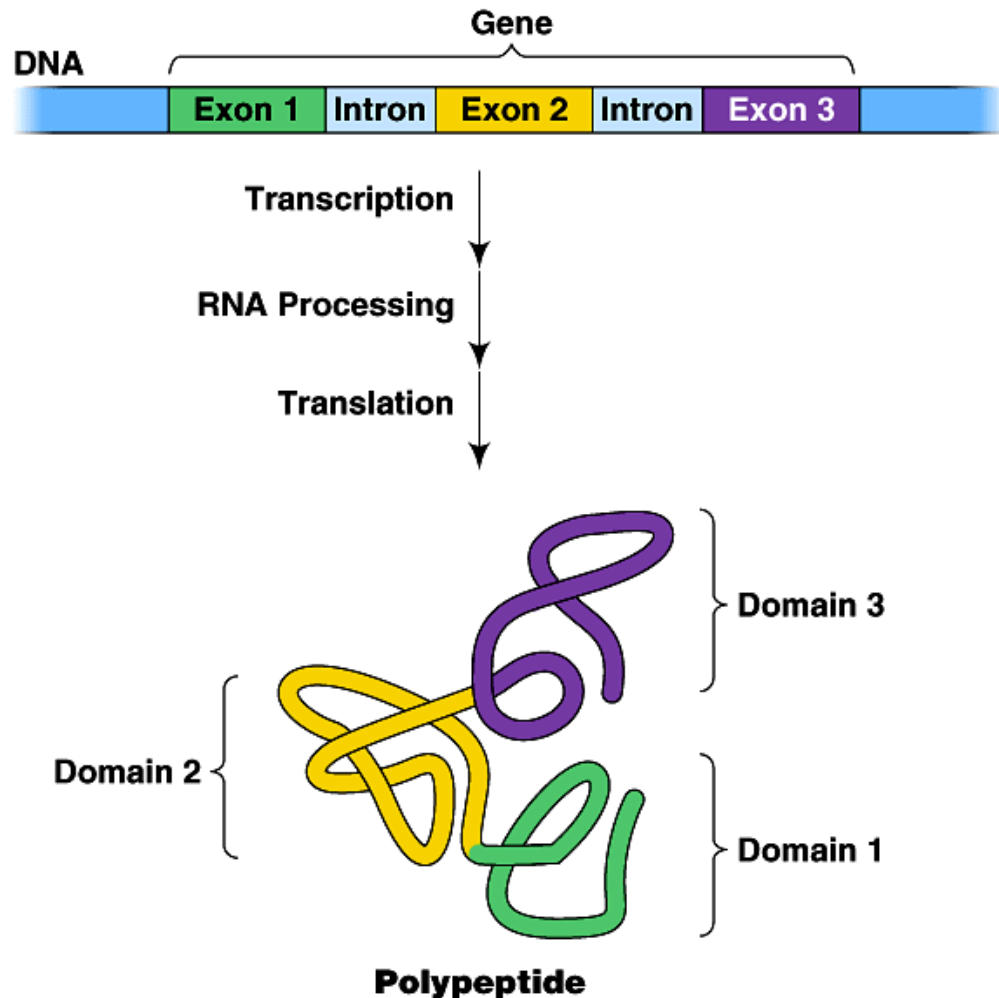
- Alternative mRNAs produced from same gene
 - ◆ when is an intron not an intron...
 - ◆ different segments treated as exons



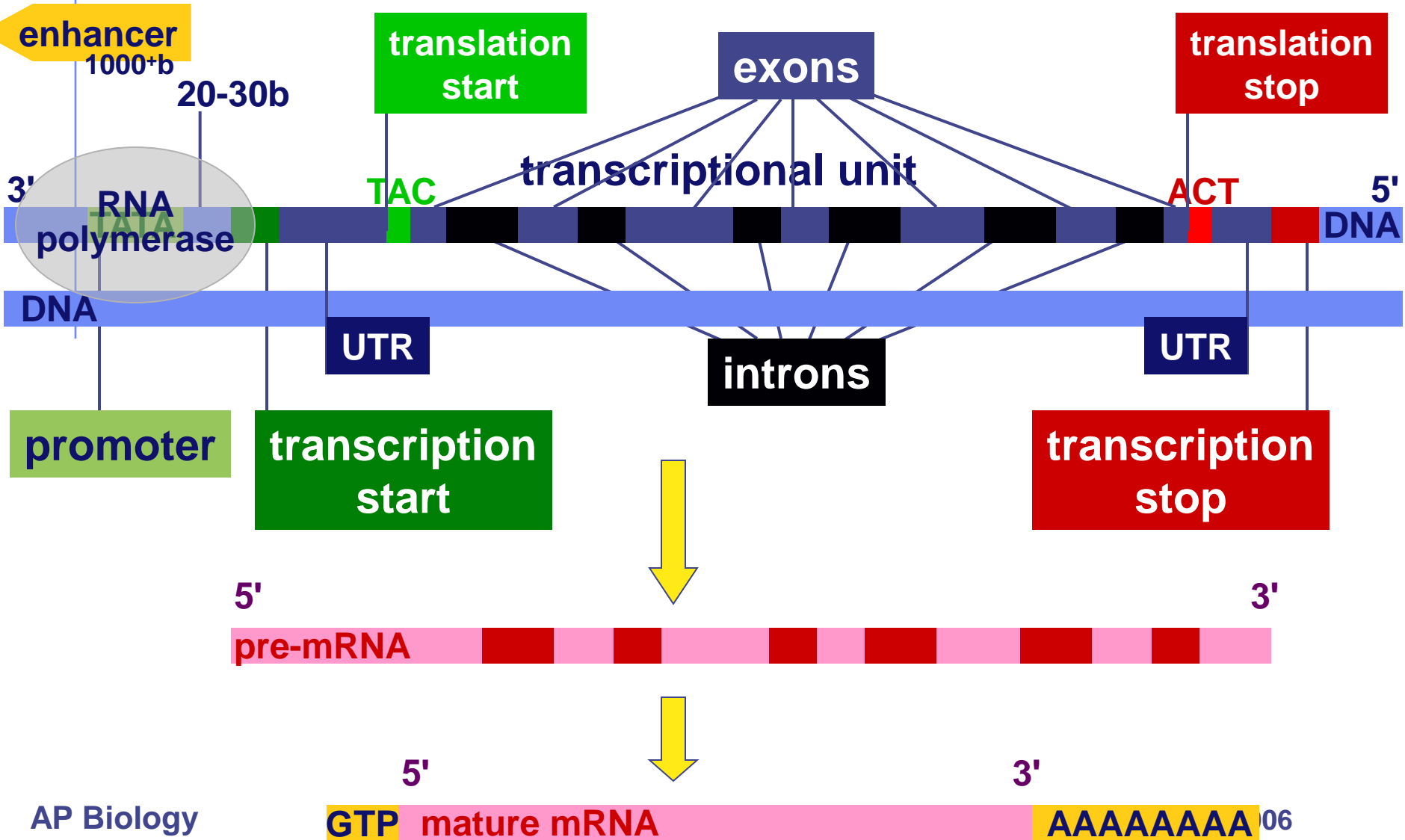
Domains

■ Modular architecture of many proteins

- ◆ separate functional & structural regions
- ◆ coded by different exons in same “gene”



The Transcriptional unit (gene?)



The Transcriptional unit

