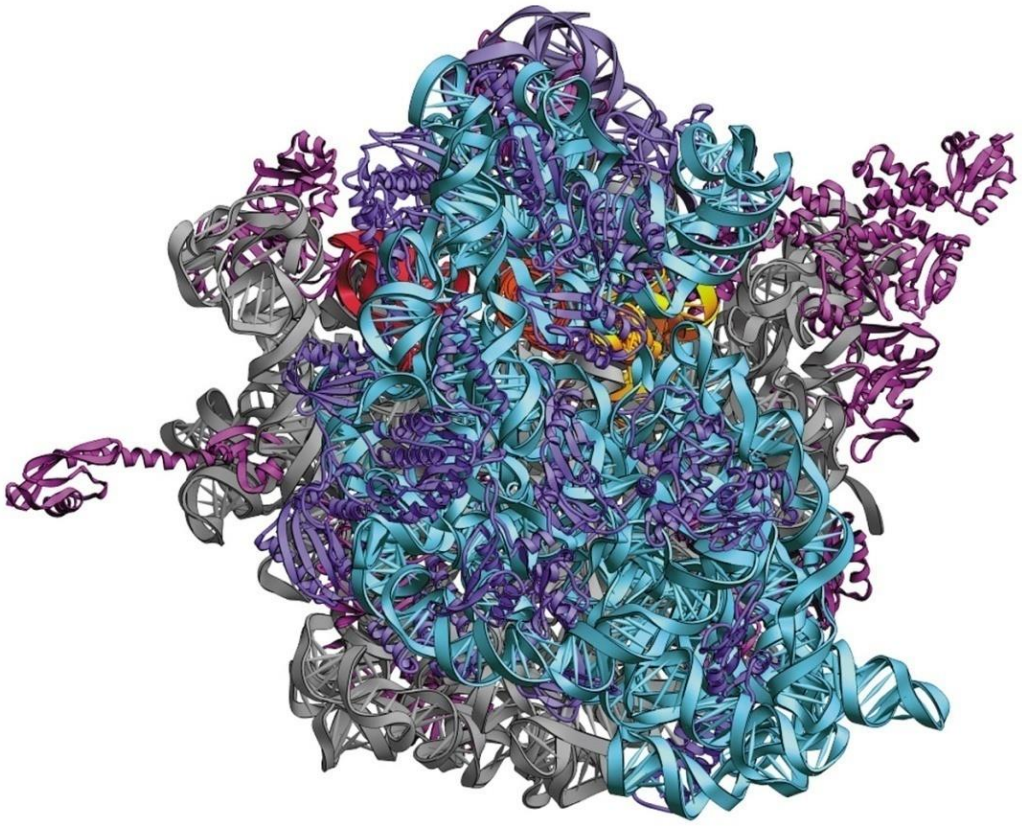
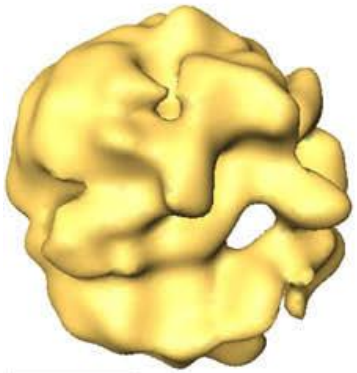
Molecular Machines

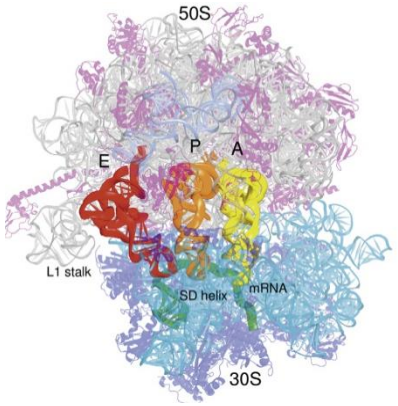


Mikołaj Olejniczak

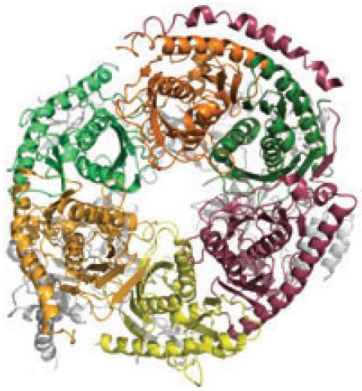
Molecular machines, which are involved in synthesis, maturation and decay of biological macromolecules



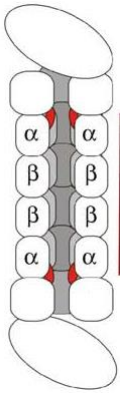
spliceosome



ribosome



exosome



proteasome

RNA structure is organized at three levels:

Primary structure is the sequence of nucleotides in polyribonucleotide chain

Secondary structure is stabilized by Watson-Crick pairs and is organized into structure motifs such as **helices, hairpins, bulges, internal loops, *helix junctions***

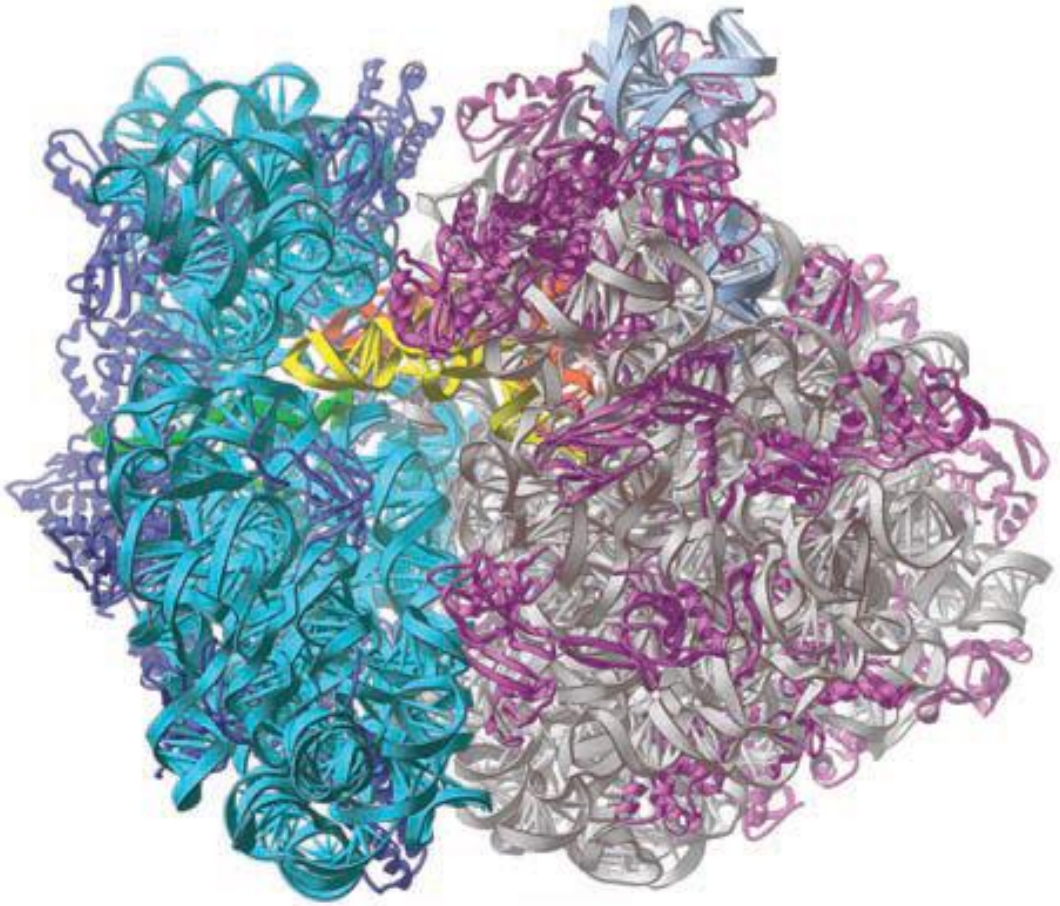
Tertiary structure is formed by nucleotides located distantly in the sequence, such as **pseudoknots, base triples, *A-minor* motifs**

