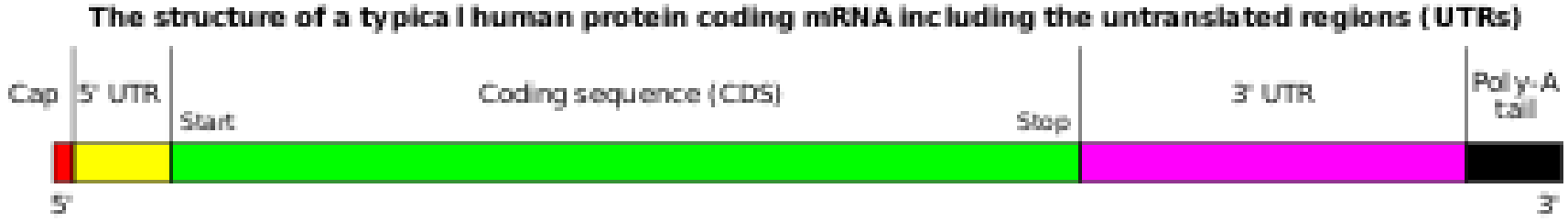
Eukaryotic mRNA Splicing

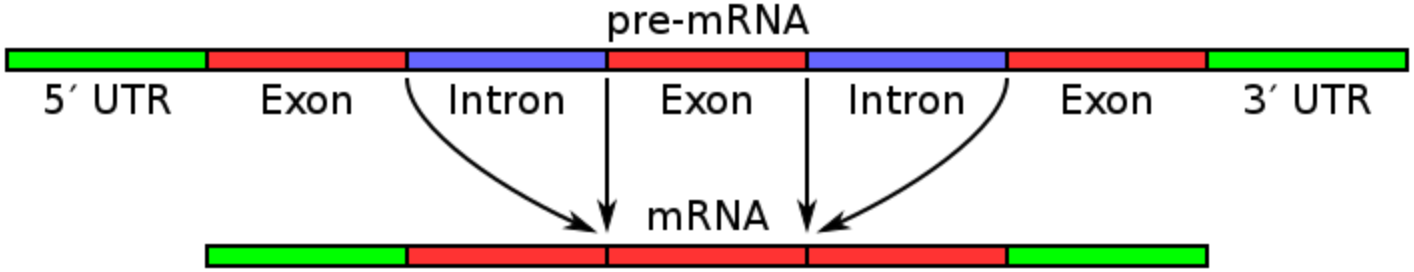
In eukaryotes messenger RNA undergoes several steps of post-transcriptional modification

- Post-transcriptional modification is the process in eukaryotic cells where primary transcript RNA is converted into mature RNA.
- The process includes three major steps: addition of a 5' cap, addition of a 3' poly-adenylation tail, and splicing.



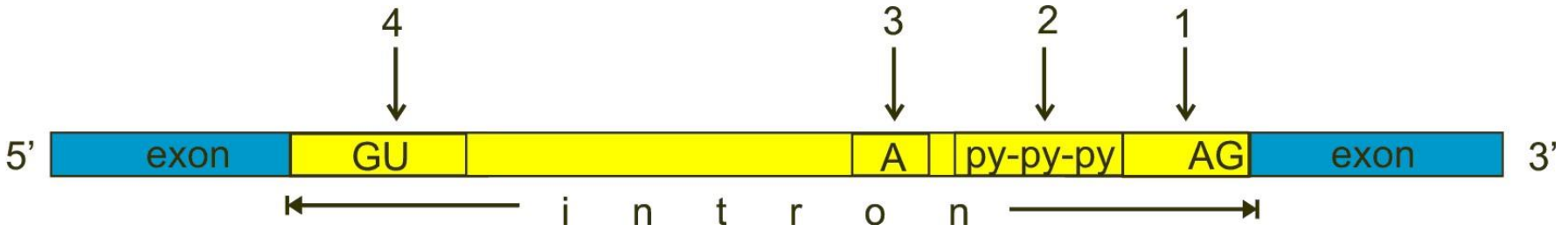
Splicing of RNA

- Eukaryotic genes are often interrupted. They contain sections of DNA called *exons*, which are expressed as mature mRNA and protein, interrupted by sections of DNA called *introns*, which are transcribed from the DNA, but absent in the mature mRNA product and therefore are not expressed as a protein.
- Introns are removed from the pre-mRNA gene transcript by a process called *RNA splicing* during maturation of the final RNA product.

