Combinatorial approaches to RNA folding
Part I: Basics

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- DNA (*Deoxyribonucleic acid*)

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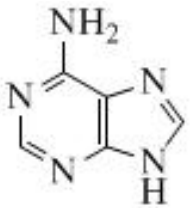
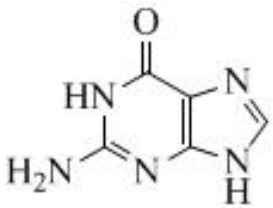
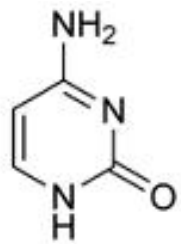


adenine



guanine



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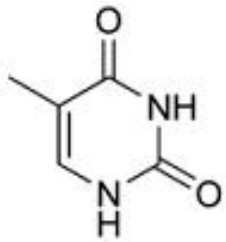
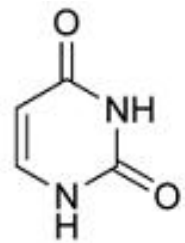


thymine



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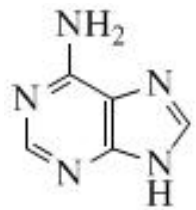

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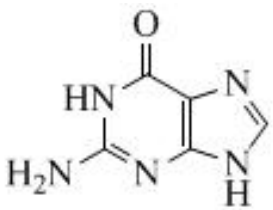

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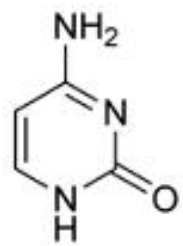

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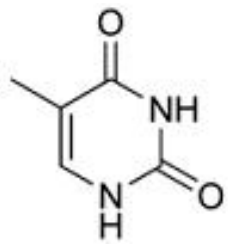

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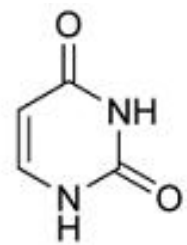

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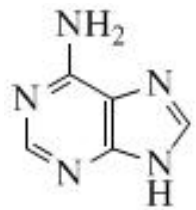

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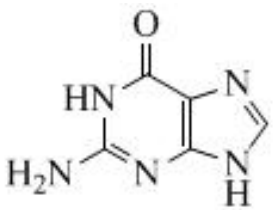

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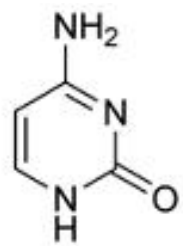

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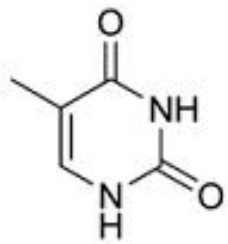

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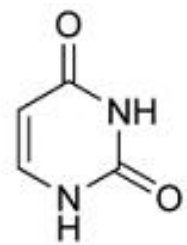

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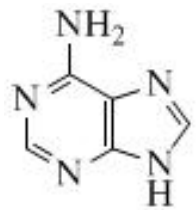

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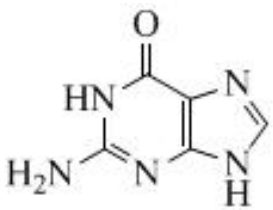

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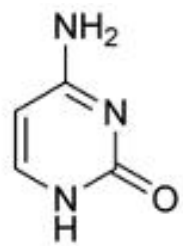

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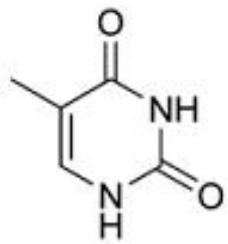

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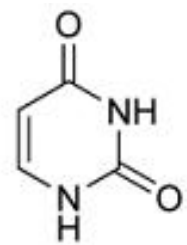

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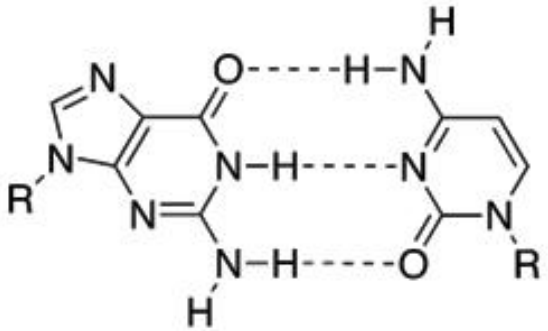