Complex RNA molecules contain multiple structure elements

RNA molecules form complex 3-dimensional structures

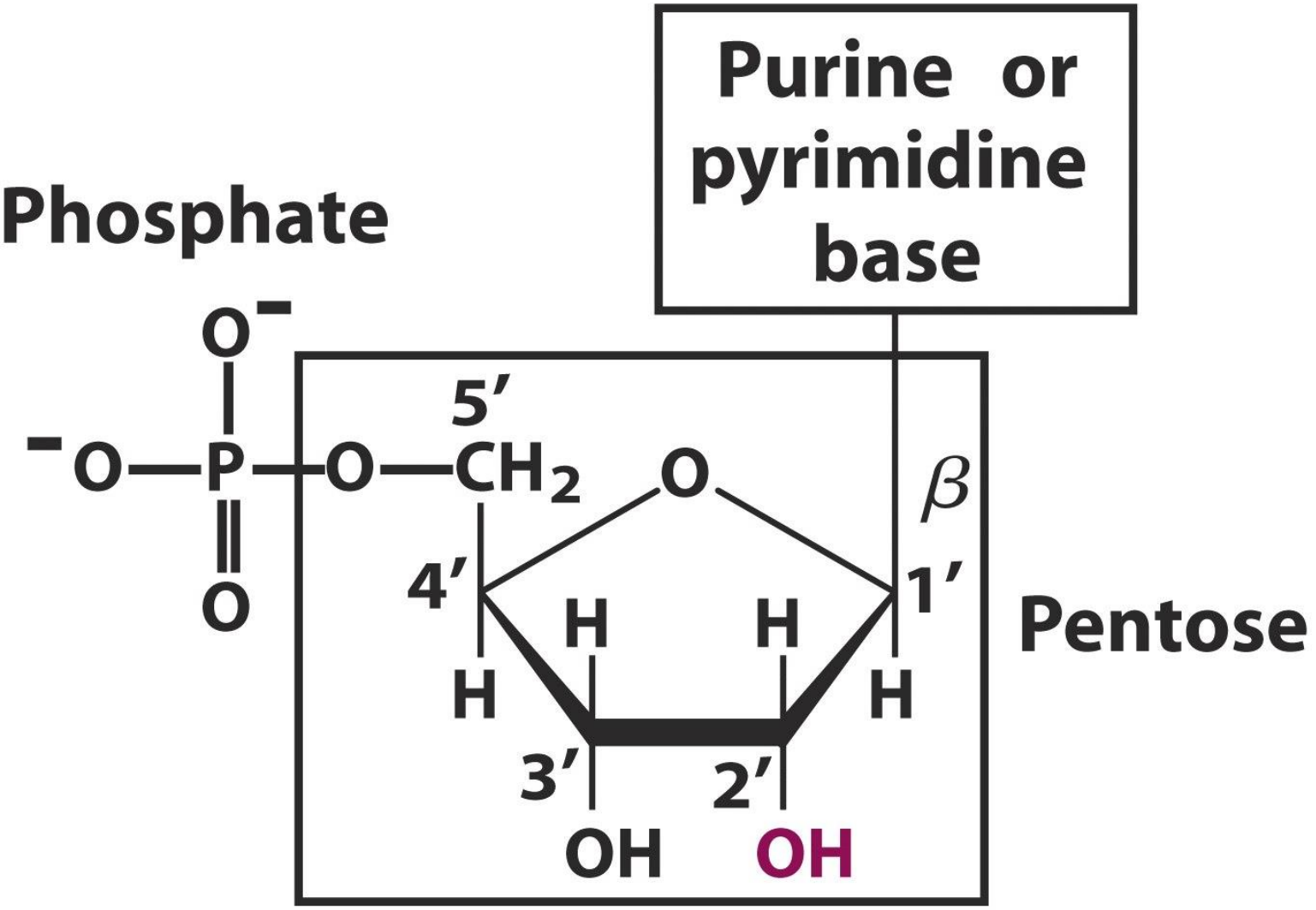
tRNA

P4-P6

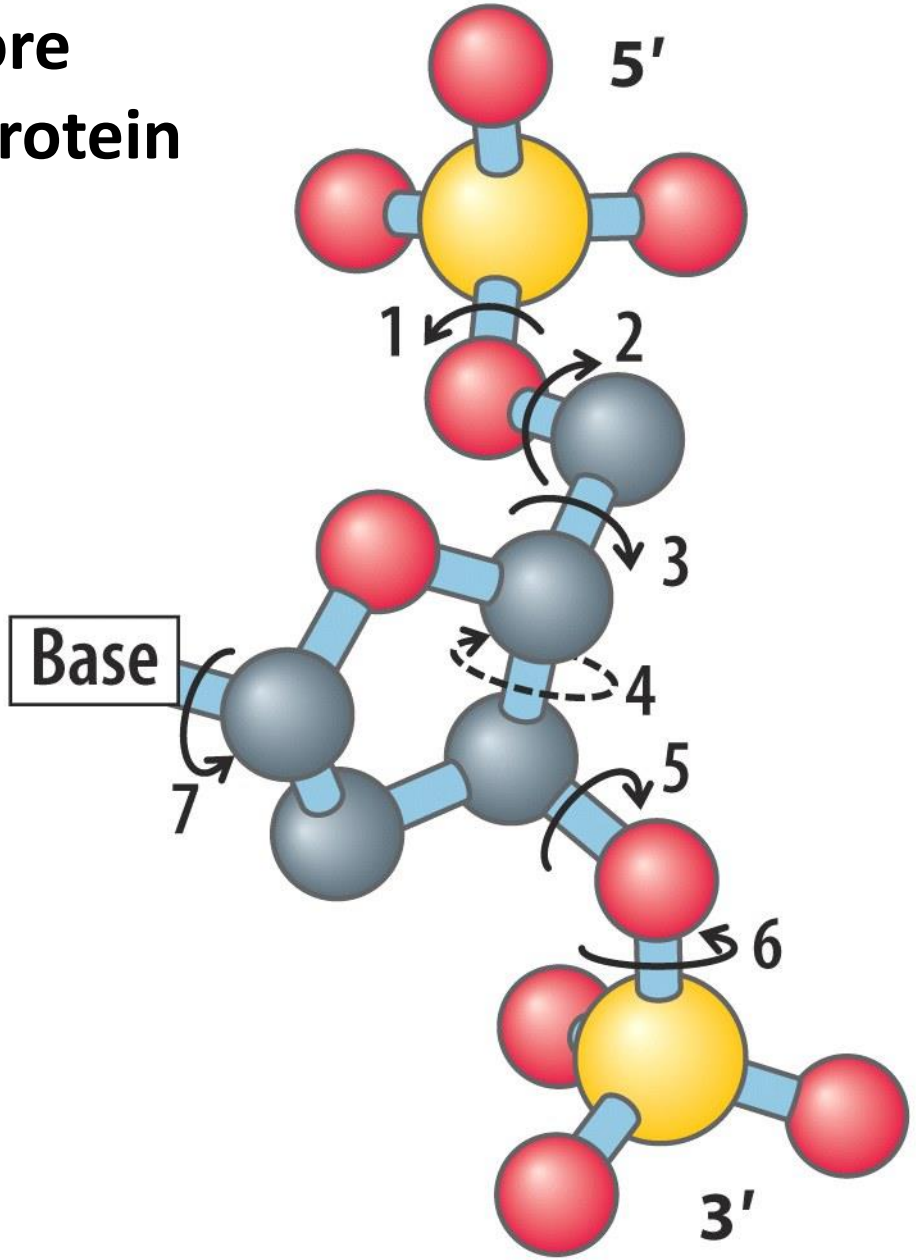


70S ribosome

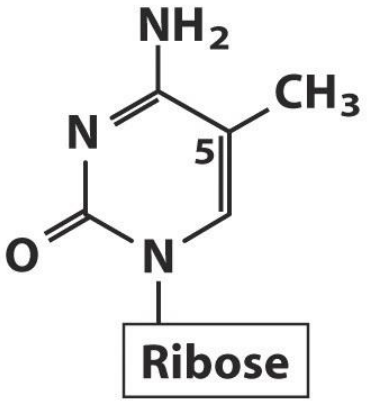
RNA properties essential for the formation of complex spatial structures



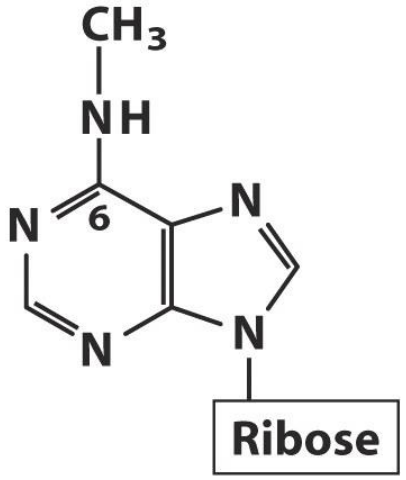
Nucleic acid chain is more flexible than that of a protein



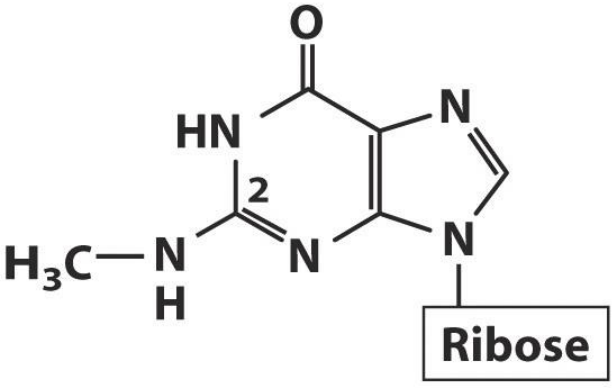
RNA molecules contain post-transcriptional modifications



