RNA structure

The Structure of tRNA.

The role of tRNA is two fold, bind to and accept the correct amino acid from the appropriate tRNA synthetase and recognize and bind the ribosome-mRNA complex to deliver the amino acid to the growing polypeptide chain. Because of its central role in gene expression (and its relative abundance), tRNA is one of the best understood, most thoroughly studied biological macromolecules.

![Figure 44](image-url)

Figure 44. Chemical structures of "new" or "minor" nucleotides and bases found in tRNAs. From [87].

![Figure 45](image-url)

Figure 45

Secondary structure

Based on base-base complementarity, the secondary structure of tRNA can be drawn as the familiar cloverleaf structure of 4 stems, each consisting of four to seven Watson-Crick type base pairs. Five regions of the tRNA are not base paired, the CCA acceptor stem, the D-loop (named for the presence of dihydrouridine), the anti-codon loop which interacts with the mRNA, the "extra arm" and the TYC loop (named for the presence of the pseudouridine base. (FIGURE 45).
The three dimensional structure of the tRNA molecule is not a cloverleaf, the molecule instead folds back on itself, forming two segments of double helix and most of the upaired bases in the T and D loops form base pairs with each other (FIGURE 46). One of the two segments of double helix are formed by the stacking of bp region of the T and acceptor stems, the other by the stacking of the D-arm base paired region on the base paired part of the anticodon loop. This tertiary structure of the molecule is L-shaped and is held together by base pairs between the bases in the upaired regions of the stems and by unique stacking interactions (Figure 47).

Base modifications and base pairings (see Figure 48)

m$^1$A$_{58}$-T$_{54}$ This base pair is a reversed Hoogstein type, with the chains from each base pair running in an antiparallel direction. The m$^1$A is unable to form a normal Watson-Crick base pair because the N1, normally a W-C acceptor is methylated, rendering it refractory to H-bonding.

m$^2$G$_{26}$A$_{44}$ is a purine-purine base pair who normally pair in a wobble fashion. However, this configuration is altered due to the presence of the bulky methyl groups on G N2. This pushes this base pair further apart, more than even in the usual wobble situation. This base pair is at the junction of the anticodon and D-stems, and is stacked with both and is thus responsible for the 26° kink between these two helices.
A number of triplet interactions are formed which also help hold the structure together (Figure 48).

Primary sequence conservatism gives all tRNAs the same structure. An examination of the places in tRNA where the base are conserved turns out to be in the non-base paired loops. As we have just seen, these are the bases which are involved in stabilizing the tertiary structure of the tRNA molecules (Figure 47 & 48).

Base stacking

The strength and utility of base stacking to hold together the structure of a polynucleotide is illustrated by tRNA. Only 42 of the 76 bases in the yeast tRNA are involved in A-RNA double helical structures. Yet, however, 71 of the 76 are involved in stacking interactions. Of the five that are not, one is the terminal A in the acceptor stem and the two others are the modified dihydrouridines in the D-stem, which are non-planar, non-aromatic and hence oppose stacking. The base stacking in the double helical regions resembles that we have seen in A-DNA. A very interesting stacking interaction is seen where the individual bases of one strand are tucked between the bases of an adjacent strand. These interactions occur where three strands meet; inside the L corner and in the T-loop region.

FIGURE 49 shows the case of A\textsubscript{9} intercalated between the bases G\textsubscript{45} and m\textsuperscript{2}G\textsubscript{46}. Because the base inserts between the two others, and the base has finite van der Waals distance (this is a stacking interaction after all), the receiving bases must move apart by at least 3.4\text{Å}. For this to occur, the ribose phosphate backbone must readjust accordingly. The most obvious way for the chain to readjust is by changing its sugar pucker, such that the bases can separate—a change from the A-RNA C\textsubscript{3}’endo to the more B-DNA-like C\textsubscript{2}’endo. As you should recall this increases the intrastand phosphate-phosphate distance from 5.9 to 7.0 (just like in B-DNA).