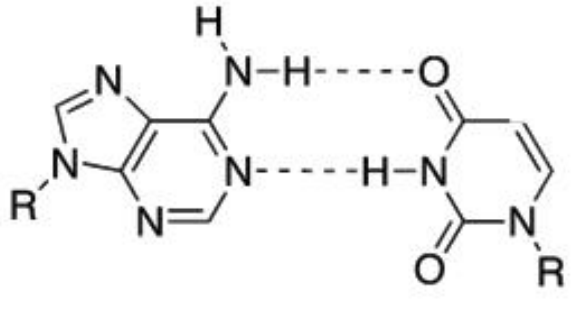

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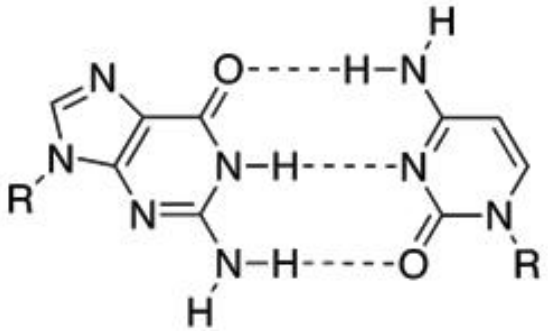
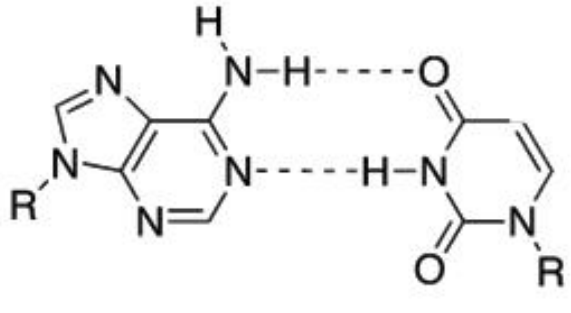
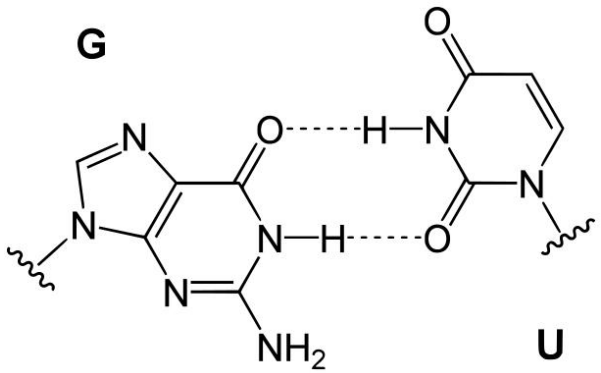




Additionally, U can bond with G. (Called a *wobble-pair*).



