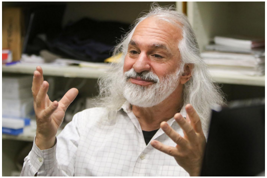
Distribution of endhered patterns in RNA-related secondary structures

Célia Biane[1], Greg Hampikian[2], Sergey Kirgizov[3],
Khaydar Nurligareev[4], Daniel Pinson[3]

[1]LaBRI (Bordeaux), [2]CompGenomics (USA), [3]LIB (Dijon), [4]LIP6 (Paris)

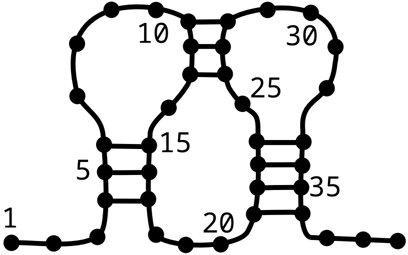
SeqBIM
2024 – 28-29 nov.
Rennes

No occurrences of these patterns in the human genome	CGCTCGACGTA, GTCCGAGCGTA, CGACGAACGGT, CCGATACGTCG

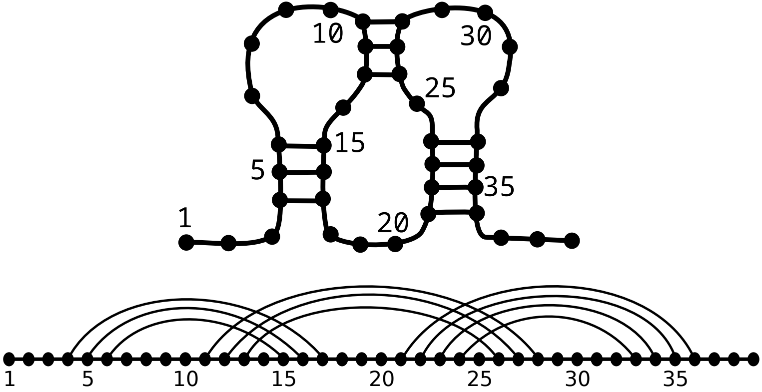
Absent sequences: nullomers and primes, 2007
by Greg Hampikian and Tim Andersen

Explore absense and presence of patterns in RNA secondary structures

RNA secondary structures and matchings



RNA secondary structures and matchings



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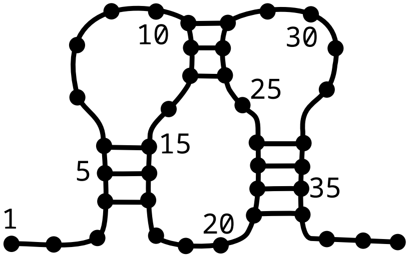
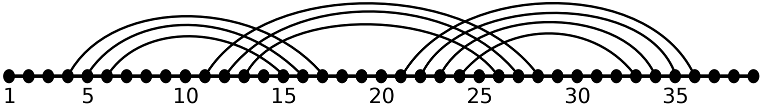
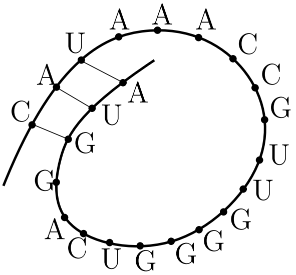
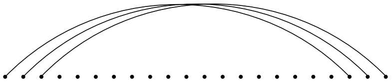




...(((....[[[.)))...((((.]]]....))))...

Snail-like pseudoknotted RNA

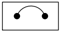




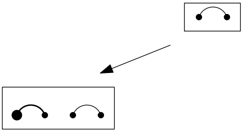
```
([{...............)]}
CAUAAACCGUUGGGUCAGGUA
```

Does it exist in nature ?

Perfect matchings



Perfect matchings



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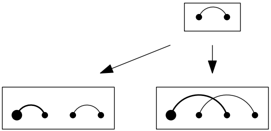
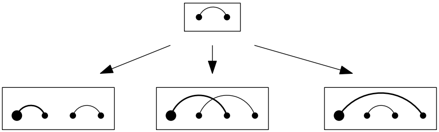
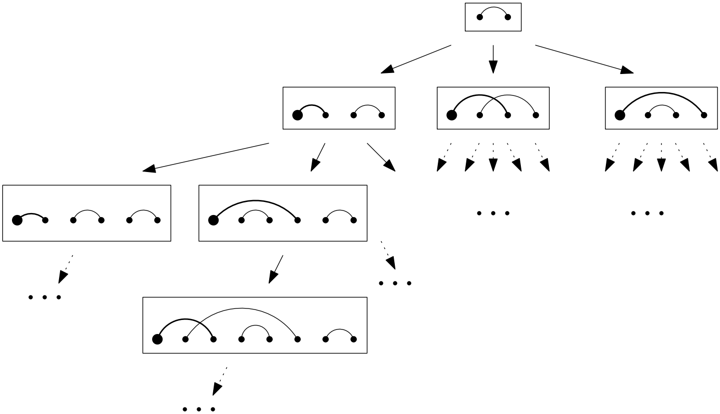


