

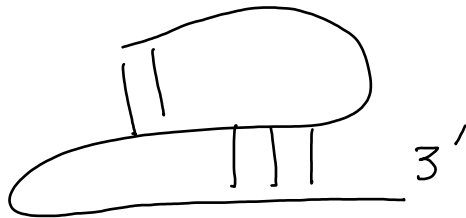
RNA secondary structures with pseudo-knots

A) What is a pseudo-knot?

- RNA secondary structure S wch that $\exists i < k < j < l$ s. t. (i, j) & (k, l) are base pairs σ_S

sec. structures with "crossing interaction"

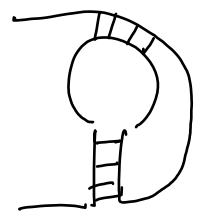
ex:



- important for RNA functions
 - -1 frameshift element
 - human telomerase
 - p. k. in viruses to create t-RNA-like structures & infiltrate cells.
 - * self-splicing introns

• Classification

most common is H-type PK



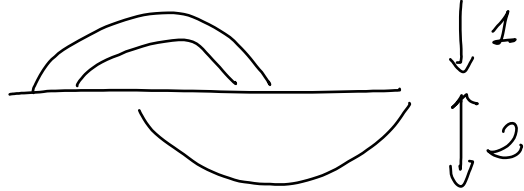
• page classification

secondary structure without pseudo-knot
 can be represented linearly using half-page

ex:



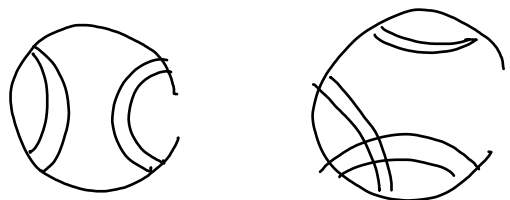
odd half page to represent H-type



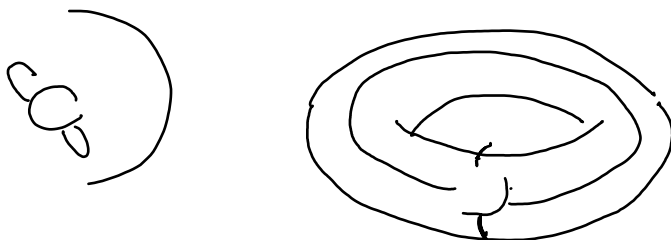
p.k. can be classified by the number of
 arcs needed to draw them without
 interaction crossing each other

genus classification (Bon et al. 2008)

holes in torus needed to draw a
 circular RNA sec struct. w/o crossing
 interactions.



measure the
 openness of
 R & also the
 seric hindrance

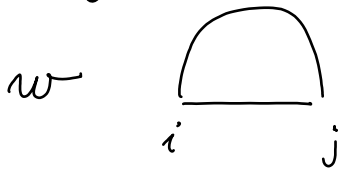


we see that the abundance of PK is correlated with genus

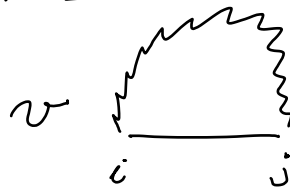
B. Prediction of RNA sec. structures with pseudo-knots.

1st Algo: Rivas & Eddy, 1999)