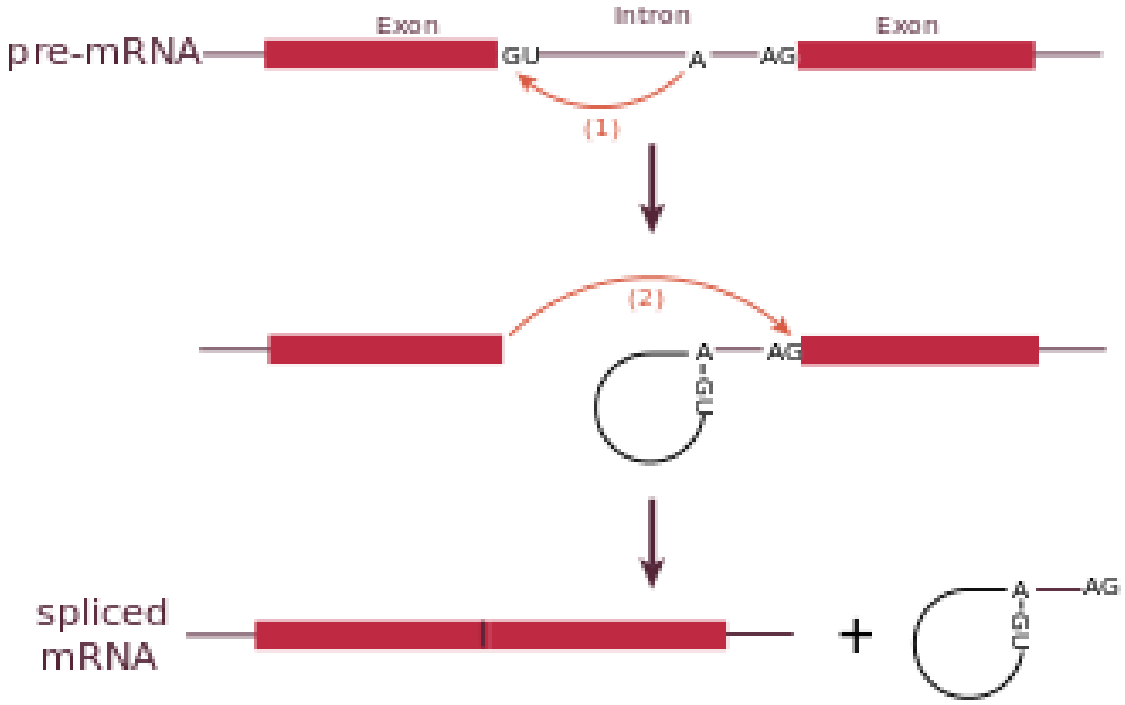


- Introns often reside within the sequence of eukaryotic protein-coding genes. Within the intron, a donor site (5' end of the intron), a branch site (near the 3' end of the intron) and an acceptor site (3' end of the intron) are required for splicing.
- The splice donor site includes an almost invariant sequence GU at the 5' end of the intron
- The splice acceptor site at the 3' end of the intron terminates the intron with an almost invariant AG sequence.

- Upstream (5'-ward) from the AG there is a region high in pyrimidines (C and U), or polypyrimidine tract
- Further upstream from the polypyrimidine tract is the branchpoint, which includes an adenine nucleotide involved in lariat formation.