Perfect matchings



Perfect matchings



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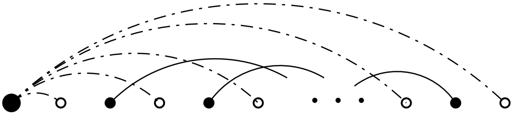


$2(n-1)$ old points

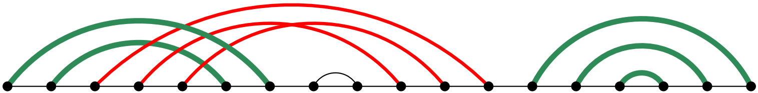
$2(n-1)+1$ possible new arcs endings

$a_n = (2n-1)\cdot(2n-3)\cdots 5\cdot 3\cdot 1 = (2n-1)!!$

A1147 in Sloane's Encyclopedia : 1, 3, 15, 105, 945, 10395,...

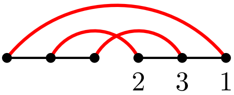
Endhered patterns in perfect matchings

(endhered = **end**-ad**hered**)

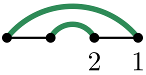


This matching contains

1 occurrence of pattern



3 occurrences of pattern



We write patterns in condensed form, indicating sequentially the order of starting points corresponding to arc ends.

(En français.... les motifs collex = **coll**és par leurs **ex**trémités)

What's the distribution of endhered patterns in perfect matchings?

Let's start with  and 

Distribution of  in perfect matchings

k \ n	1	2	3	4	5	6	7	8	9	OEIS
0	1	2	10	68	604	6584	85048	1269680	21505552	A165968
1	0	1	4	30	272	3020	39504	595336	10157440	A179540
2	0	0	1	6	60	680	9060	138264	2381344	
3	0	0	0	1	8	100	1360	21140	368704	
4	0	0	0	0	1	10	150	2380	42280	
5	0	0	0	0	0	1	12	210	3808	
6	0	0	0	0	0	0	1	14	280	
7	0	0	0	0	0	0	0	1	16	
8	0	0	0	0	0	0	0	0	1	

Let $a_{n,k}$ be the number of matchings with n arcs and k occurrences of pattern . Exponential generating function is

$$\sum_{n=0}^{\infty}\sum_{k=0}^{n} a_{n+1,k}\frac{z^n}{n!}u^k = \frac{e^{z(u-1)}}{\sqrt{(1-2z)^3}}$$

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Let $a_{n,k}$ be the number of matchings with n arcs and k occurrences of pattern . Asymptotics

$$a_{n,k} \sim \frac{1}{2^k k!} \left(\frac{2}{e}\right)^{n+1/2} n^n \qquad \frac{a_{n,k}}{a_{n,k+1}} \sim 2(k+1).$$

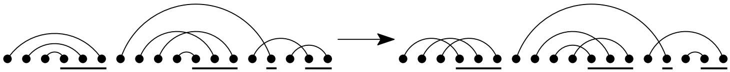
Does the distribution of  differ from the distribution of ?

Endhered twist

Left endhered twist
All runs of consecutive **starting points** are reversed.

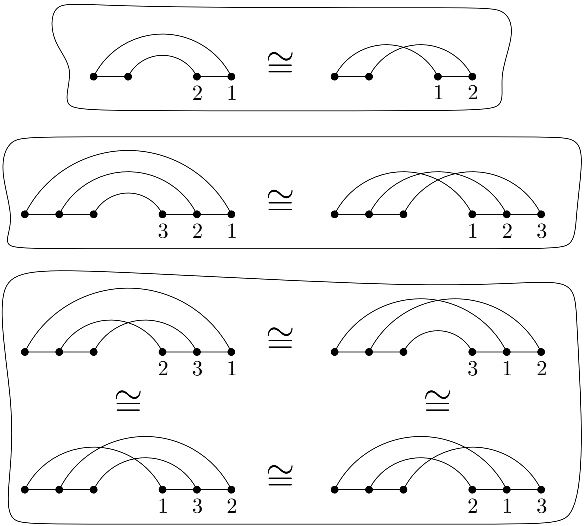
Right endhered twist
All runs of consecutive **ending points** are reversed.