Feynman Diagrams



(i, j) unknown

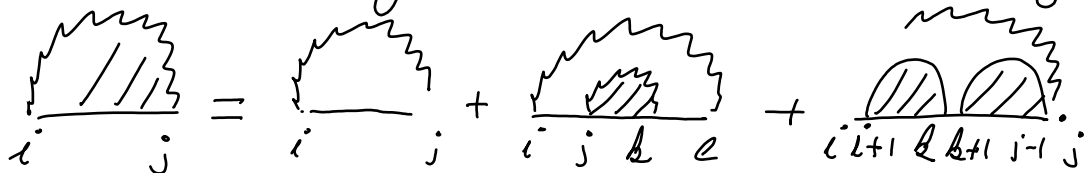


(i, j) base pair

Recursion for w in nested algo



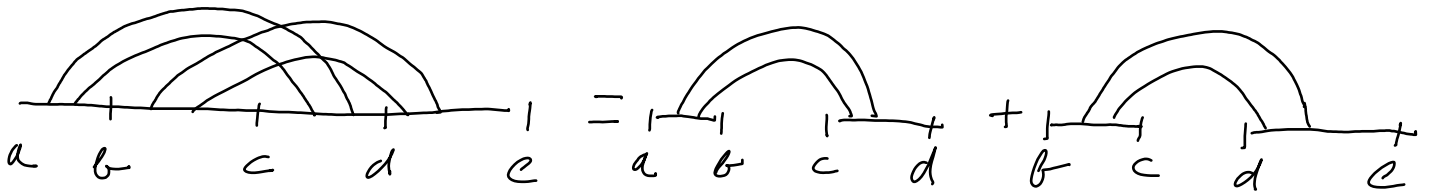
Recursion for v in nested algo



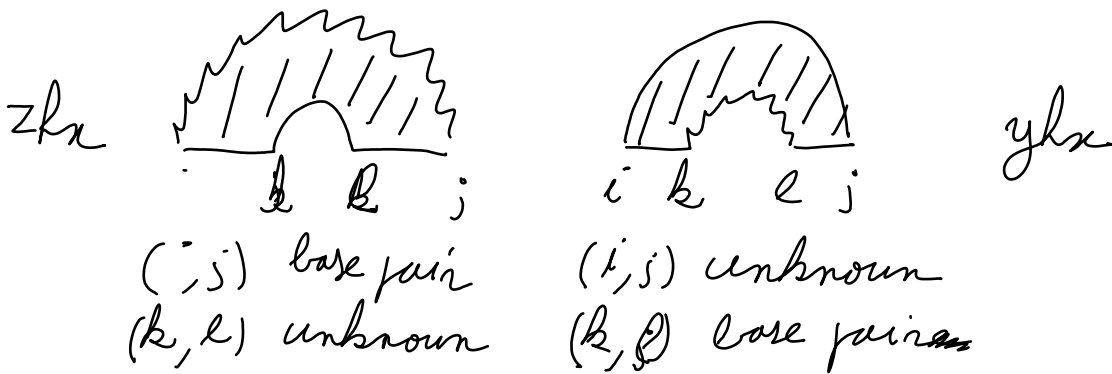
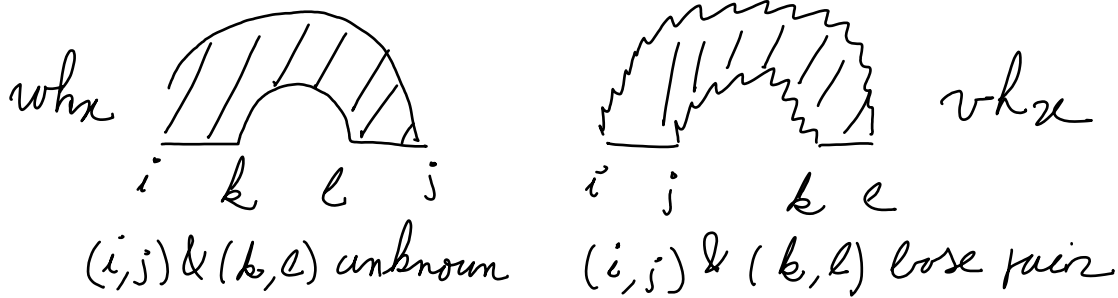
Rd: each case matches an energy case (hairpin, stack, etc.)

Limitation: base pairs are added in the recursion of v. But cannot cross each other (nested)