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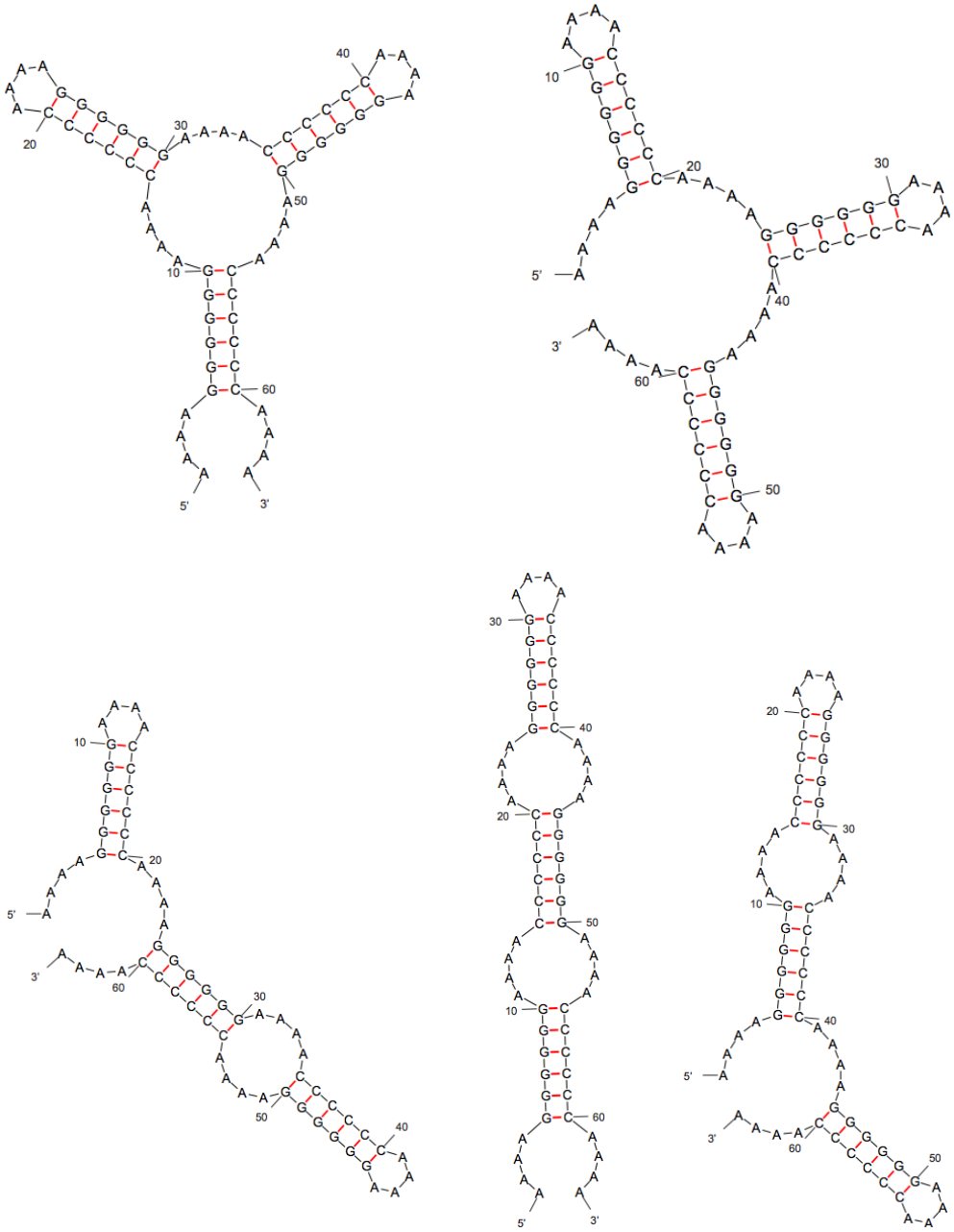
How does RNA fold? [image from C. Heitsch; Georgia Tech]