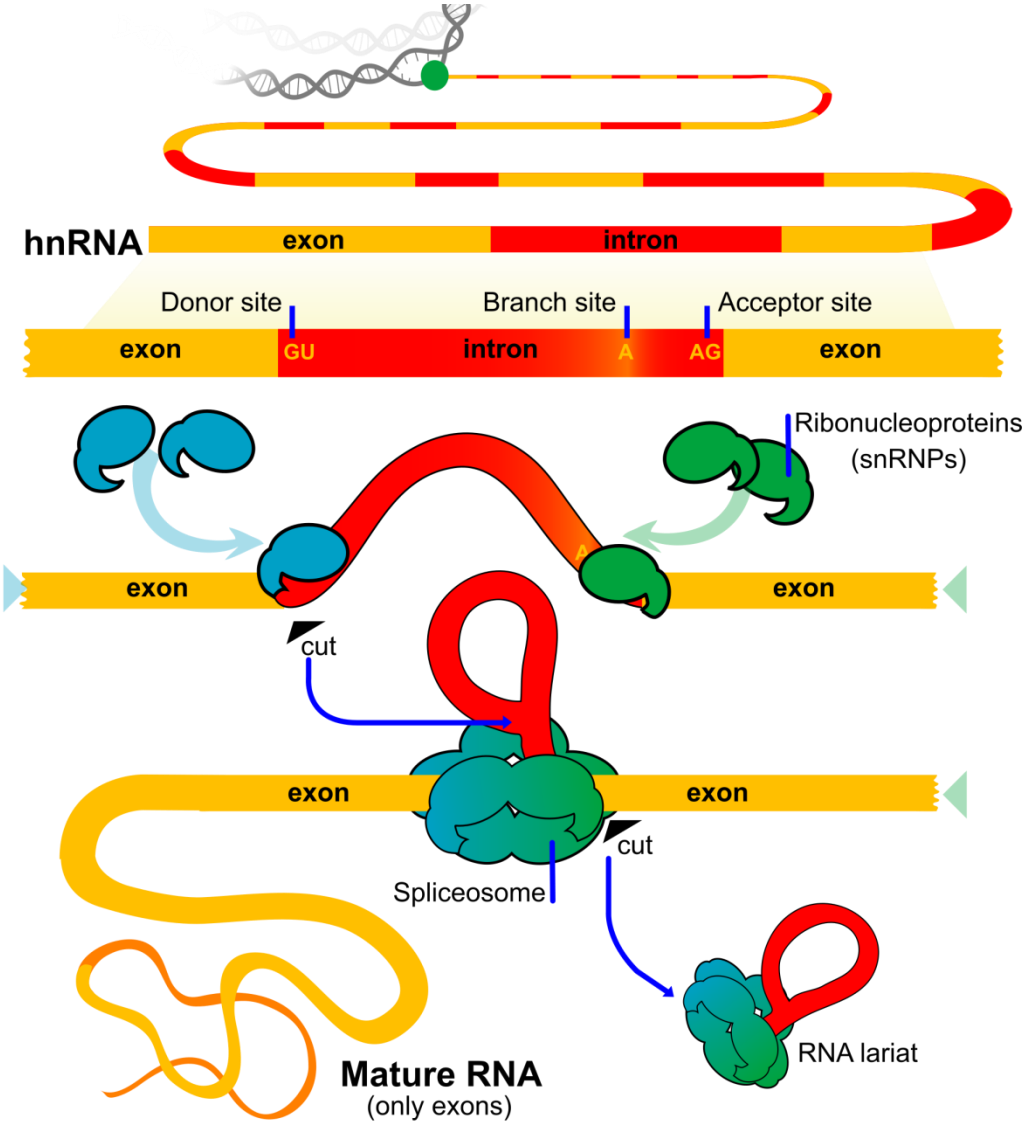


1 – acceptor site
2 - polypyrimidine tract
3 – branching site
4 – donor site


pre-mRNA
Exon
Intron
Exon
GU
A
AG
(1)
(2)
A
AG
UG
spliced
mRNA
+
A
AG
UG

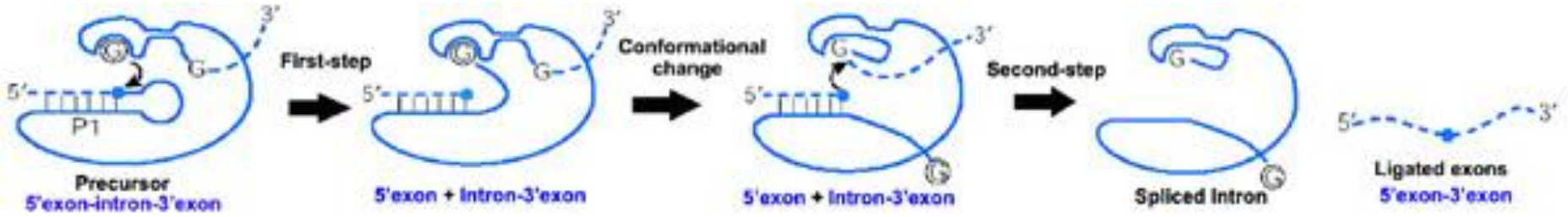
Spliceosome

- Splicing is catalyzed by the **spliceosome**, a large RNA-protein complex composed of five small nuclear ribonucleoproteins (snRNPs). Assembly and activity of the spliceosome occurs during transcription of the