

Bioinformatics II:

RNA structure and function

(structure prediction)

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What types of RNA Structure & Function

- The main cause of the divergence of species and the evolution is the RNA processes e.g splicing etc.
- So it important to study such process on RNA and the structure and the function of the RNA
- RNA structure
 - Levels of organization
 - Energetics
- RNA types & functions
 1. Genomic information storage/transfer
 2. Structural
 3. Catalytic
 4. Regulatory

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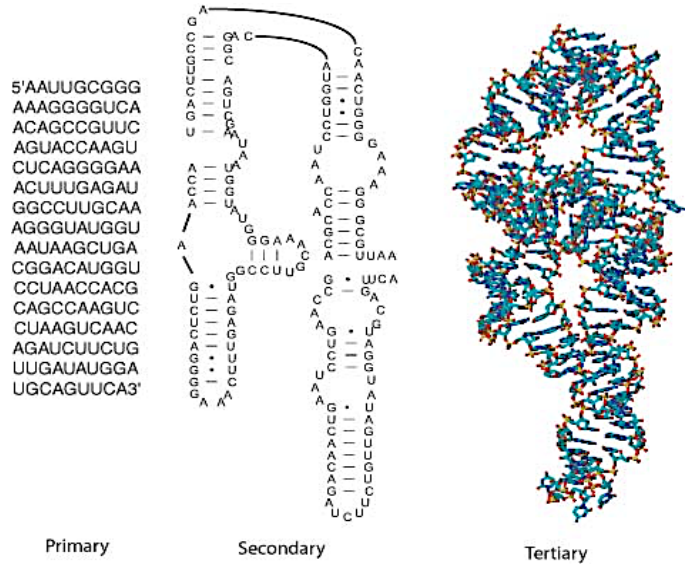
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What are the types of bonds in the RNA structure? Covalent & non-covalent bonds in RNA

1-Primary:
Covalent bonds

2-Secondary/Tertiary
Non-covalent bonds

- H-bonds
(base-pairing)
- Base stacking



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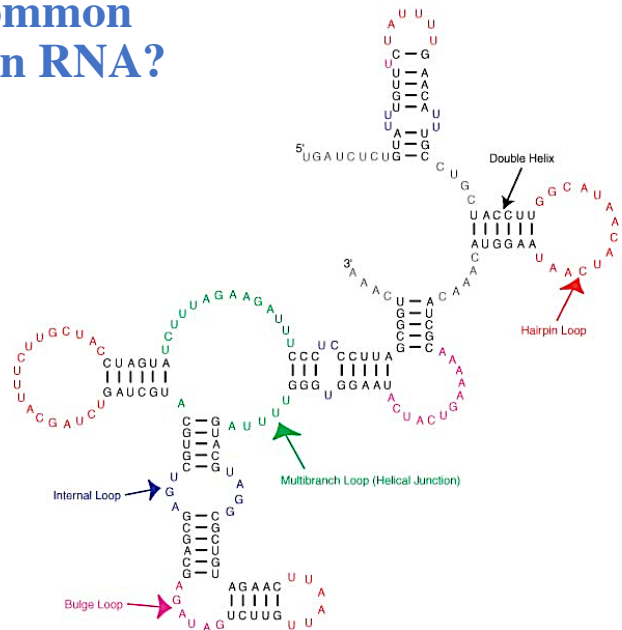
What are the Common structural motifs in RNA?

Helices

Loops

- Hairpin
- Internal
- Bulge
- Multibranch

Pseudo-knots



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What are the RNA functions?

Storage/transfer of genetic information

- **Genomes**
 - many viruses have RNA genomes
- **Transfer of genetic information**
 - mRNA = "coding RNA" - encodes proteins