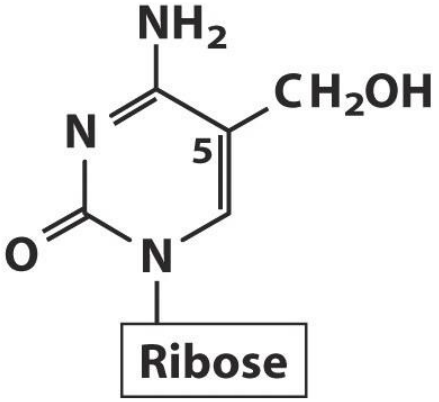
5-Methylcytidine



N^6-Methyladenosine

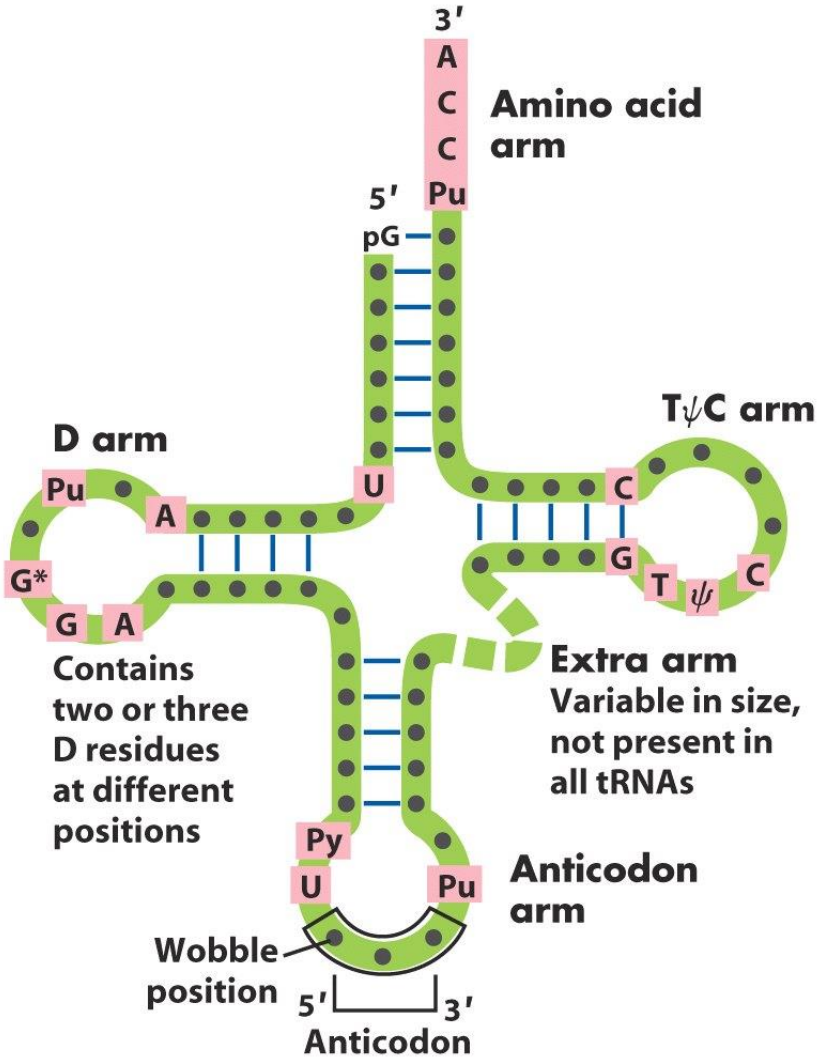


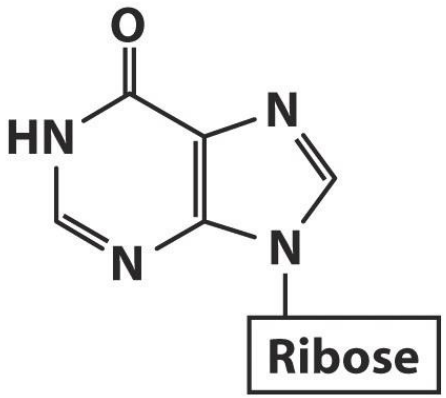
N^2-Methylguanosine



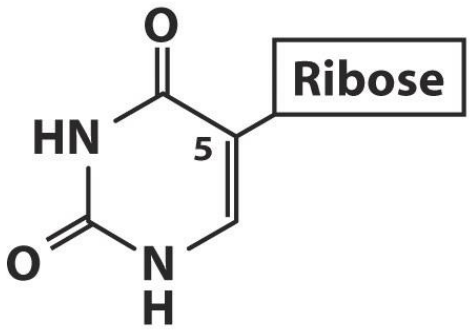
5-Hydroxymethylcytidine

Modified bases in tRNA are essential for Its structure and for accurate decoding of mRNA

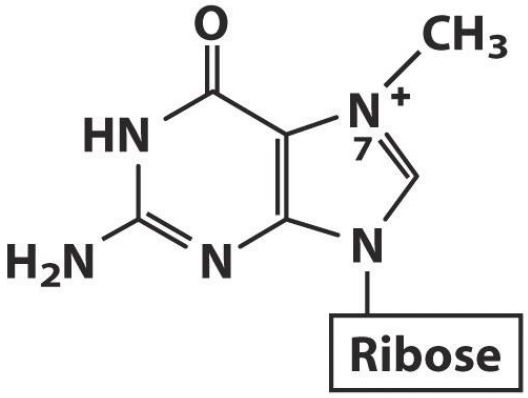




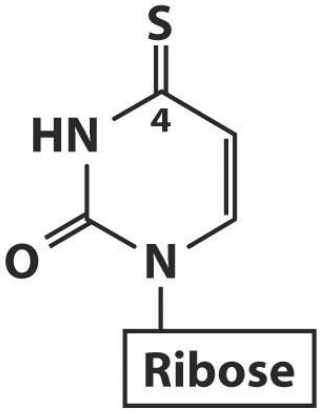
Inosine



Pseudouridine

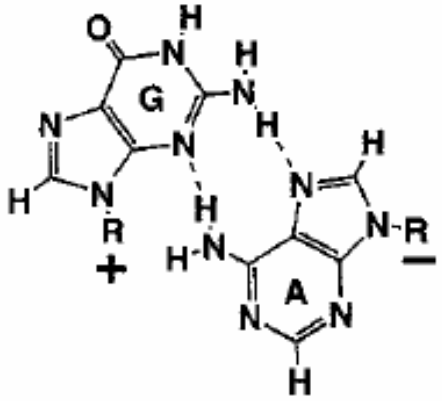


7-Methylguanosine

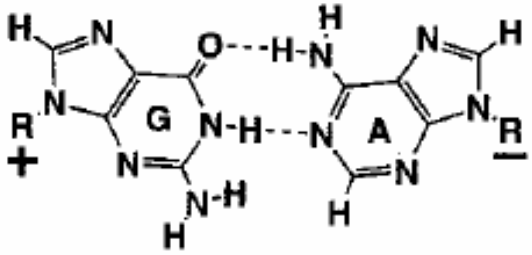


4-Thiouridine

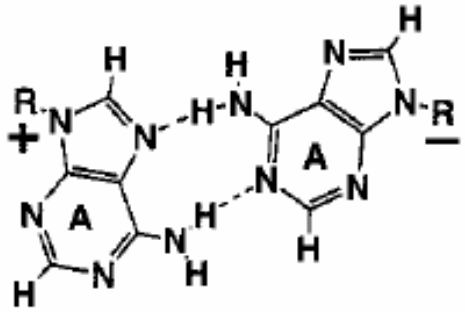
More than 70 types of noncanonical basepairs are known