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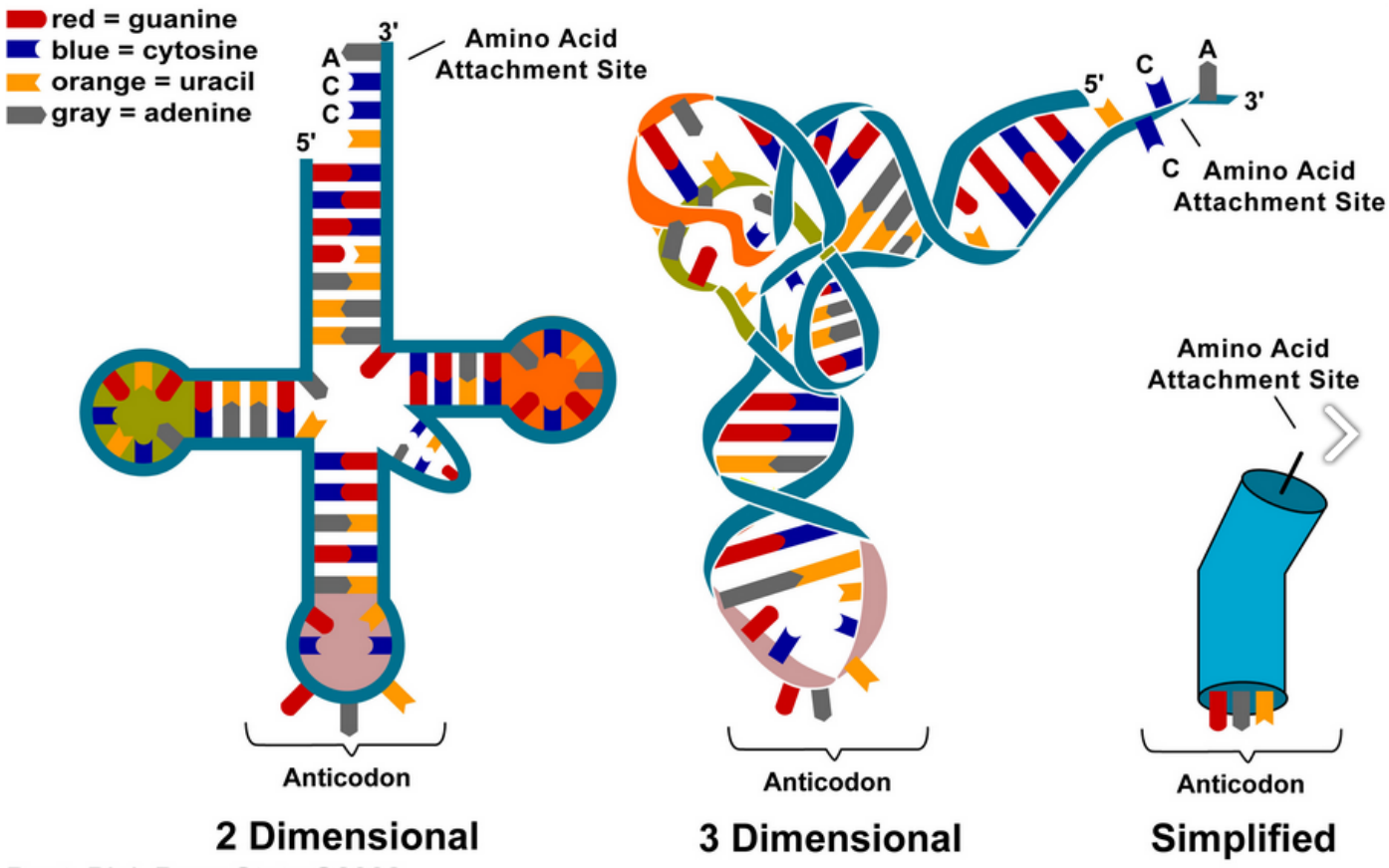
- *Tertiary structure*: Embedding (e.g., twisting, knotting, etc.) of the strand in 3-dimensional space.



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Before we proceed, we will need to establish a combinatorial framework for describing RNA strands.

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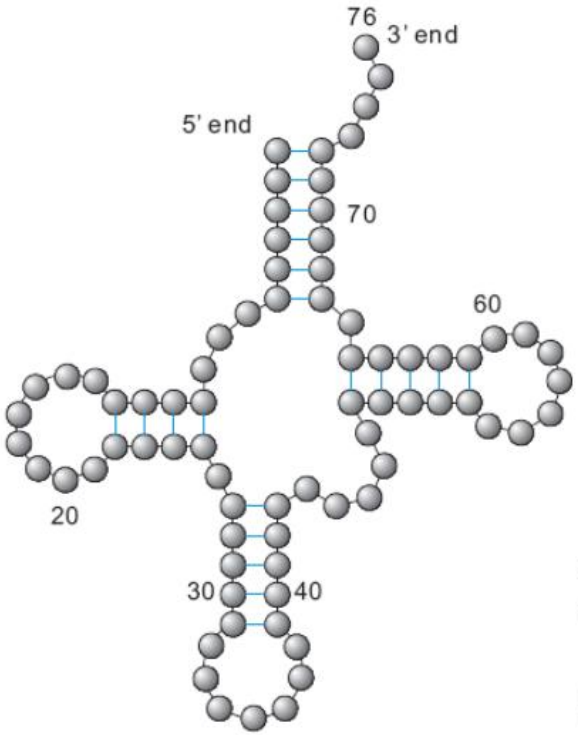

