Pseudoknot RNA structures with arc-length $\geq 4$

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Abstract

In this paper we study $k$-noncrossing RNA structures with minimum arc-length 4 and at most $k - 1$ mutually crossing bonds. Let $T_k^{[4]}(n)$ denote the number of $k$-noncrossing RNA structures with arc-length $\geq 4$ over $n$ vertices. We prove (a) a functional equation for the generating function $\sum_{n \geq 0} T_k^{[4]}(n) z^n$ and (b) derive for $k \leq 9$ the asymptotic formula $T_k^{[4]}(n) \sim c_k n^{-((k-1)^2+(k-1)/2)} \gamma_k^{-n}$. Furthermore we explicitly compute the exponential growth rates $\gamma_k^{-1}$ and asymptotic formulas for $4 \leq k \leq 9$.

Keywords: RNA pseudoknot structure, generating function, singularity analysis, $k$-noncrossing diagram, exponential growth rate.
1. Introduction

RNA pseudoknot structures [2, 28] are a reality. They occur in functional RNA (RNaseP [18]), ribosomal RNA [17] and are conserved in the catalytic core of group I introns. Due to the crossings of arcs their theory differs considerably from RNA secondary structures. Pseudoknots are inherently noninductive and the standard dynamic programming folding paradigm employed for RNA secondary structures can only generate particular subclasses of pseudoknot structures [21]. Recently the concept of $k$-noncrossing RNA structures has been introduced [14]. Here the idea is that the complexity of the structure is captured by an inherently “local” property: the maximal number of mutually crossing bonds. A structure is $k$-noncrossing, if there exists no $k$-set of mutually crossings arcs. The locality is in fact of central importance: point in case are RNA bisecundary structures introduced by P.F. Stadler [12]. These structures are constructed as superpositions of two RNA secondary structures and correspond to planar $3$-noncrossing structures [14]. The planarity property is clearly non-local and at present time the generating function for RNA bisecundary structures is not known.

A very intuitive approach to the $k$-noncrossing property of RNA molecules is their diagram representation [12]. It is obtained by drawing the nucleotide-labels 1, . . . , $n$ in increasing order in a horizontal line and drawing the arc-labels $(i, j)$ in the upper half-plane, if and only if $i$ and $j$ are paired in the structure, see Figure 1. We
call a diagram \( k \)-noncrossing, if it does not contain \( k \) mutually crossing arcs. The length of an arc \((i, j)\) is given by \( \lambda = j - i \) and a stack of length \( \sigma \) is a sequence of “parallel” arcs of the form \(((i, j), (i + 1, j - 1), \ldots, (i + (\sigma - 1), j - (\sigma - 1)))\). A \( k \)-noncrossing RNA structure is a \( k \)-noncrossing diagram over \([n]\) having minimum arc-length \( \lambda > 1 \). These structures have been studied in \([14, 15]\) via a bijection into vacillating tableaux in the context of tangled diagrams \([4]\). For the enumeration of structures with crossing arcs the tableaux-interpretation is non-optional. There is, to the best of our knowledge, no way to inductively construct \( k \)-noncrossing structures, despite the fact that they are \( D \)-finite.

For RNA secondary structures (2-noncrossing RNA structures), certain combinatorial restrictions, for instance minimum arc-length or stack-size are relatively straightforward to deal with. The combinatorics and prediction of RNA secondary structures has been pioneered by Waterman et al. in a series of excellent papers \([20, 26, 25, 27, 10]\). He proved for the number of RNA secondary structures of length \( n \) (arc-length \( \geq 2 \)), \( T_{2}^{[2]}(n) \), the fundamental recursion

\[
T_{2}^{[2]}(n) = T_{2}^{[2]}(n - 1) + \sum_{s=0}^{n-3} T_{2}^{[2]}(n - 2 - s)T_{2}^{[2]}(s),
\]