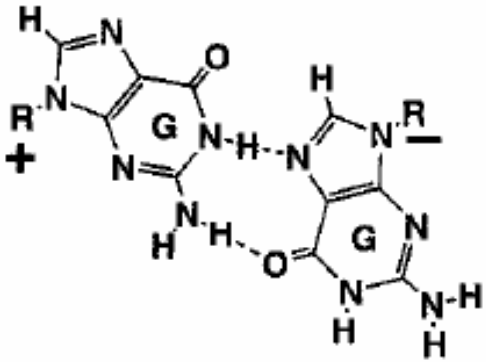
Sheared G•A



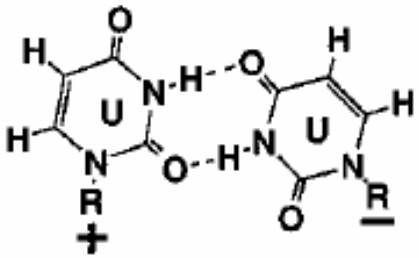
G•A imino



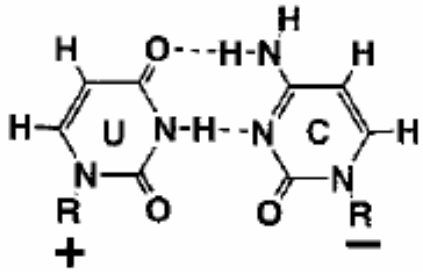
A•A N7-amino



G•G N7-imino

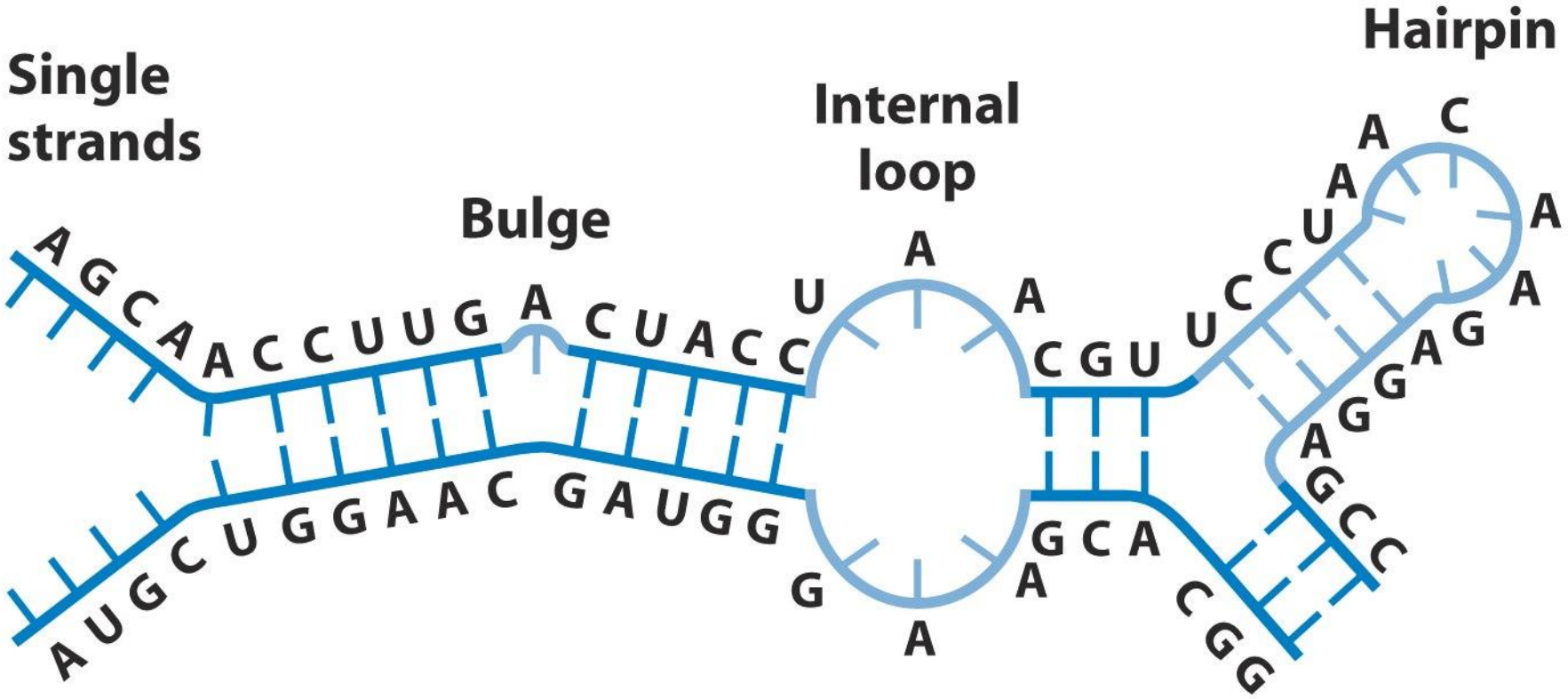


U•U imino-carbonyl

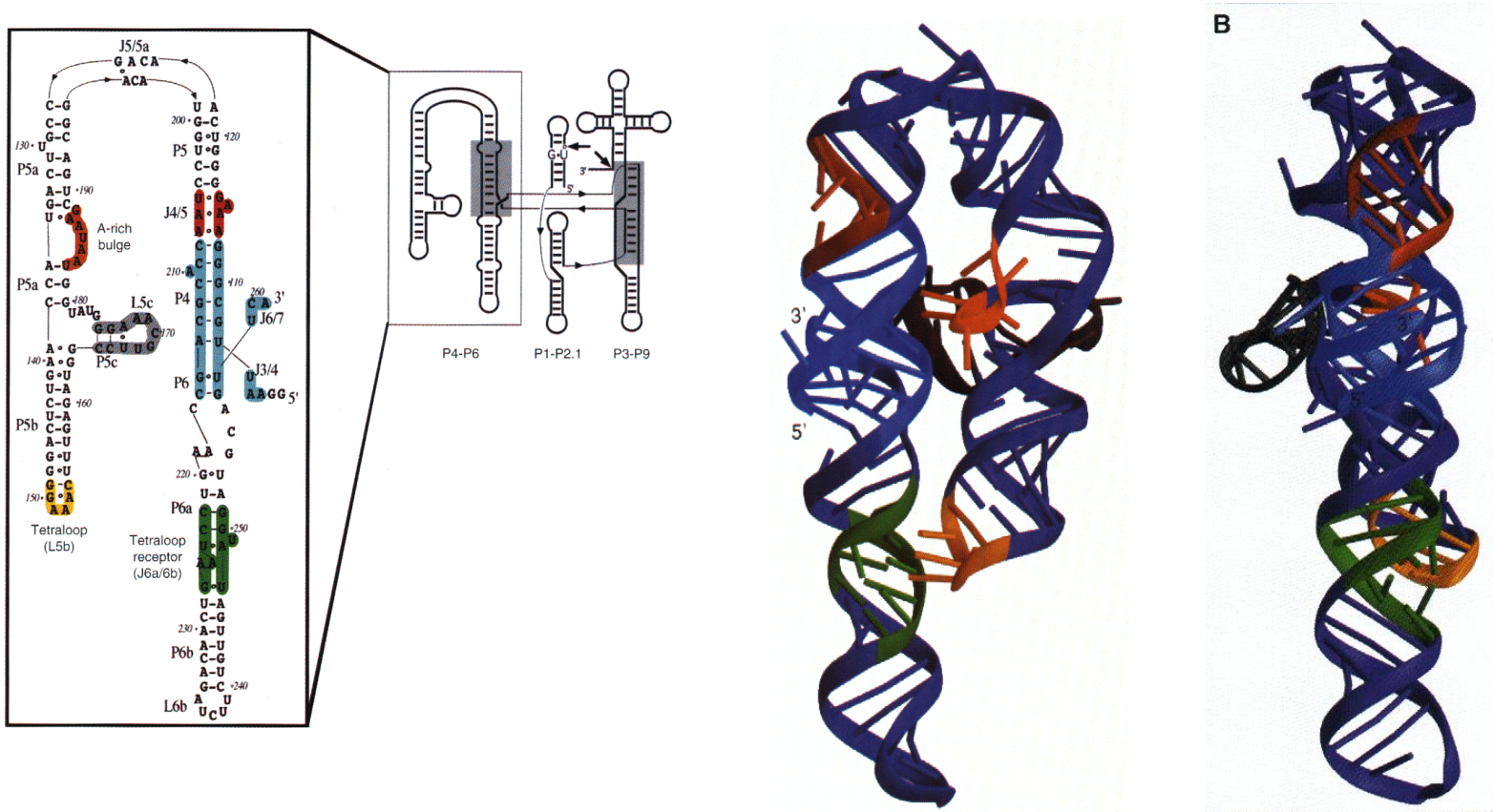


U•C 4-carbonyl-amino

RNA secondary structure motifs