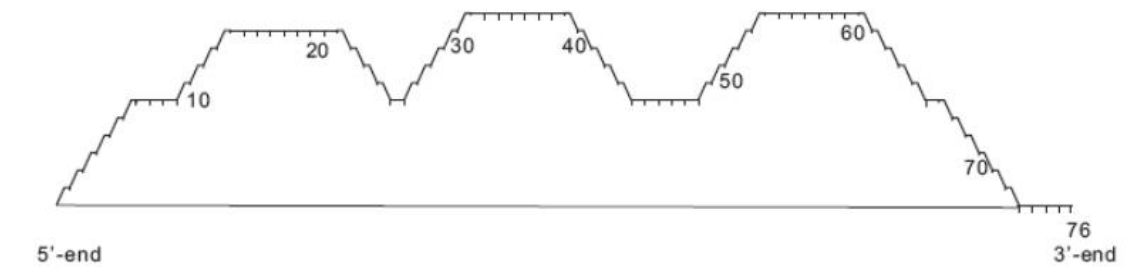

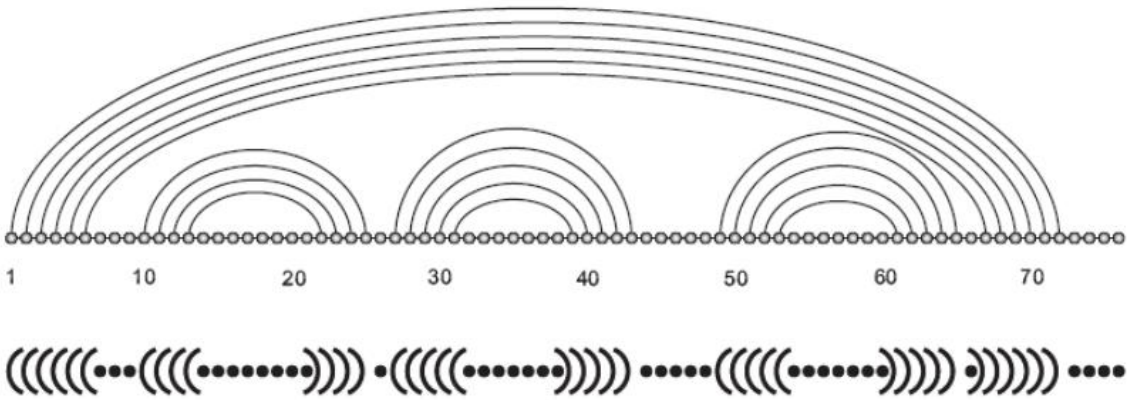

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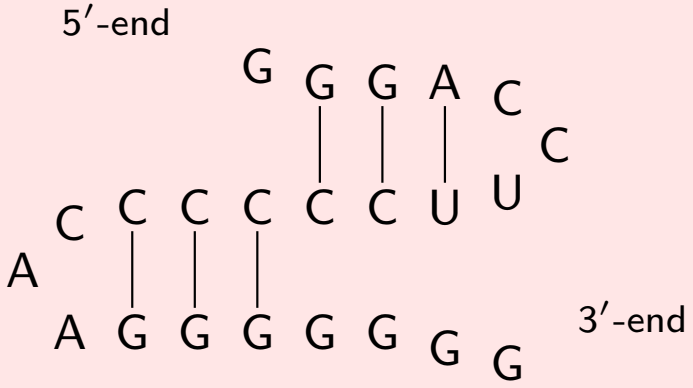

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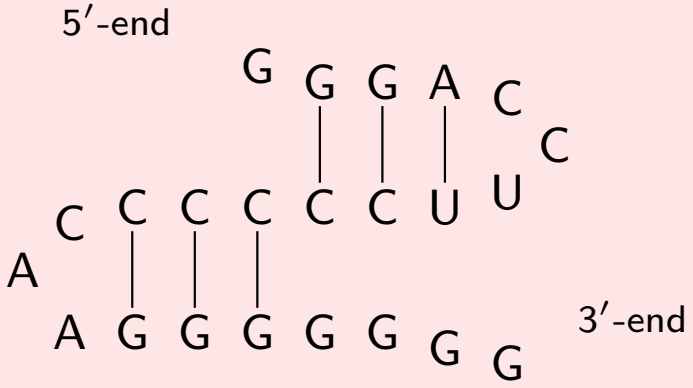