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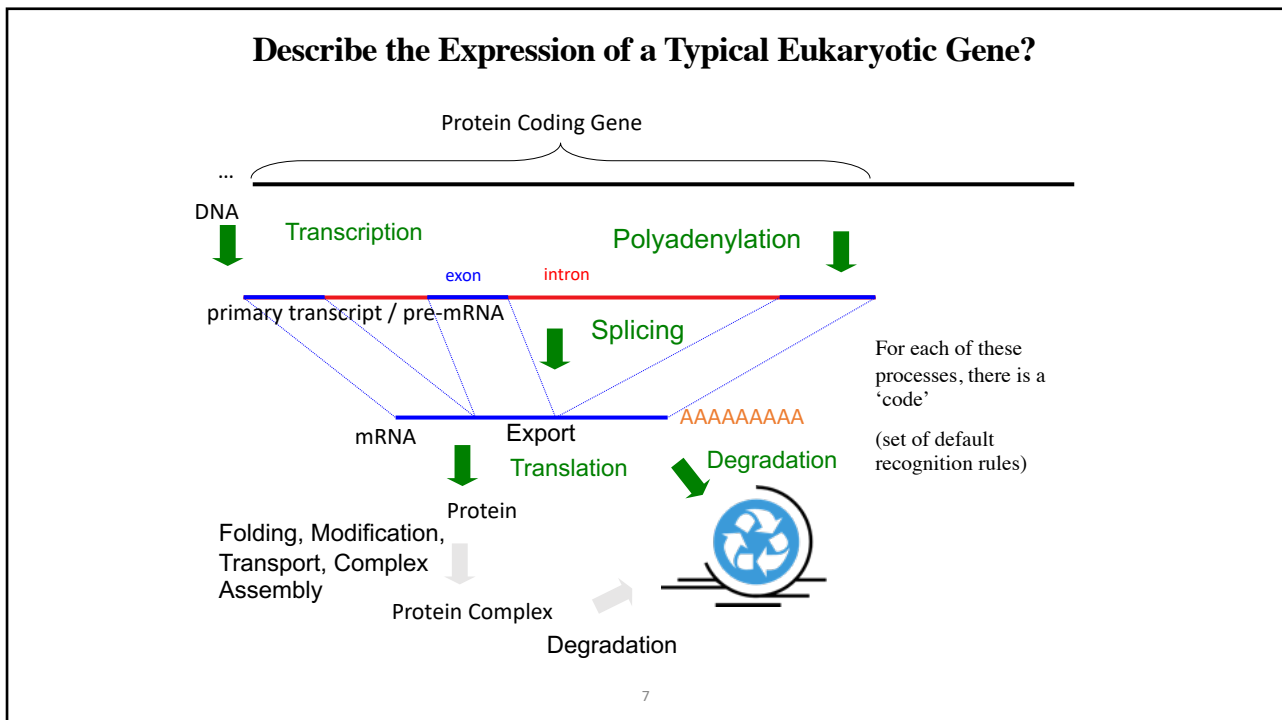
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RNA types & functions

Types of RNAs	Primary Function(s)
mRNA - messenger	translation (protein synthesis) regulatory
rRNA - ribosomal	translation (protein synthesis) < catalytic >
t-RNA - transfer	translation (protein synthesis)
hnRNA - heterogeneous nuclear	precursors & intermediates of mature mRNAs & other RNAs
scRNA - small cytoplasmic	signal recognition particle (SRP) tRNA processing < catalytic >
snRNA - small nuclear snoRNA - small nucleolar	mRNA processing, poly A addition < catalytic > rRNA processing/maturation/methylation
regulatory RNAs (siRNA, miRNA, etc.)	regulation of transcription and translation, other??

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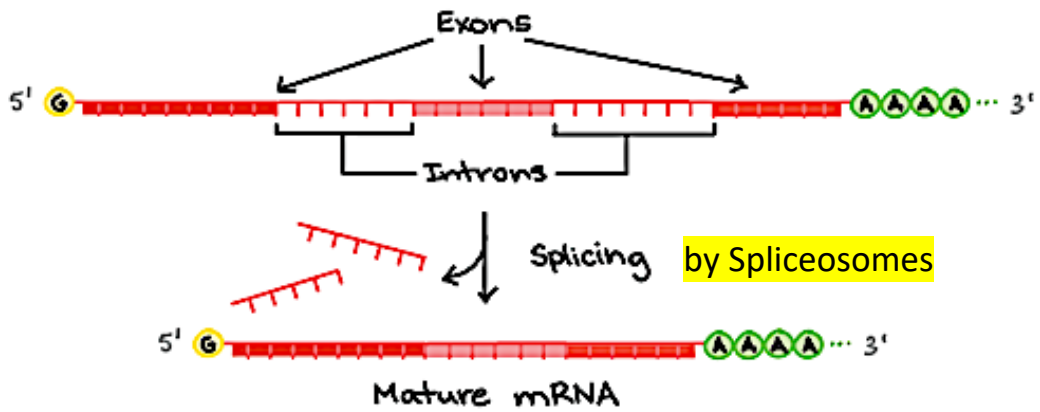
Describe the process of RNA splicing?

1. RNA splicing occur only in eukaryotic cells.(not prokaryotic) This is because the genes in eukaryotic DNA are made up of exons and introns.(prokaryotes do not have introns).
2. Exons are coding regions and introns are non coding regions.
3. During transcription all the exons and introns are transcribed to make a primary RNA.
4. This primary RNA undergoes splicing, by **splicesosomes**.
5. That means the introns(non coding regions) are removed and the exons are joined together. So that m-RNA formed after splicing does not have introns. It only has exons.

Note:-> 50% of human genes undergo alternative splicing.