Tertiary contacts in P4-P6 domain of group I intron

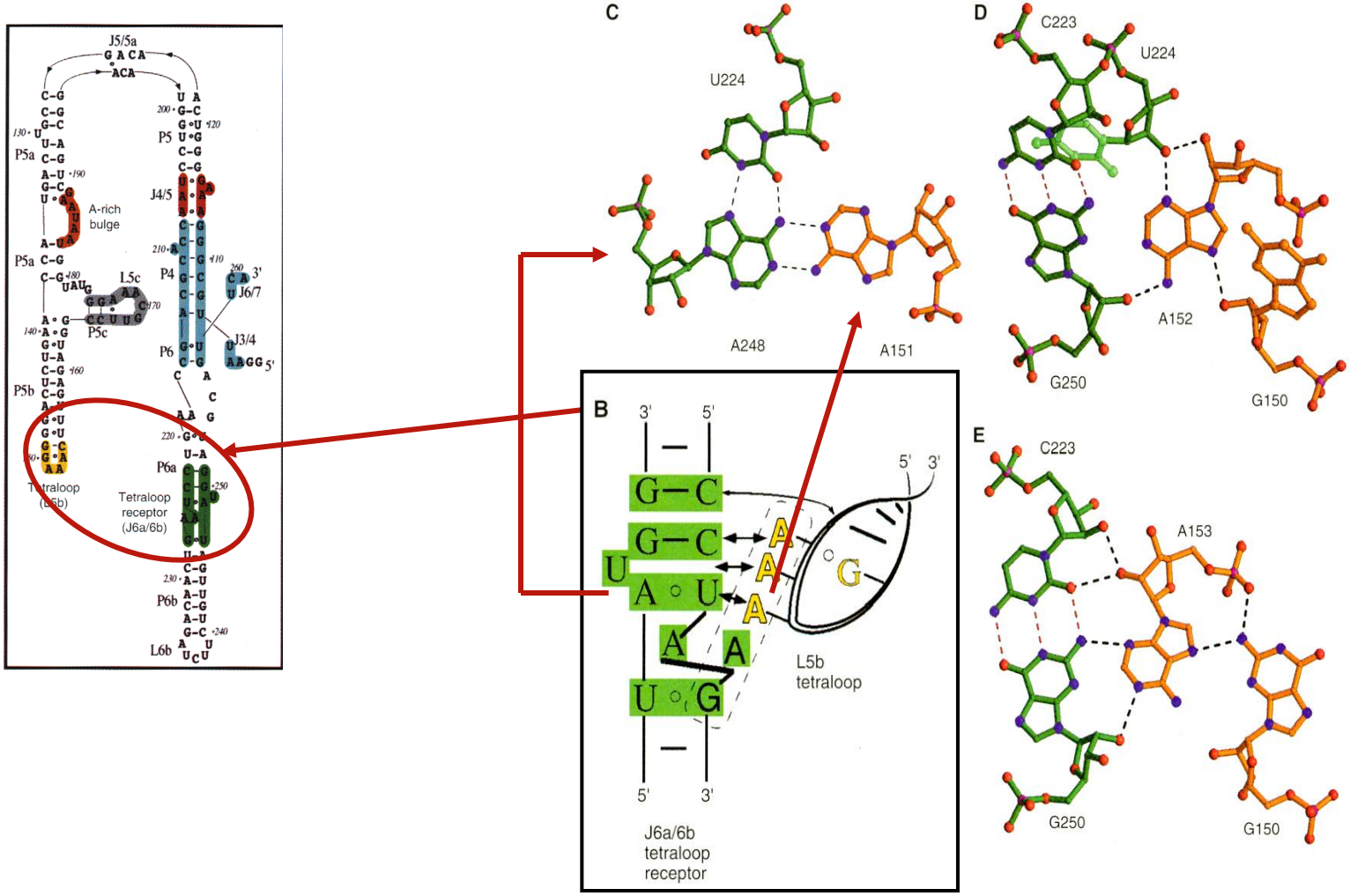


Two parallel helical regions stabilized by tertiary contacts

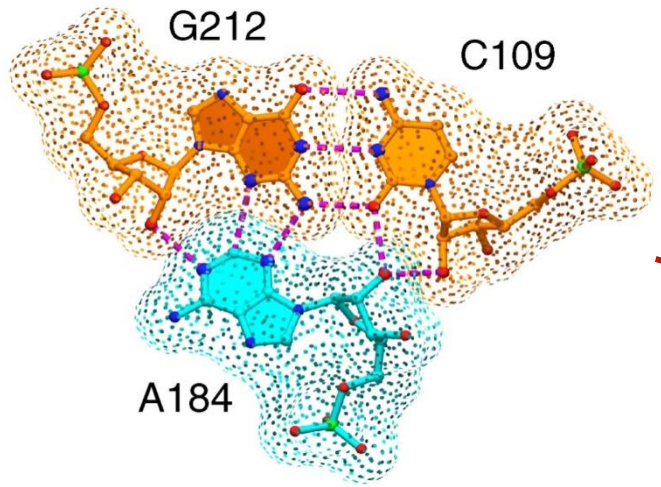
1. tetraloop/tetraloop-receptor

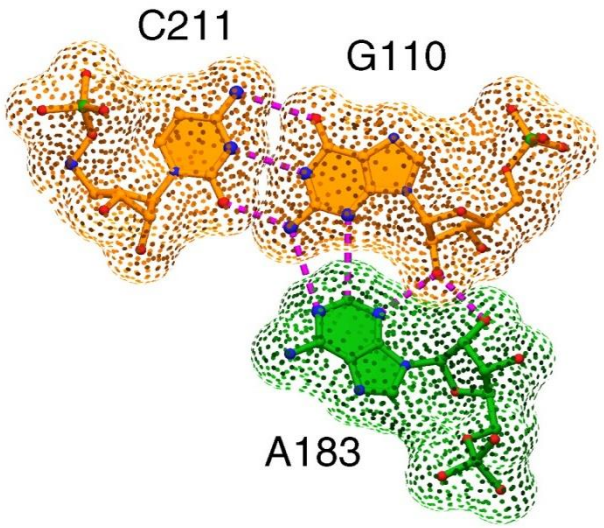
2. A-minor interactions

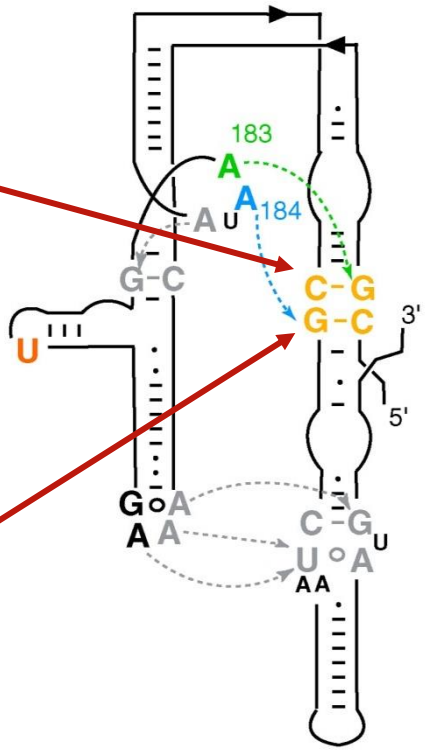
