RNA structure (Uracil replaces thymine)

RNA does not adopt the classic B-DNA helix conformation when it forms a self-complementary double helix.

Reason: RNA has ribose sugar ring, with a hydroxyl group (OH). If RNA in B-form conformation there would be unfavorable steric contact between the hydroxyl group, base, and phosphate backbone.
At least 50% double stranded in solution of any random RNA molecule incl.. mRNA (~55-60% in tRNA)

Most bases are stacked

short-range pairings > hairpins, loops, bulges, junctions

Compacted globular fold

long-range pairing > intramolecular structural roles stabilizing 3D folding
Secondary structural elements

- single nucleotide bulge
- three nucleotide bulge
- hairpin loop
- mismatch pair
- symmetric internal loop
- asymmetric internal loop
RNA tertiary structure
Mainly based on transfer RNA structures

Yeast phenylalanine transfer RNA (tRNA$^{\text{Phe}}$)
-Findings universal.

L -shape
(solution -elongation experiments)

Two segments of double Helix
(A-DNA like)

10 base pairs in length
Non helical regions participate
in unusual hydrogen bonding interactio
I. Primary structure: sequence

II. Secondary structure: Watson Crick base pairs

III. Tertiary structure (tertiary interactions):
- ‘unusual‘ base pairs
- base triples
- loop-loop interactions
- cross strand stacking

> increase the stability of tertiary structure
> enable interactions with proteins and/or nucleic acids
THREE commonly found RNA-binding domains

Ribonucleoprotein (RNP) domain

Double stranded RNA binding domain (dsRSB)

K homology (KH) domain

ALL shown to have $\alpha/\beta$ domain similar to ribosomal proteins

Specific RNA-protein interactions play crucial roles in gene regulation through transcription control, RNA processing, transport and translational control.
Ribonucleoprotein (RNP) domain

Very common

Contains two short conserved sequences within a weakly conserved motif

70-90 aa
RNP1 (RNP octamer)
RNP2 (RNP hexamer)

4 anti-parallel β stands
flanked by 2 α helices
β–α–β–α–β topology
RNP1 and RNP2 located on central strands
(crucial role in RNA binding)
Aromatic aa exposed on β-sheet sheet provides a large surface area
Double stranded RNA binding domain

Short motif 65 aa

α–β–β–α topology
3 anti-parallel β stands

flanked by 2 α helices

Conserved positive charged residues
hydrogen donor/acceptors in loops 2 and 4

dsRBD and N-terminal domain of
ribosomal protein s5 share sequence and structure similarities

Fold specific
The KH domain

Short conserved sequence found in heterogeneous nuclear RNP (hnRNP) K, associated with mRNA precursors.

Domain $\beta-\alpha-\alpha-\beta-\beta-\alpha$ topology

3 anti-parallel $\beta$ stands and 3 $\alpha$ helices
Aminoacyl-tRNA synthetases complexed with cognate tRNAs

Transfer RNA (tRNA) is the 'adaptor' molecule that enables the Genetic Code contained in the nucleotide sequence of a messenger RNA (mRNA) molecule to be translated into the amino acid sequence of a polypeptide chain. The key to this process lies in the specific recognition of the correct tRNA molecule by an aminoacyl-tRNA synthetase enzyme which attaches the correct amino acid for the tRNA to the acceptor stem at the 3' end of the molecule.
Aminoacyl-tRNA synthetases from all organisms belong to one of two classes depending on the amino acid they are responsible for. Class I enzymes are generally (though not always) monomeric, and attach the carboxyl of their target amino acid to the 2' OH of adenosine 76 in the tRNA molecule. Class II enzymes are generally dimeric or tetrameric, and attach their amino acid to the 3' OH of their tRNA, except for phenylalaninyl-tRNA synthetase which uses the 2' OH.
Two distinct domains (connected by hinge module)
20% of tRNA surface is buried (2500 Å)
When function as dimers each bind one tRNA

Structure of Glutaminyll-tRNA synthetase

Acceptor stem
Hinge region
Anticodon recognition
C-terminal domain (241-557)
6 anti-parallel β-strands enclosed by loops and α-helices
Interact with acceptor stem of tRNA and perform catalysis

The structure also contains a classic 'Rossman Fold'
nucleotide binding domain
Hinge connection (207-240)
Consists of 4 short α-helices
Interact with ribose and phosphate groups
N-terminal domain (1-206)

Recognition of anticodon (Specific interaction)
Consist of 5 stranded β-barrel
Lies on the side of the major groove
Strands S1, S4, S5, S3, S2, (S1) anti-parallel except between S5 and S3
α-helix between S3 and S4
Protein-RNA and RNA-RNA interactions
Glutaminy1-tRNA synthetase

D loop
Acceptor Stem
TΨC loop
Anticodon Stem

Interactions

○ Specific
☐ conformational
— Non-specific
**MS2 bacteriophage**

**ssRNA genome**

5 anti-parallel β-strands flanked with α-helices
MS2 capsid protein binds to sequence specific RNA stem-loop structure (controls assembly of virus)

RNA bases A4, C5, U6, and A10
(A10 shown to ‘flip out’ from unbound state)
RNA-binding proteins

RNA seems to bind to surface of β-sheet

RNA bases in ss loop regions seem to be able to conformationally move to base stack with adjacent bases or aromatic side chains

Not possible in dsDNA unless helix distorted (bent) as seen in TATA box-binding protein

ssDNA proteins may function the same way as RNA binding proteins