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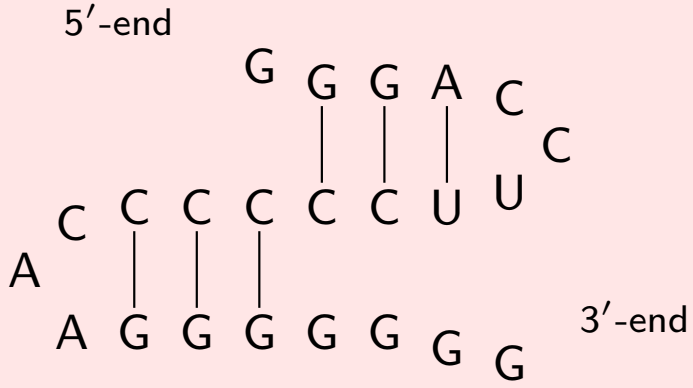

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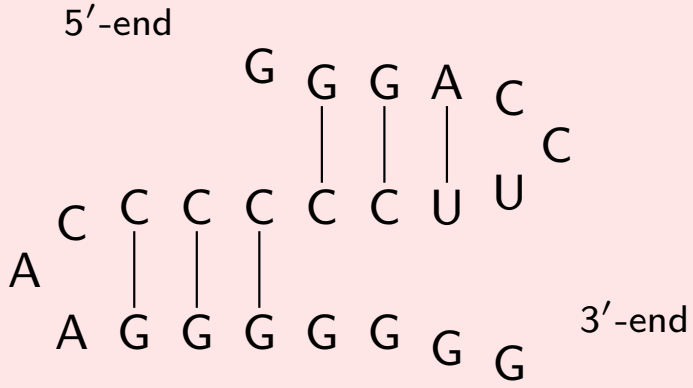

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Pseudoknots

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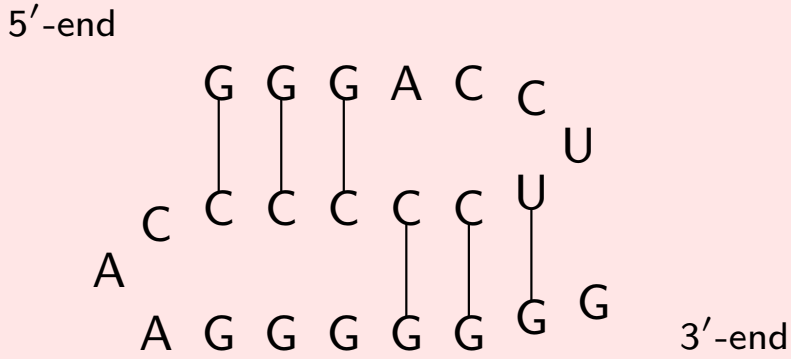
Consider the following fold of the same RNA sequence:



(i) Draw the corresponding arc diagram.

(ii) Write out this secondary structure in point-bracket notation.

(iii) Draw the corresponding Motskin path.

Which of these go wrong, now that there are crossing arcs?

An RNA structure is a pseudoknot if its arc diagram has crossings.

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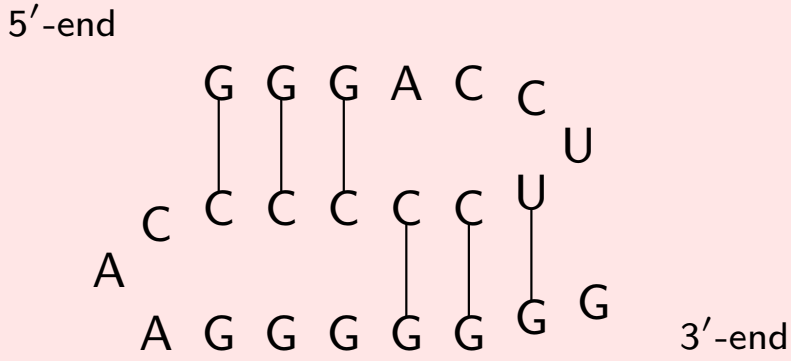

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An arc diagram is k-noncrossing if there is no set of k mutually crossing arcs.

