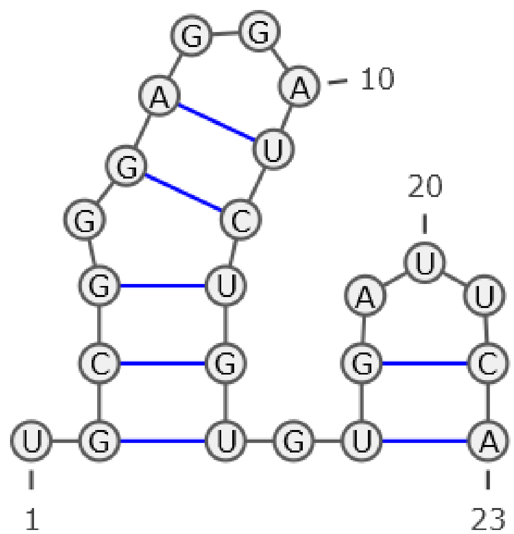
Exercise sheet 11: RNA Bioinformatics

Exercise 1

RNA secondary structures can be represented using a graph notation, where nodes represent nucleotides and edges encode the molecule's backbone or intramolecular base pairs between nucleotides. Below, an RNA molecule graph is depicted that encodes base pairs in blue.

Decide for the following properties whether they are correct or wrong given the RNA secondary structure graph.



1a)

Position 23 represents the 5'-end

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Solution wrong; We always encode in the 5' (=1) to 3' (=n) direction.

1b)

the graph is invalid

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Solution wrong

1c)

contains invalid base pairs

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Solution wrong; all base pairs depicted in the graph are valid

1d)

contains a pseudoknot

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Solution wrong; There are no pseudoknot structures in this graph.

1e)

non-crossing

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Solution correct; There are no pseudoknot structures in this graph.

1f)

nested

Hide

Solution correct

1g)

contains base pair (5,12)

Hide

Solution wrong; Position 5 is unpaired.

1h)

contains base pair (4,13)

Hide

Solution correct

1i)

base pair (1,10) would be crossing

Hide

Solution correct

1j)

obeys a minimal loop length of 4

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Solution wrong; The minimum loop length for this graph is 3. (number of unpaired bases in loops)

1k)

encoded by ((...)).(((((...)).))).

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Solution wrong

1l)

encoded by .(((.((...))))).((...))

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Solution correct

Exercise 2

You are given the following dot-bracket string: (((...)))...((((...))..))

2a)

Draw graph representations of all nested structures that can be encoded by the dot-bracket string. Assume a minimal loop length of 3.

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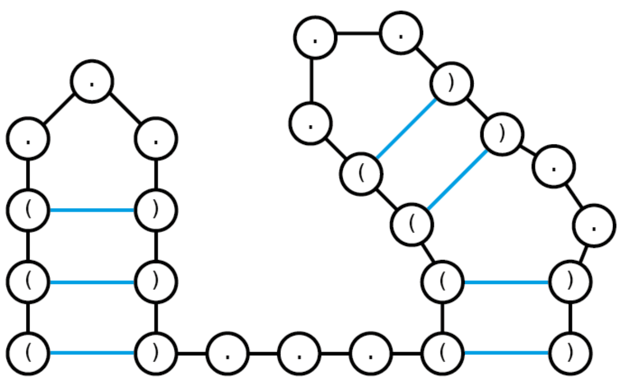
Solution



This is the only possible nested structure based on the dot-bracket string given.

2b)

Draw a graph representation of one possible crossing structure that can be encoded by the dot-bracket string. Assume a minimal loop length of 3.