pre-mRNA. The RNA components of snRNPs interact with the intron and are involved in catalysis.


hnRNA
exon
intron
Donor site
Branch site
Acceptor site
exon
GU
intron
A
AG
exon
Ribonucleoproteins
(snRNPs)
exon
exon
cut
exon
exon
cut
Spliceosome
RNA lariat
Mature RNA
(only exons)

Self-splicing introns

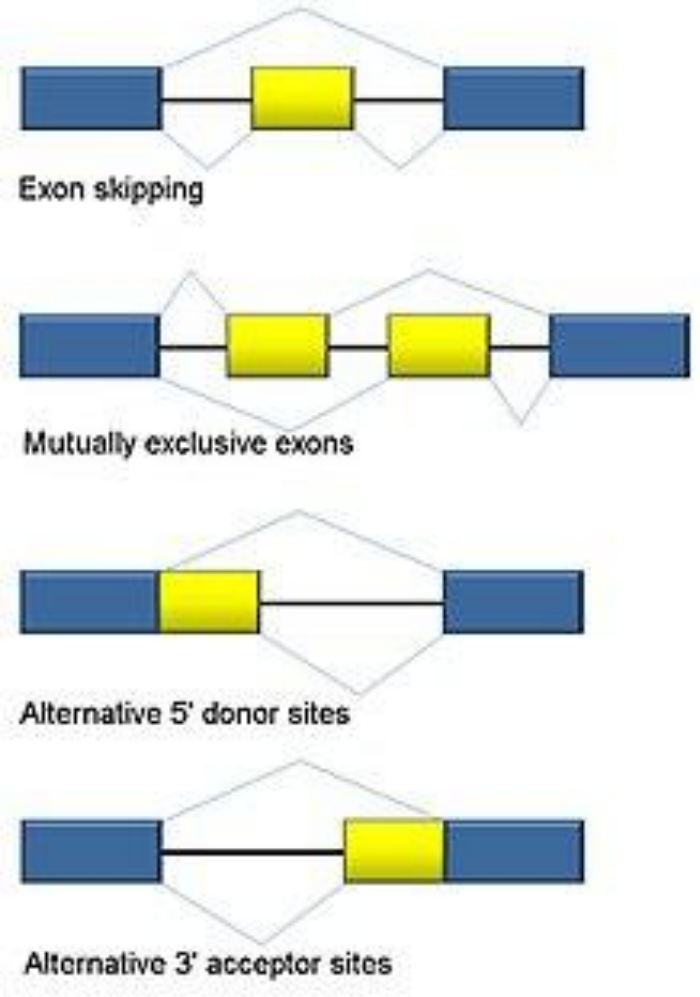
- Self-splicing occurs for rare introns that form a ***ribozyme***, performing the functions of the spliceosome by RNA alone.



