

Chapter 26.1: RNA metabolism Part I

RNA structure:

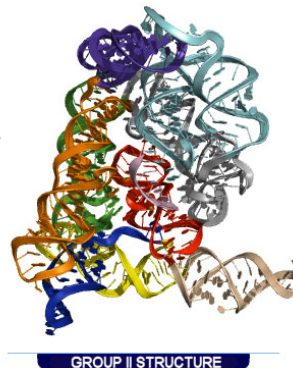
- Structural elements and complexity of RNA structure
- How are RNA structures determined?
 - 1) X-ray/NMR
 - 2) Phylogeny
 - 3) Structure probing
 - 4) Computational approaches

RNA structure

The RNA folding problem... Why?

The ultimate goal- predict structure from sequence

GUCUGAAUC.....



Toor et al, Science 2008

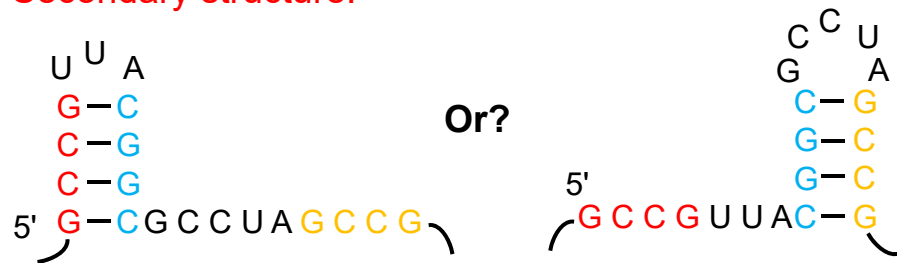
RNA structure

Examples of:

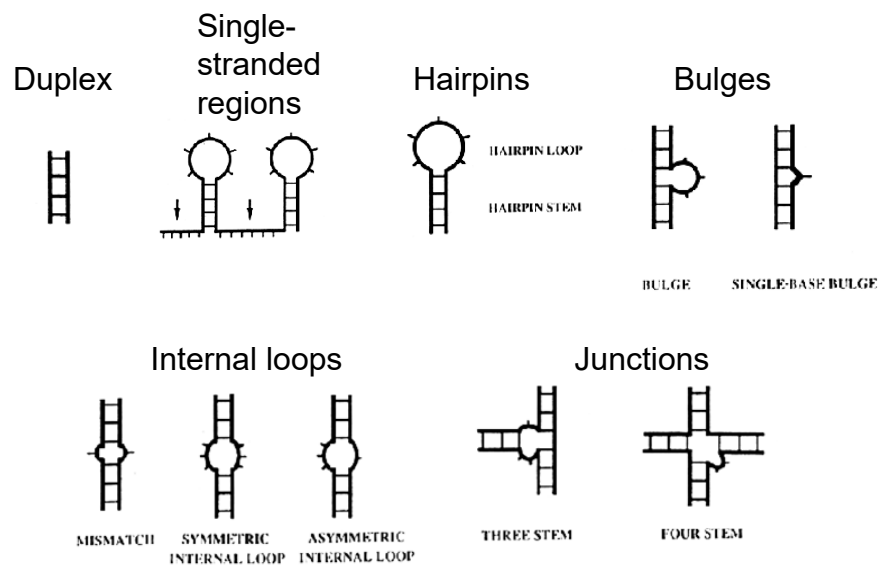
Primary sequence:

---G C C G U U A C G G C G C C U A G C C G---

Secondary structure:

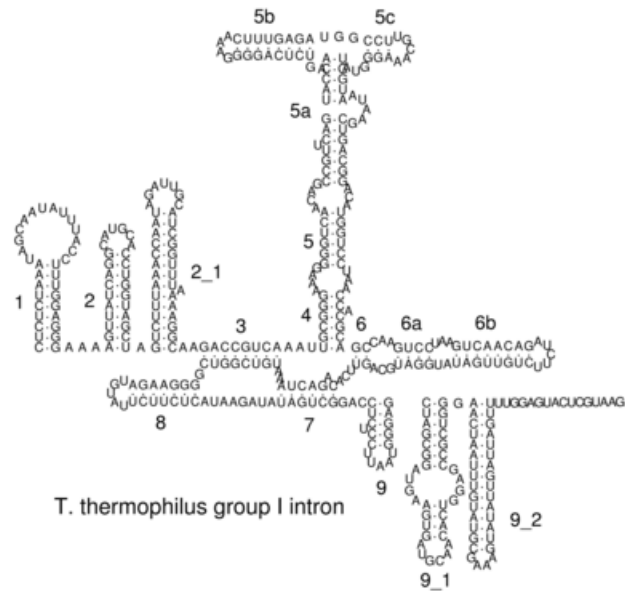


Secondary structure terminology



Tinoco et al, The RNA World (CSHL Press)

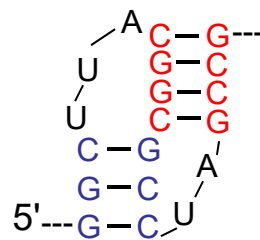
Secondary structural elements in biological RNAs



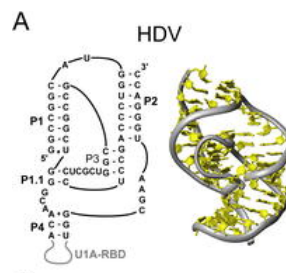
RNA structure

Tertiary structure (or tertiary interaction):

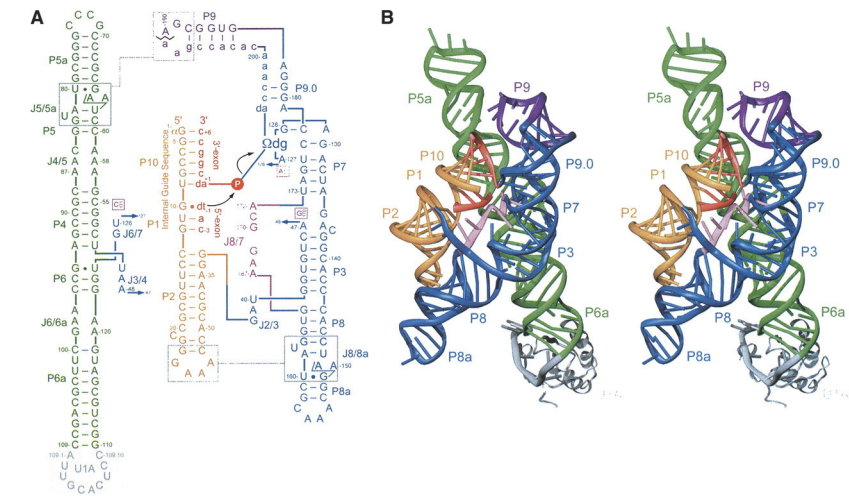
---G G C U U A C G G C G C C U A G C C G---



"pseudoknot"



Staple DW, Butcher SE (2005) Pseudoknots: RNA Structures with Diverse Functions. PLoS Biol 3(6): e213



ADAMS P L et al. RNA 2004;10:1867-1887

RNA

Copyright 2004 by RNA Society

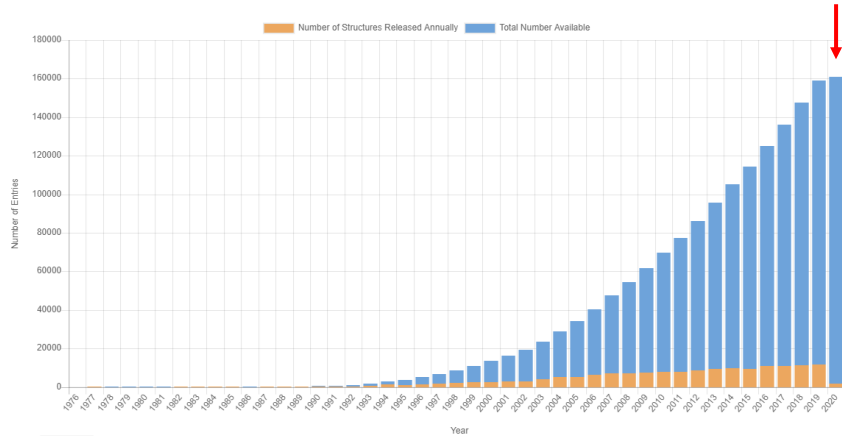
How are RNA structures determined?