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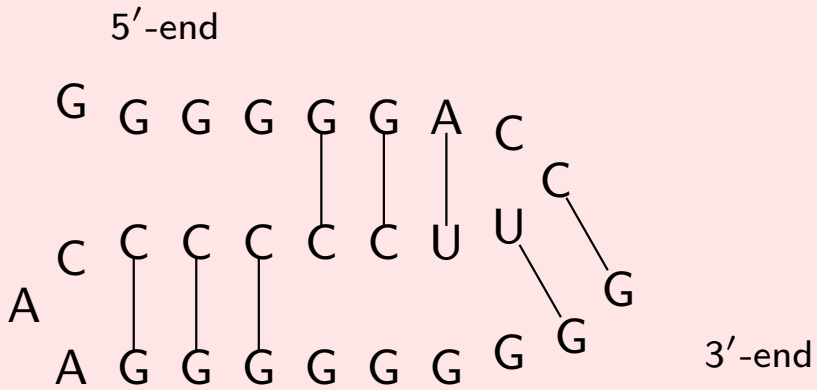

(i) Draw the corresponding arc diagram. What is the smallest k for which this is k-noncrossing .

(ii) What if the first G bonds with the C "directly below" it (vertex 17). Does this change the k from the previous part?

(iii) Draw a picture of a folded RNA strand (like the one above) that is 4-noncrossing but not 3-noncrossing.

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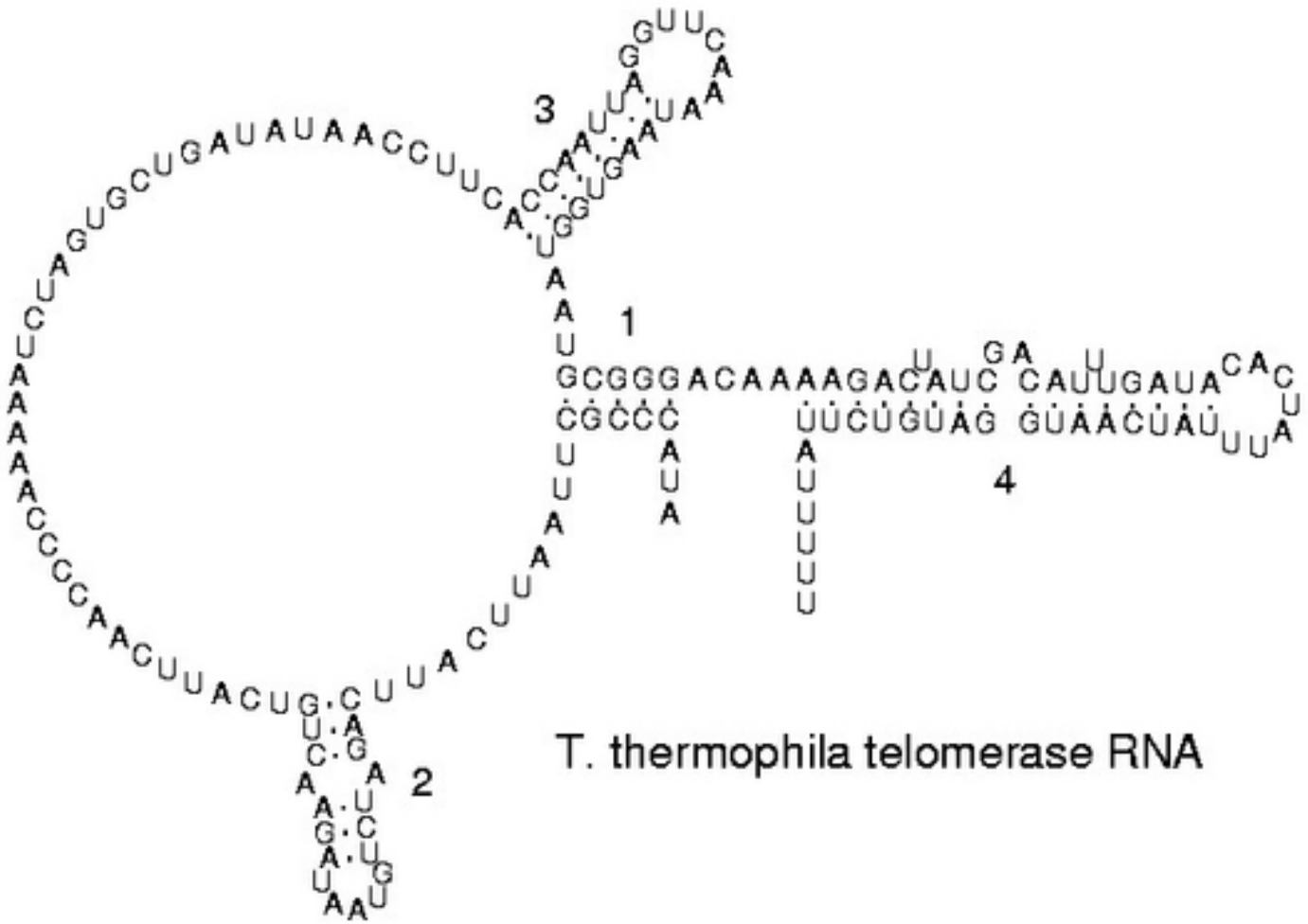