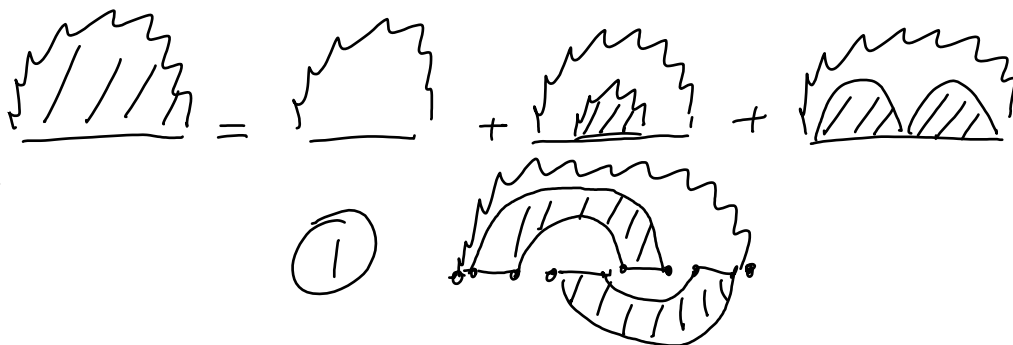
How can we build pseudo-knots?
 i.e. decompose)



Generalization of N.J. matrices to
 gap matrices (4 types)



recursion for $x \Rightarrow$ add a case



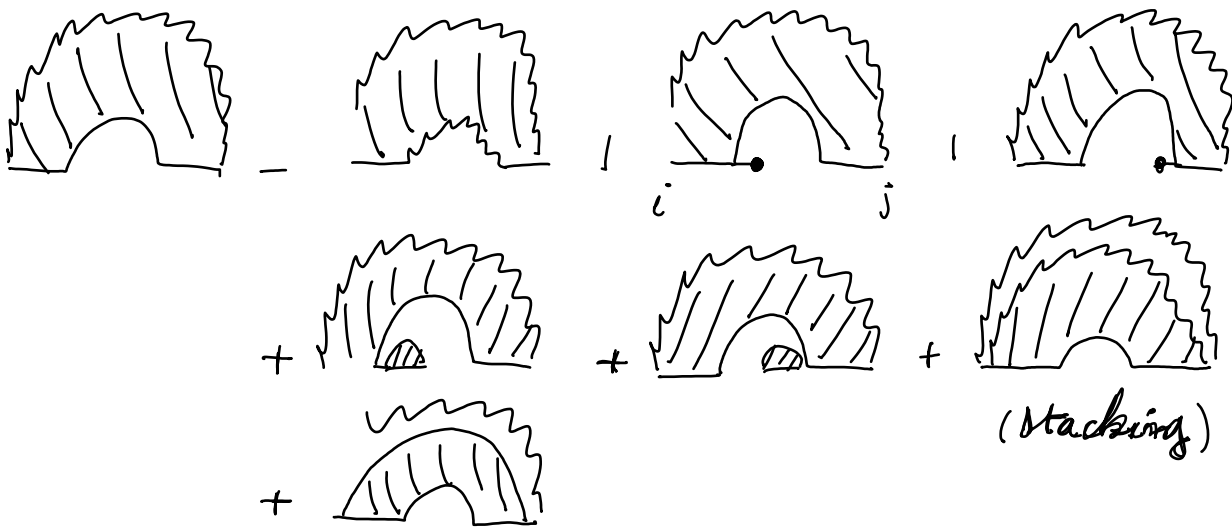
recursion for vhx



important for stacking

all other cases

recursion for Bhx



this decomposition expands 2 cases:

extension of the inner gap with unknown status

- addition of external base pair

recursions of yxh vxh in the assignment.

Energy model: extended nearest neighbor energy model.

- ⊕ penalty for new pair in non-nested multi-loop
- ⊖ penalty for creation of a non-nested M-L
- ⊙ creation of a P.K.

complexity: $O(n^6)$ - time

$O(n^4)$ space

Q: Does this algo cover all Pseudo-knots?

ABAB, ABACBC, ABA BDCD ✓ ok
(planar)

ABCABC ok too

But ABCADB E DE ✗ Fails

we cannot ~~decide~~ characterize a priori

In fact, RNA folding with P.K. is NP-hard.

(Lyngst ~~2004~~ 2000) (Abutsu, 2000)

∴ why? ~~needing all~~
max weighted matching problem
(RNA with max base pair weight) can be
solved in $O(n^3)$.

⇒ the problem is NP-hard with stacking
(Lyngst, 2004)

In Practice. algo implemented

- PKnots (Rivas & Eddy 1999) - t ne Bon & Orland, 2011)
- PKnot (Sato et al. 2011)
- nobknot (Jellousov & Matheus, 2010)