tetraloop/tetraloop-receptor



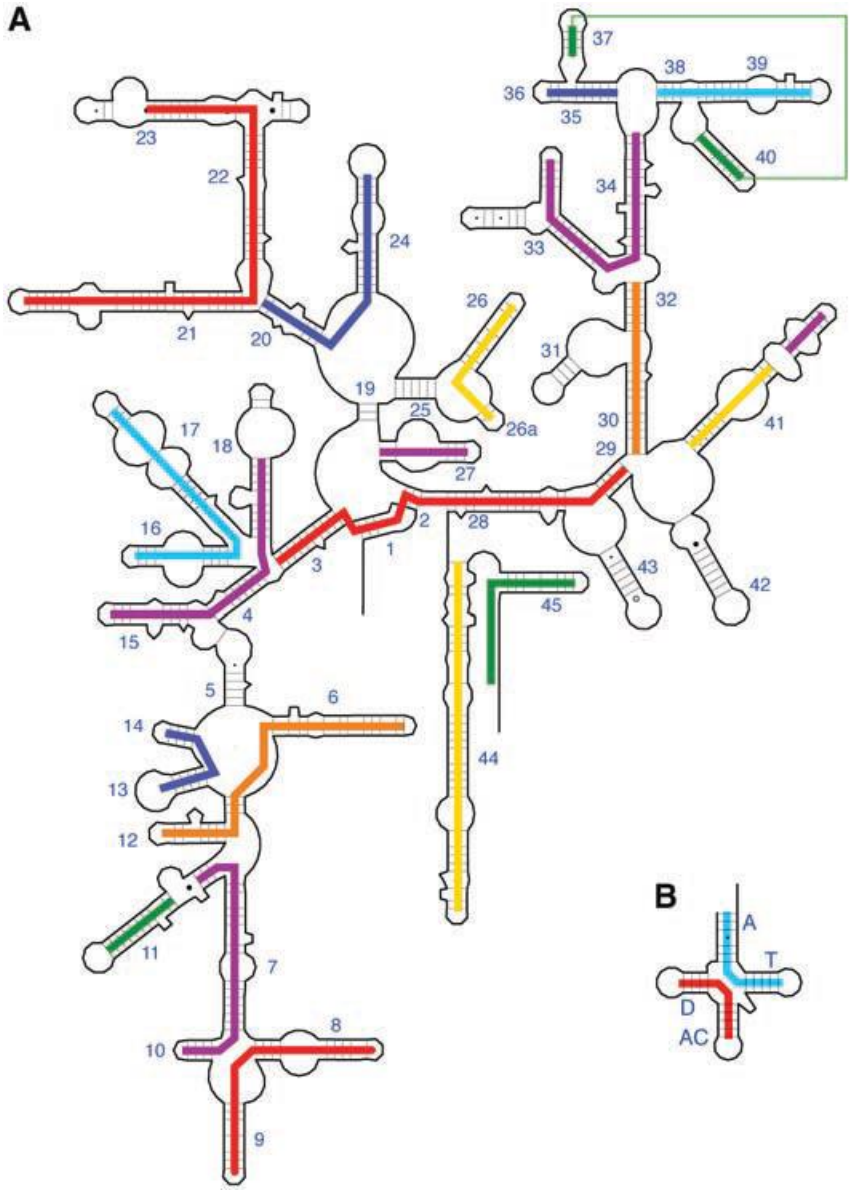
A-minor motif



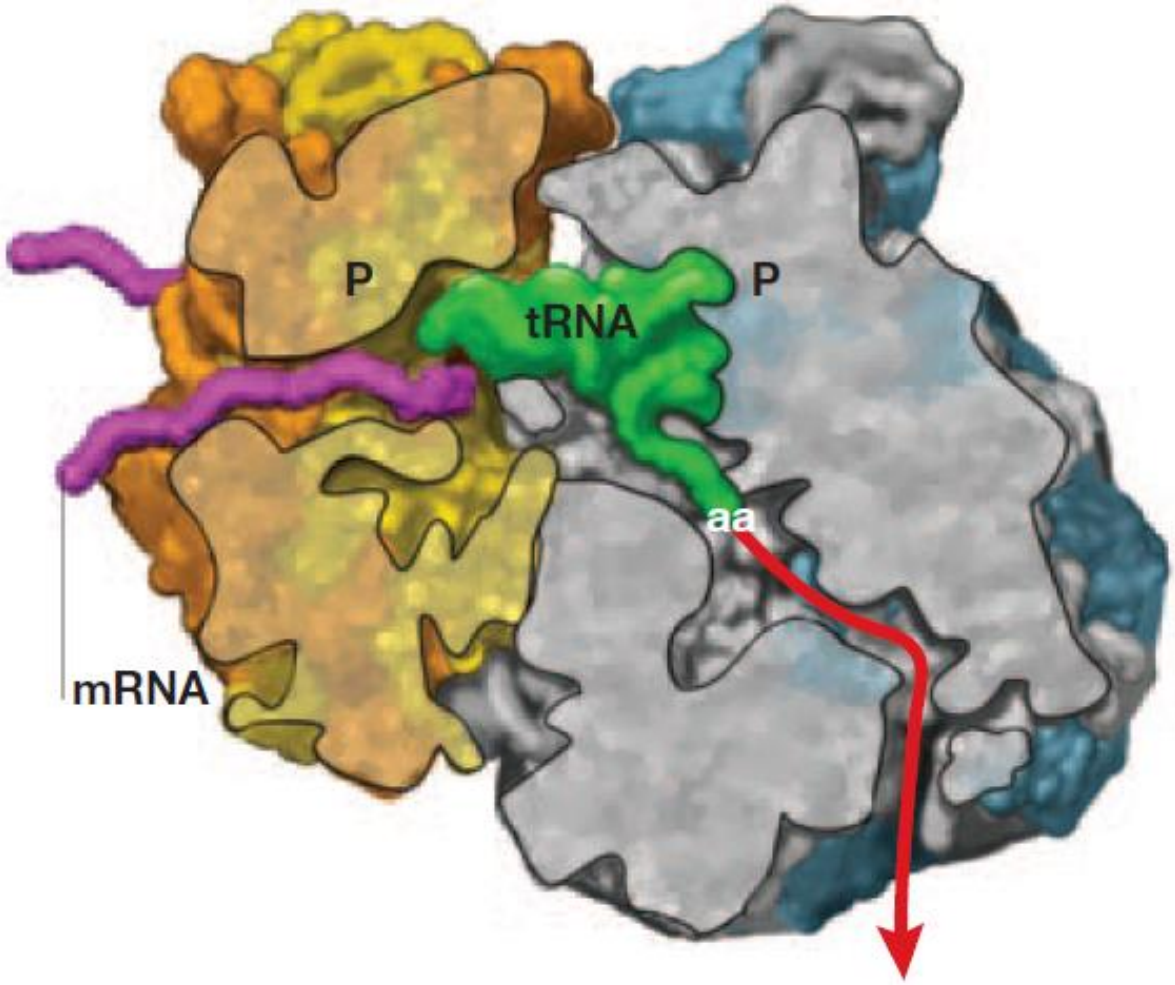




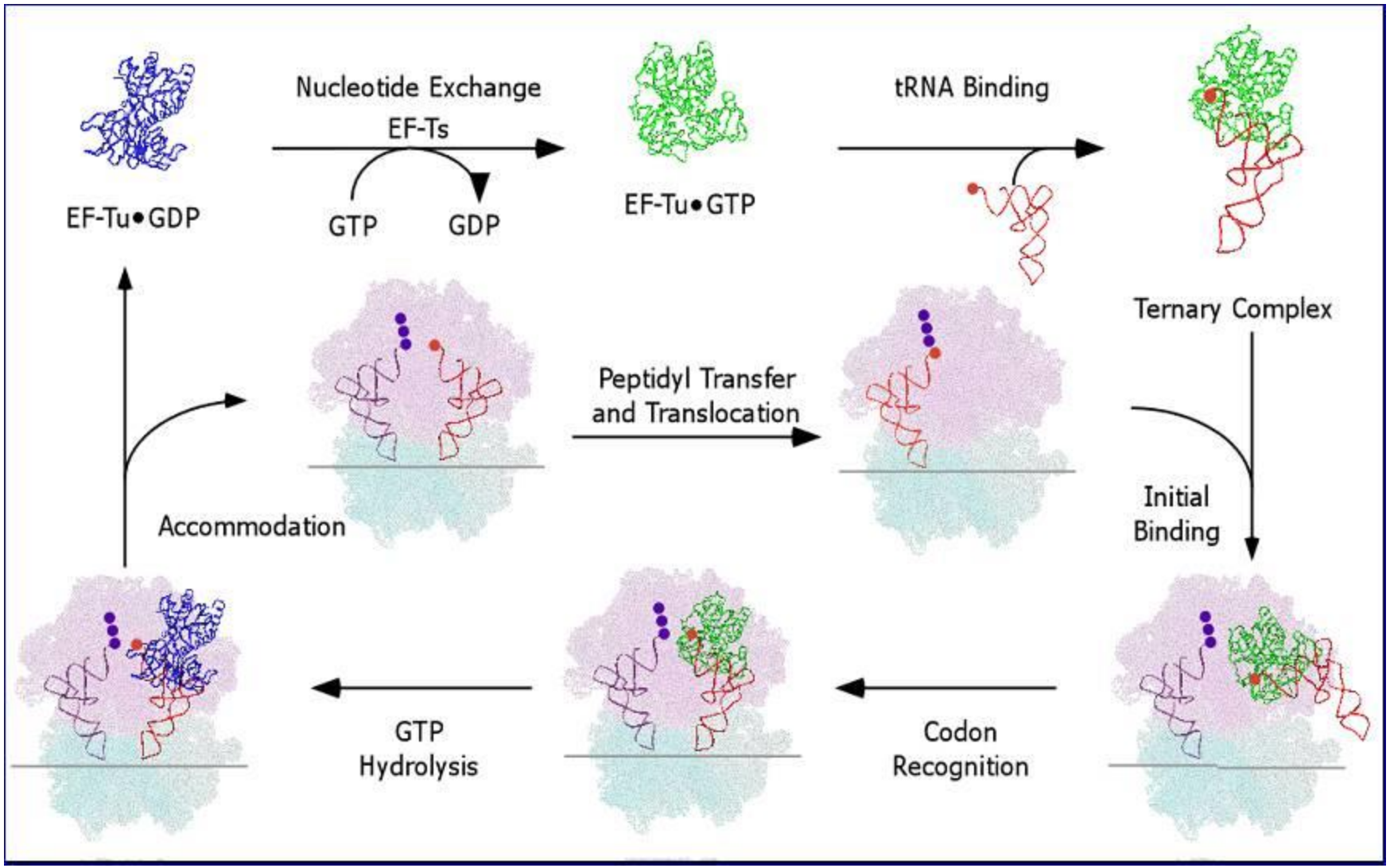
coaxial stacking in 16S rRNA



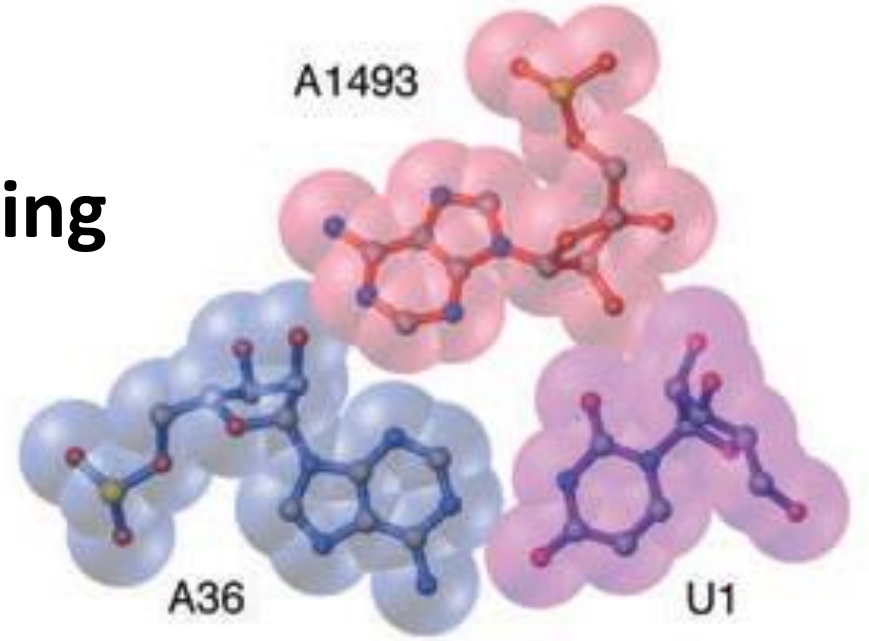
Ribosome is a molecular machine, in which RNA is the peptide bond formation catalyst