Example of right twist:



Thanks to an endhered twist
 **and**  **have the same distribution!**

Endhered pattern equivalence



equivalence = same distribution

Goulden-Jackson cluster method and endhered patterns

Endhered pattern enumeration in matchings

Imagine we have g.f. for a distribution of a given pattern μ:

$$D_\mu(z,u) = \sum_{n=0}^{\infty}\sum_{k=0}^{\infty} d_{n,k} z^n u^k.$$

There are $d_{n,k}$ matchings of size n with k occurrences of μ.

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We label some occurrences by variable v,
i.e. u is replaced either by 1 or by v.

$$H_\mu(z,v) = \sum_{n=0}^{\infty}\sum_{k=0}^{\infty} h_{n,k} z^n v^k = D_\mu(z, 1+v).$$

It is simplier to construct H_μ than D_μ !

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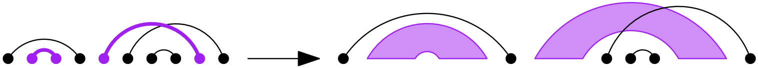
It is simplier to construct H_μ than D_μ !
Then we recover by the symbolic inclusion-exclusion:
$D_\mu(z,u) = H_\mu(z,u-1)$

Idea: replace some arcs by patterns

(simple case without self-overlappings)



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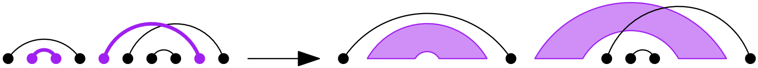


We label certain arcs by v, these arcs will be replaced by occurrences of pattern μ.

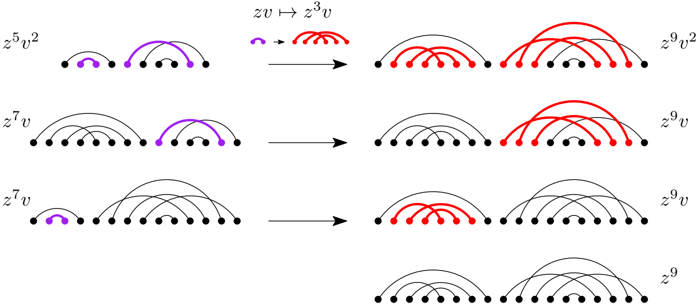
$$F(z + zv),$$

where $F(z)$ is the ordinary g.f. for all matchings.

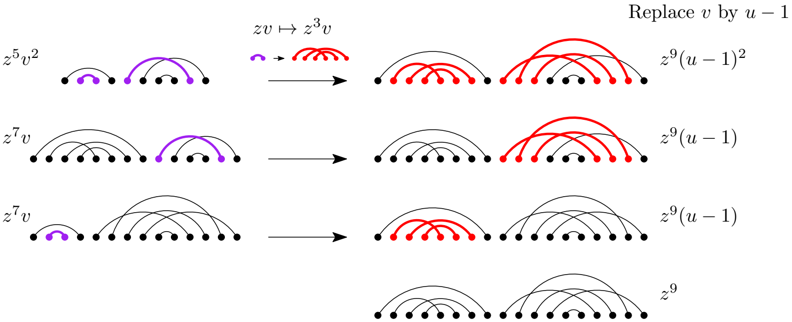
$$F(z) = \sum_{n=0}^{\infty} (2n-1)!!\, z^n = 1 + z + 3z^2 + 15z^3 + 105z^4 + \dots$$

Consider, for instance, the endhered pattern

Zero self-overlappings



Zero self-overlappings



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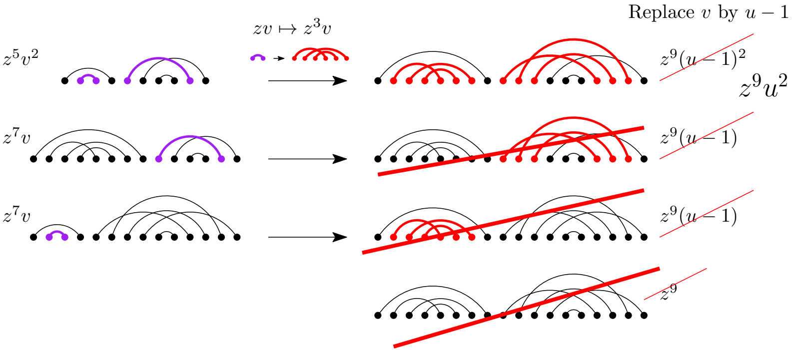

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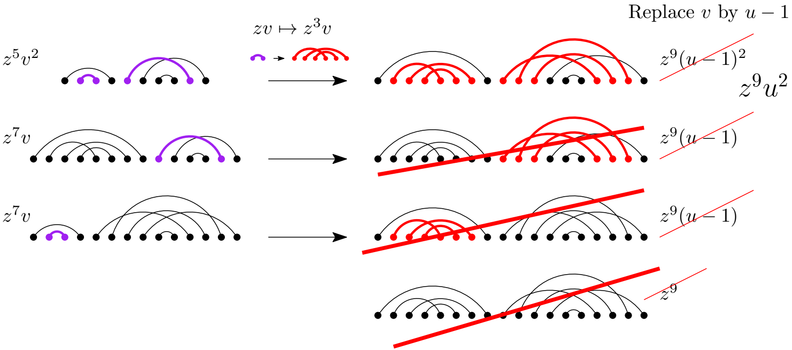

$$H_\mu(z, v) = F(z + z^\ell v),$$

$$D_\mu(z, u) = H_\mu(z, u-1),$$

where ℓ is the size of pattern μ.