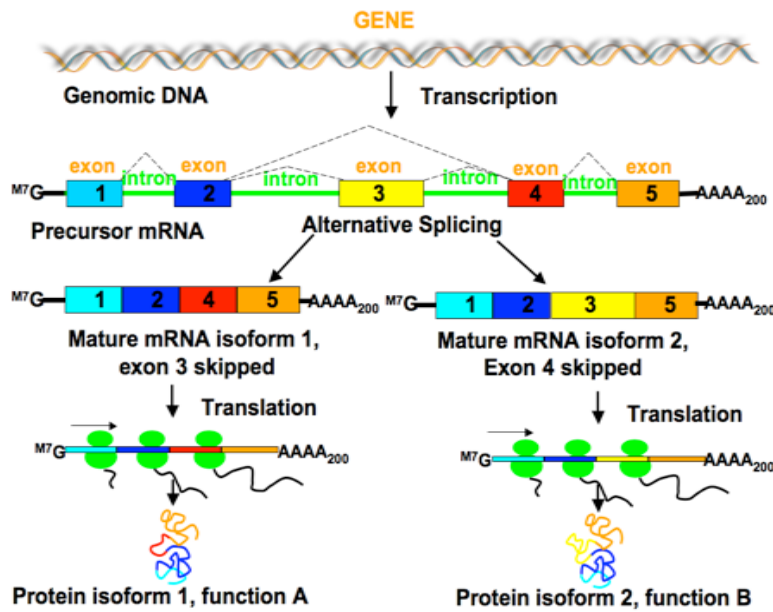
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Draw the process of RNA splicing?



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An example of a gene gives 2 isoforms (2 different proteins)



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What are the RNA structure prediction strategies?

Secondary structure prediction

- 1) Energy minimization. (thermodynamics)
- 2) Comparative sequence analysis (co-variation).
- 3) Combined experimental & computational

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Secondary structure prediction strategies

1) Energy minimization (thermodynamics)

- **Algorithm:**
e.g Dynamic programming to find high probability pairs
(also, some Genetic algorithms)
- **Software:** such as
RNA structure - [Mathews](#)



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What are the Experimental RNA structure determination?

1. X-ray crystallography
2. NMR spectroscopy
3. Enzymatic/chemical mapping

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1) Energy minimization method

What are the assumptions?

Native tertiary structure or "fold" of an RNA molecule is (one of) its "lowest" free energy configuration(s)

Gibbs free energy = ΔG in kcal/mol at 37°C

= equilibrium stability of structure

lower values (negative) are more favorable

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What is Gibbs Free energy (G)?

Gibbs Free energy (G) is formally defined in terms of state functions **enthalpy** & **entropy**, & state variable, **temperature**

$$G = H - TS$$

$$\Delta G = \Delta H - T\Delta S \text{ (for constant temp)}$$

Enthalpy (H) = amount of heat absorbed by a system at constant pressure

Entropy (S) = measure of the amount of disorder or randomness in a system

Note = this is not the same as "entropy" in information theory, but is related

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Free energy minimization

What are the rules?



$$\Delta G = -1.2 \text{ kcal/mole}$$

What gives here?

Why 1.2 vs 1.6?



$$\Delta G = -1.6 \text{ kcal/mole}$$

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Energy minimization calculations: *Base-stacking is critical*

AA UU	-1.2	CG GC	-3.0
AU or UA UA AU	-1.6	GC CG	-4.3
AG, AC, CA, GA UC, UG, GU, CU	-2.1	GU UG	-0.3
CC GG	-4.8	XG, GX YU, UY	C

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Nearest-neighbor parameters

- Most methods for free energy minimization
- use nearest-neighbor parameters (derived from experiment) for predicting stability of an RNA secondary structure (in terms of ΔG at 37°C)
- most available software packages use the same set of parameters: by [Mathews, Sabina, Zuker & Turner, 1999](#)

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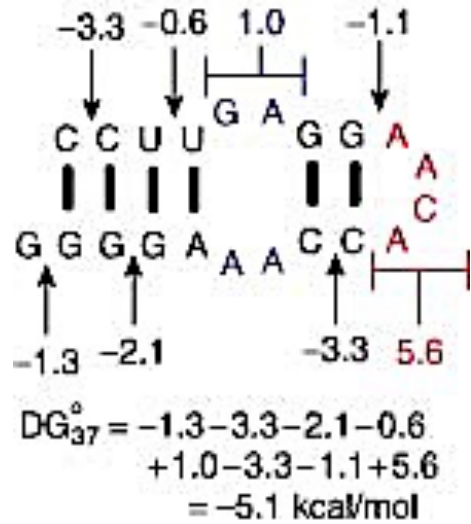
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Energy minimization - calculations: a good method to predict RNA structure

Total free energy of a specific conformation for a specific RNA molecule
= sum of incremental energy terms for:

- helical stacking
 (sequence dependent)
- loop initiation
- unpaired stacking

(favorable "increments" are < 0)



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