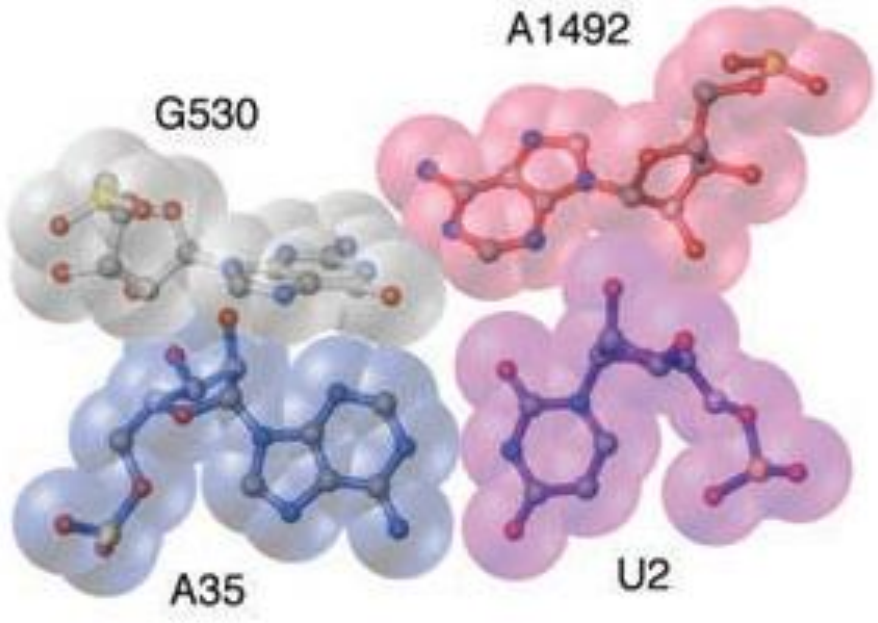


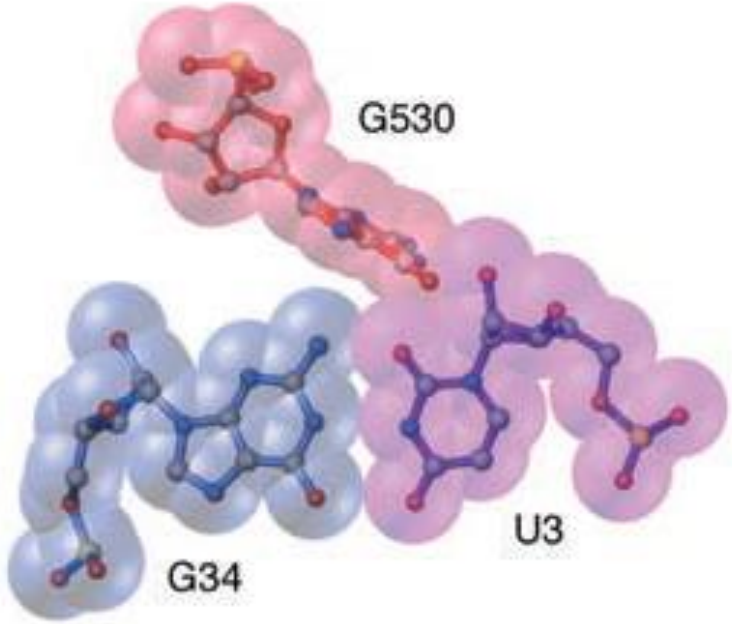
Translation elongation cycle



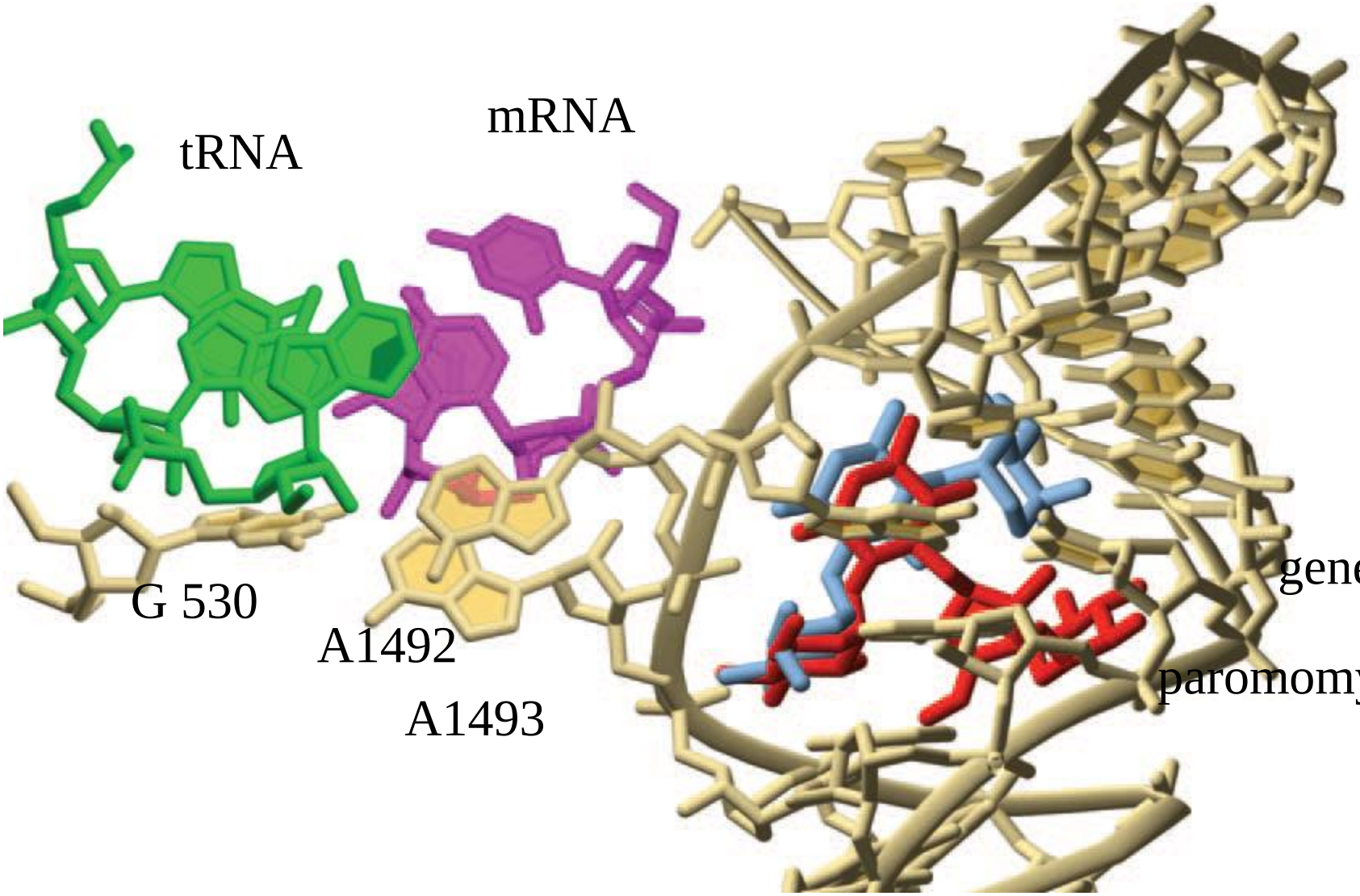
A-minor interactions are essential for mRNA decoding