WITH SELF-OVERLAPPINGS ?

Autocorrelation encodes self-overlappings

An *autocorrelation polynomial* $A(\pi; z)$ for an endhered pattern π of size n is

$$A(\pi; z) = 1 + \sum_{k \in S} z^{n-k},$$

where S is the set of lengths of possible overlappings of two different occurrences of the pattern π in some matching.
In other words, z^{n-k} means that two occurrences have k edges in common.

$A(21; z) = A($  $; z) = 1 + z,$

$A(12; z) = A($  $; z) = 1 + z,$

$A(132; z) = A($  $; z) = 1,$

$A(321; z) = A($  $; z) = 1 + z + z^2,$

$A(3412; z) = A($  $; z) = 1 + z^2,$

$$A(7564231; z) = 1 + z^3 + z^6.$$

Enumeration and asymptotics

Let π be an endhered pattern of size ℓ, with autocorrelation $A(\pi; z) = 1 + z^m + \dots$ (m is the smallest positive power)
If $A(\pi; z) = 1$, then we let $m = 0$.
Generating function:

$$\sum_{n,k \geq 0} a_{n,k}\, z^n u^k = F\left(z + \frac{(u-1)z^\ell}{1 - (u-1)(A(\pi; z) - 1)}\right)$$

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Asymptotics by Borinsky's approach: as $n \to \infty$,

$$\frac{a_{n,k}}{(2n-1)!!} \sim \begin{cases} \dfrac{1}{k!\, 2^{k(\ell-1)}} \cdot \dfrac{1}{n^{k(\ell-2)}} & \text{if} \quad m = \ell - 1 \text{ or } m = 0 \\ \dfrac{1}{(2n)^{k(\ell-2)}} \displaystyle\sum_{s=1}^{k} \frac{1}{s!\, 2^s} \binom{k-1}{s-1} & \text{if} \quad m = \ell - 2 \\ \dfrac{1}{2(2n)^{km+(\ell-2-m)}} & \text{if} \quad 0 < m < \ell - 2 \end{cases}$$

Well... what about real-world data ?

Real-world data

Data comes from PDB, we have used X3DNA-DSSR to obtain dot-bracket notations from 3D coordinates of atoms.
FR3D Python can also be used.

Our database looks like this:

```
2GQ5 ((((((((&))))))))&((((((((&))))))))
2IRN (((..(((.&)))..))).
2IZ8 (((.((....))))).&((.((....))))
3VAL ......&......&......&.....
437D ..(((((..[[[.)))))).......]]]
4M40 ((((((.(((((.((.......((((.(.[.(..])..).)))))).))))).))))))
6IV6 ....(((((.....))))).......
7K16 {{...((((((((....))))))((((...[[[...))))}}.))...]]]
```

Interactive web application by Daniel Pinson

https://rna.kirgizov.link

Possible research directions

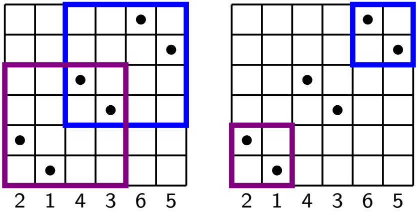
- Explain possible autocorrelations or endhered patterns, (in other words, period sets)

  1, 2, 4, 4, 7, 7, 11, 12, 18, ... ? (shift of A304178 ?)
  Bijection with sets of palindrome prefix lengths, over all binary palindromes of length n ???

- Characterise real-world RNA secondary structures by pattern distributions (avoidance-presence)

Endhered patterns in matchings and RNA
Célia Biane, Greg Hampikian, Sk, Khaydar Nurligareev
https://arxiv.org/abs/2404.18802
To appear in *Journal of Computational Biology*

Asymptotics of self-overlapping permutations
Sk and Khaydar Nurligareev
https://arxiv.org/abs/2311.11677
To appear in *Discrete Mathematics*



Interactive web application by Daniel Pinson *et al.*
https://rna.kirgizov.link

Clusters of endhered patterns in permutations and matchings. In preparation.

Merci !