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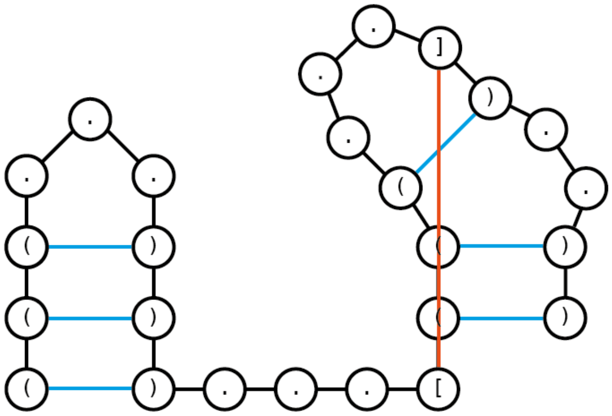
Solution



Dot-bracket string: (((. . .))). . . [(((. . .])..))

There are multiple other possible crossing structures. (e.g. (((. . .))). . . [((<. . .])..>))

Exercise 3

Given the following partially filled Nussinov matrix N using a minimal loop length $l = 0$, i.e. neighbored nucleotides are allowed to pair.

i		G	C	C	G	G	A	C	G	
1	0	0	1	1	?					G
2		0	0	0	1	2				C
3			0	0	1	1	1			C
4				0	0	0	0	?		G
5					0	0	0	1	1	G
6						0	0	0	1	A
7							0	0	1	C
8								0	0	G
j	0	1	2	3	4	5	6	7	8	

3a)

What are the values of the green and red entry?

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Solution green: 2

red: 1

3b)

How many tracebacks exist for the red entry using the original recursion by Nussinov?

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Solution There exist two tracebacks for the red entry; pairing with either G.

Exercise 4

Given any matrix N filled by Nussinov's algorithm for and RNA sequence S of length n. Discuss which of the following statements are correct or wrong.

The entry $N_{1,n}$ of the Nussinov matrix encodes ...

4a)

... the optimal structure.

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Solution wrong; It only encodes the base pair number for the optimal structure.

4b)

... the minimum free energy (mfe) structure.

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Solution wrong; No energy minimization is done.

4c)

... the maximal number of base pairs for sequence $S_1..S_n$.

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Solution correct

4d)

. . . the traceback end.

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Solution wrong; It encodes the traceback start.

4e)

. . . the maximal number of base pairs for any structure.

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Solution correct

4f)

. . . information for a unique structure.

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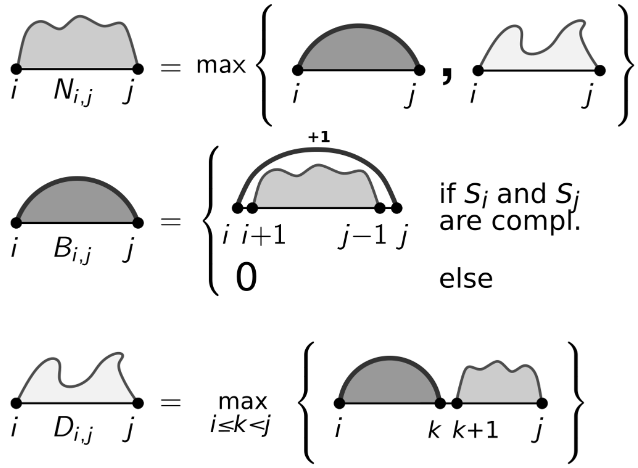
Solution wrong; Typically there is more than one optimal structure with maximal number of base pairs.

Exercise 5



5a)

Provide all recursion and initialization details for the following recursion depictions. Note, also ensure a minimal loop length l within your recursions.

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Solution

$$
\begin{aligned}
N_{i,i} = N_{i,i-1} &= && 0 \text{ (no init for } B \text{ and } D \text{ needed)} \\
\forall_{1 \leq i < j \leq n} : N_{i,j} &= && max\left\{B_{i,j}, D_{i,j}\right\} \\
B_{i,j} &= && \begin{cases} N_{i+1,j-1} + 1 & \text{if } i + l < j \wedge S_i, S_j \text{ compl.} \\ 0 & \text{else} \end{cases} \\
D_{i,j} &= && \max_{i \leq k < j} \left\{B_{i,k} + N_{k+1,j}\right\} \text{ (only valid for } i < j\text{)}
\end{aligned}
$$