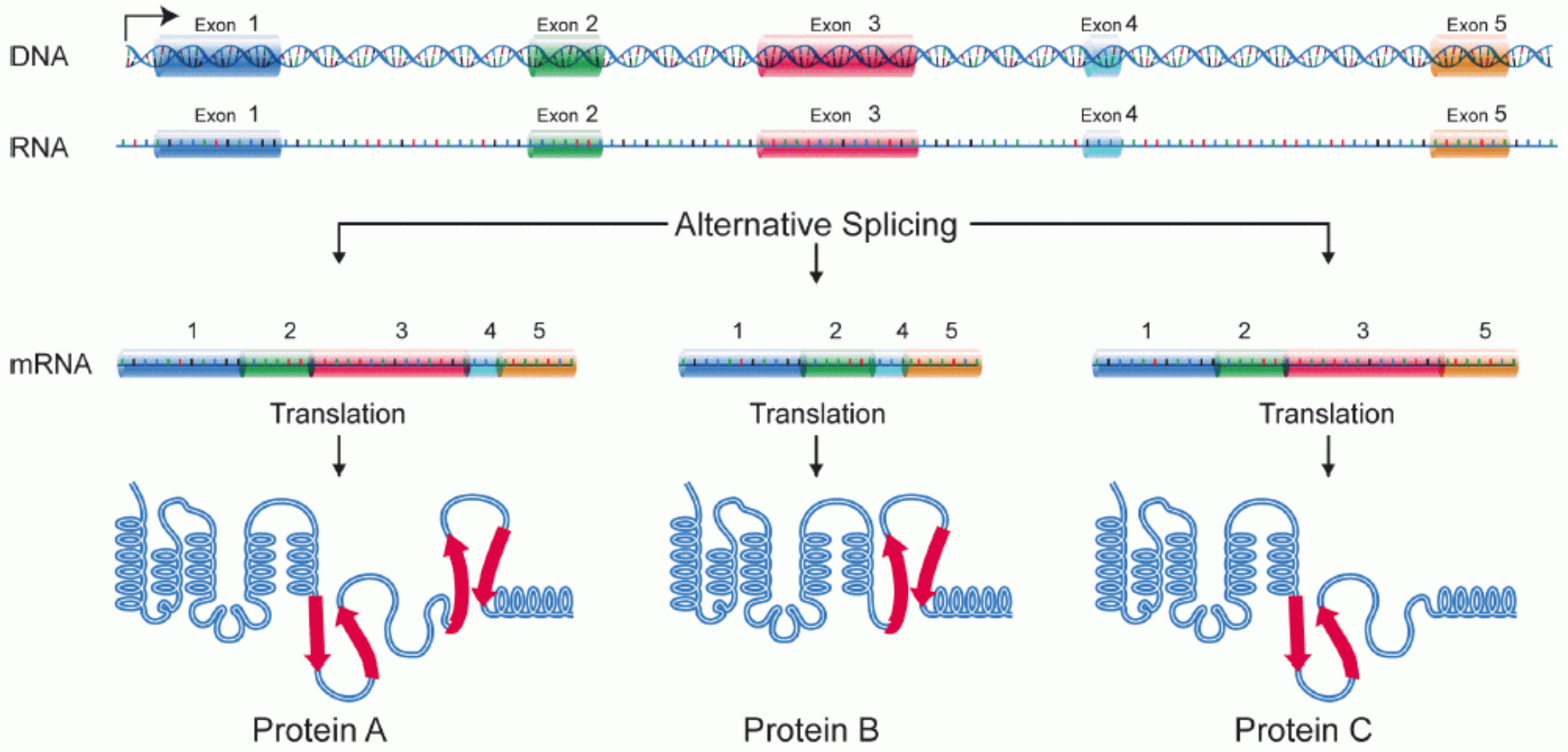
Aternative Splicing

- Sequences of donor and acceptor sites are very common. There are many factors defining which of these sequences will actually serve as donor or acceptor. In many situations this choice is not 100% certain and splicing can occur in a different pattern. This phenomenon is called *alternative splicing*.
- In this process, particular exons of a gene may be included within or excluded from the final, processed messenger RNA (mRNA) produced from that gene

Types of alternative splicing



- Alternative splicing results in a single gene coding for multiple proteins



- Alternative splicing allows a eukaryotic genome to direct the synthesis of many more proteins than would be expected from the number of its protein-coding genes. Thus it greatly increases the biodiversity of proteins that can be encoded by the genome
- in humans, ~95% of multi-exonic genes are alternatively spliced.
- Alternative splicing is regulated by complex mechanisms.