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Loop types

0. The vertices not accessible from any arcs form the unique 0-loop, or null loop L_0.
1. A 1-loop is called a hairpin loop
2. There are three types of 2-loops: bulge loops, interior loops, and stacked pairs.
3. A k-loop for $k \geq 3$ is called a multiloop.

Loop decomposition

2-loops

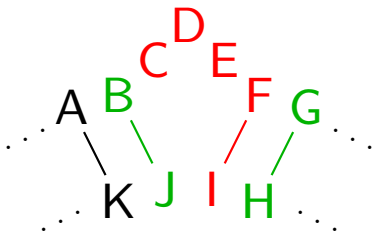
Suppose (i', j') is the unique accessible base pair from (i, j). Then the resulting 2-loop is:

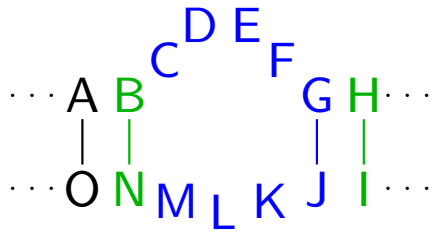
2a. a stacked pair if $i - i' = j' - j = 1$;

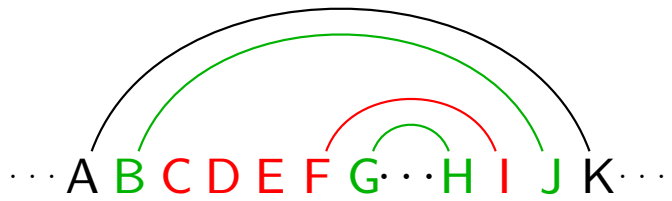
2b. a bulge loop if exactly one of $i - i'$ and $j' - j$ is > 1;

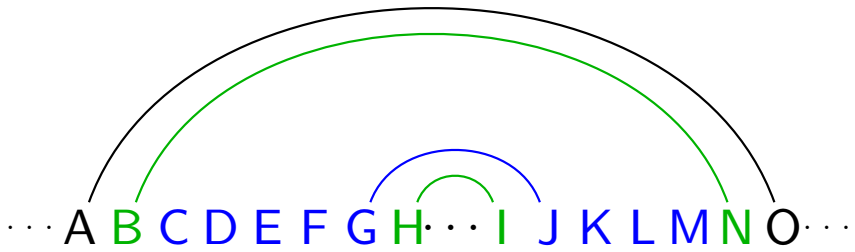
2c. an interior loop if both $i - i'$ and $j' - j$ are > 1;

Two 2-loops: a bulge loop (left) and an interior loop (right). Each secondary structure also contains two 2-loops that are stacked pairs.









Loop decomposition with pseudoknotting

Things get a little more complicated when the diagram contains a pseudoknot, but there is is still a well-defined decomposition. (We won't go into details.)