1. Xray/NMR structures
2. Phylogenetic comparison
3. Structure probing
4. Computational approaches

How are RNA structures determined?

1. X-ray/NMR structures:
growing but still a way to go

2020: 160,796 structures
(3448 Nucleic acid,
8275 Protein/NA complex)



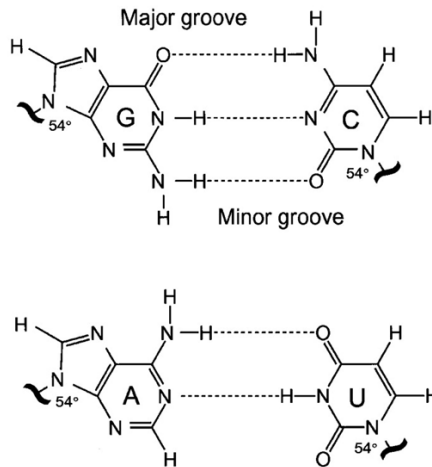
www.pdb.org

How are RNA structures determined?

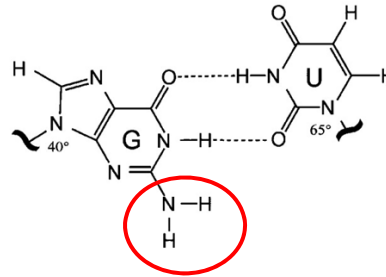
2. Phylogenetic comparison

- Comparison of sequences from different organisms
- RNA of identical function would have identical (or very similar) structure
- Look for compensatory changes in base pairing → **covariation**
- Need strong conservation- but not 100%

Alternative base pairs in RNA



G-U Wobble base pair:
Ubiquitous in structures

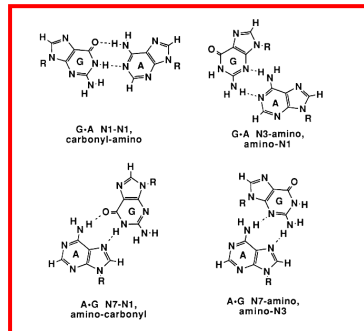


similar geometry
N2 amino tilted into minor groove
hard to do compensatory change

Varani and McClain, EMBO Rep, 2000

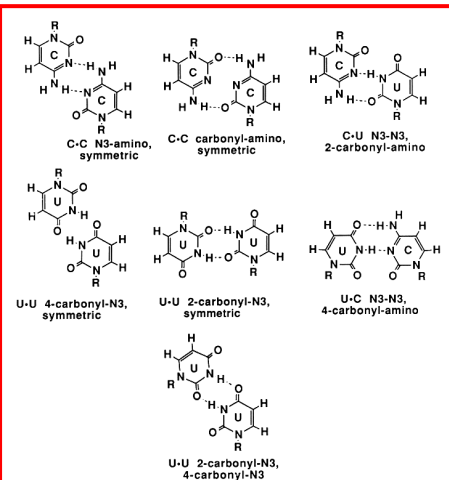
Non-canonical base pairs in RNA

purine-purine



Purine-pyrimidine: 10
Homopurine-purine: 7

pyrimidine-pyrimidine

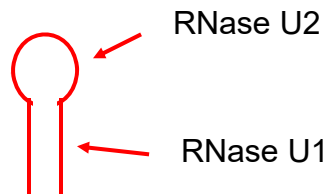


Even more complicated...

How are RNA structures determined?

3. Structure probing

- Take advantage of alternative nuclease specificities



- Or use chemicals that only modify nucleotides not involved in a base pair (DMS, kethoxal)

How are RNA structures determined?

4. Computational approaches

- Determine lowest free energy structure
- Most models focus on 2° structure
- Nearest-neighbor energy prediction (Turner rules)

For any one base pair, the energy it contributes comes from itself and its nearest neighbors...
Measure ΔG (mostly thermal denaturation)