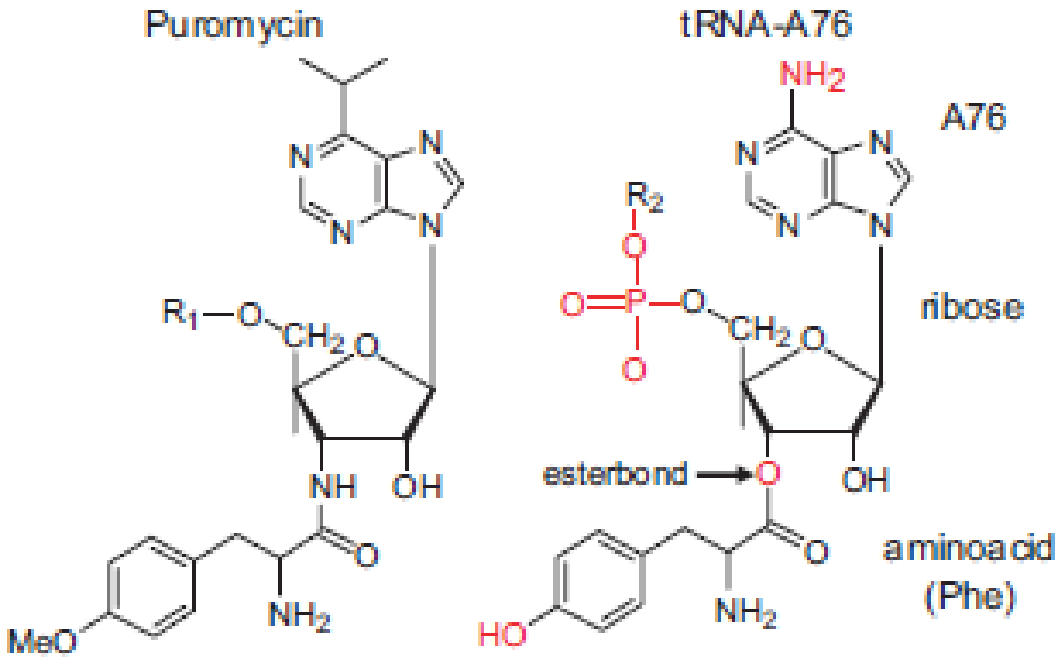




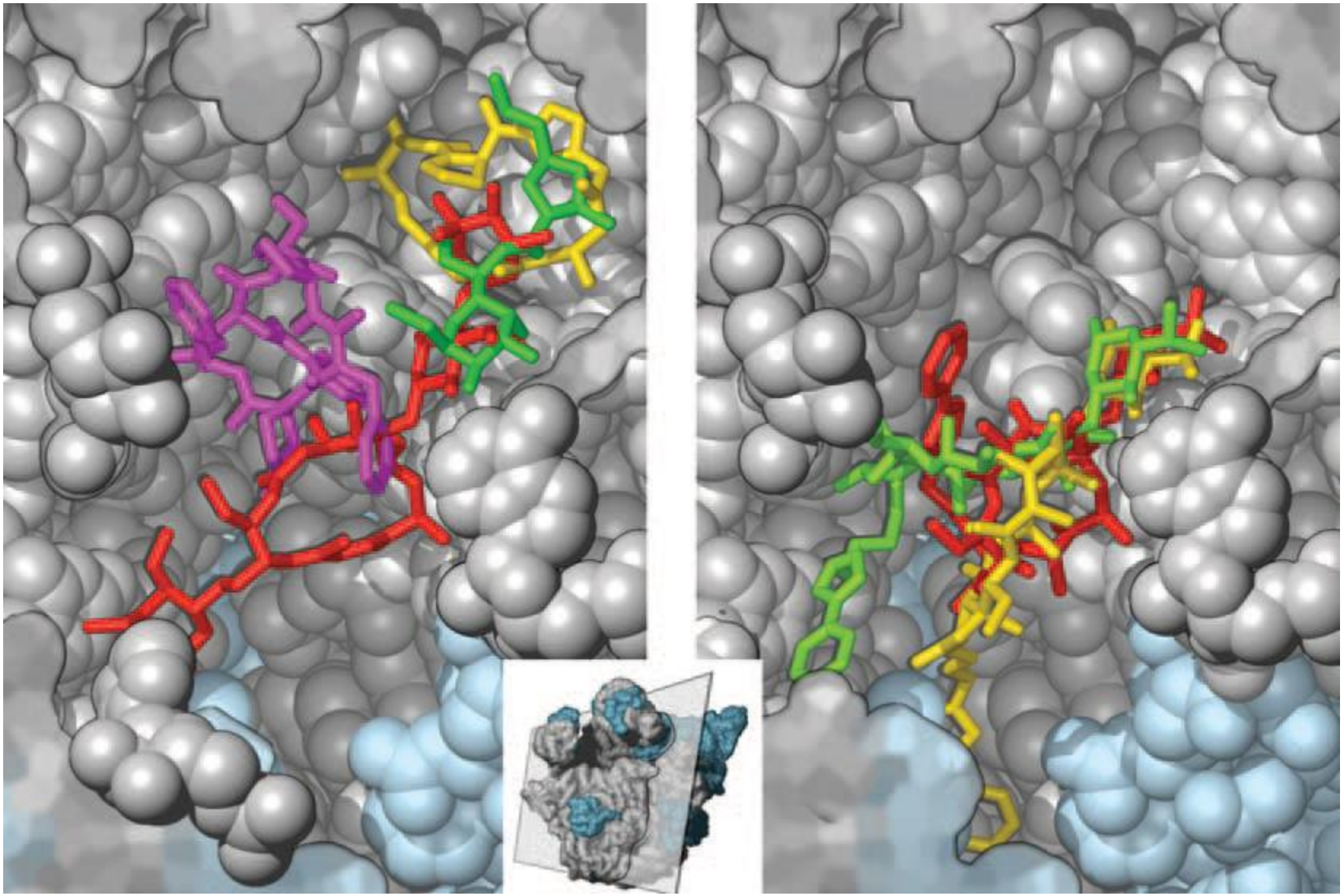
Aminoglycosides trigger conformational change at the decoding site



Puromycine mimics the 3’ end of aa-tRNA and inhibits peptidyltransferase activity

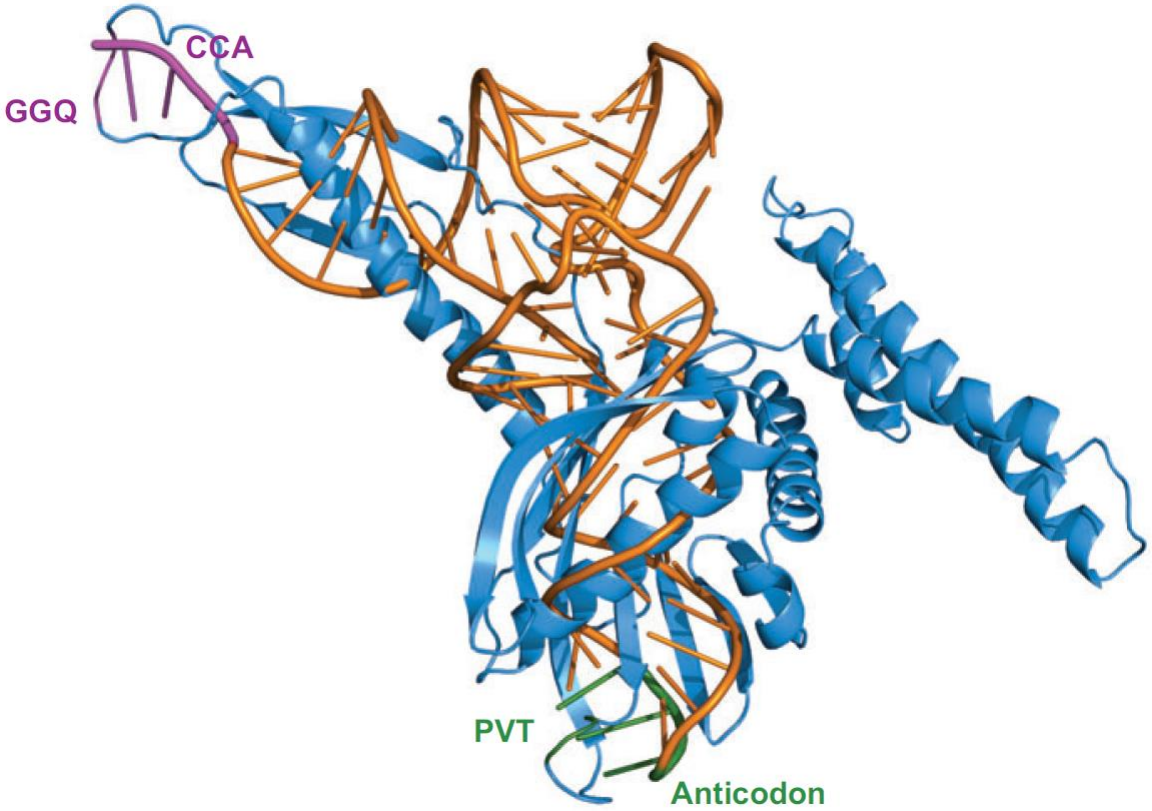


Macrolides block the exit tunnel of the 50S subunit



Molecular mimicry:

Release factors (RFs), which recognize nonsense codons to terminate translation, have the shape of tRNA molecules



Youngman et al., Ann Rev Microbiol 2008