where \( T_{2}^{[2]}(0) = T_{2}^{[2]}(1) = T_{2}^{[2]}(2) = 1 \). Eq. (1.1) is an immediate consequence considering secondary structures as peak-free Motzkin-paths, i.e., peak-free paths with \( up \), \( down \) and \( horizontal \) steps that stay in the upper halfplane, starting at the origin and end on the \( x \)-axis. The recursion is in particular the key for all asymptotic
results since it immediately implies a functional equation for the corresponding generating function. This allows the application of Darboux-type theorems \[11, 24\]. For the number of secondary structures with minimum arc-length $\lambda$, $T_2^{[\lambda]}(n)$, it is straightforward to derive

\[
T_2^{[\lambda]}(n) = T_2^{[\lambda]}(n - 1) + \sum_{s=0}^{n-(\lambda+1)} T_2^{[\lambda]}(n - 2 - s)T_2^{[\lambda]}(s). 
\]

All asymptotic formulae for secondary structures are of the same type: a square root. In other words, the asymptotic behavior is determined by an algebraic branch singularity with the subexponential factor $n^{-\frac{3}{2}}$.

The situation changes for $k$-noncrossing RNA structures. A different approach has to be made, since in lack of functional equations Darboux-type theorems \[24\], cannot be employed. The idea is to analyze the dominant singularities directly, using Hankel contours. Singularity analysis has been pioneered by P. Flajolet and A.M. Odlyzko \[7\]. Its basic idea is the construction of the “singular-analogue” of the Taylor-expansion. It can be shown that, under certain conditions, there exists an approximation, which is locally of the same order as the original function. The particular, local approximation allows then to derive the asymptotic form of the coefficients. In contrast to the subtraction of singularities-principle \[19\] the only contributions to the contour integral come from segments close to the singularity. In our situation all conditions for singularity analysis are satisfied, since the generating functions involved are $D$-finite \[22, 30\] and $D$-finite functions have an analytic
continuation into any simply-connected domain containing zero. Our approach also works for tangled diagrams [5], which represent the combinatorial framework for RNA tertiary interactions. Our analysis confirms that the particular singularity-type of the generating function of $k$-noncrossing RNA structures depends solely on the crossing number [15, 16]. While the location of the singularity shifts as a function of the arc-length, all subexponential factors remain the same. Furthermore an interesting feature is the appearance of logarithms for $k \equiv 1 \mod 2$ in the singular expansion.

Due to biophysical constraints a minimum arc-length of four can be assumed for minimum free energy RNA structures. The key objective of this paper is to derive and analyze the generating function for $k$-noncrossing RNA structures with minimum arc-length 4, see Table 1. Based on our results the next step is to compute the subset of canonical structures, i.e. the subset of structures with arc-length $\geq 4$, having no isolated arcs. While it is straightforward to obtain eq. (1.2) from eq. (1.1) considerable complication arises, when considering $k$-noncrossing structures with arc-length $> 3$. To understand why, one observes that the number of ways to place 3-arcs satisfies a new type of recursion, see eq. (3.6). As a result and in contrast to $k$-noncrossing structures with minimum arc-length $\lambda \leq 3$ the generating function $\sum_{n \geq 0} T_k^{[4]}(n) z^n$ turns out to be a sum of two power series (Theorem 2). The exponential growth rate can easily be computed via the formula given in Theorem 3, see Table 2 and Figure 3.
The paper is organized as follows: in Section 2 we provide the background on the methods used in this paper. In Section 3 we prove a functional equation relating RNA structures to $k$-noncrossing matchings. We then study the singularity of the generating function and obtain the asymptotic formula in Section 4. Finally, in Section 5 we detail some key ideas instrumental for the proof of Theorem 2.
2. Preliminaries

In this Section we provide some background on the generating functions of $k$-noncrossing matchings \cite{3} \cite{13} and $k$-noncrossing RNA structures \cite{14} \cite{15}. We denote the numbers of $k$-noncrossing matchings and RNA structures with arc-length $\geq \lambda$ by $f_k(2n)$ and $T_k^{[\lambda]}(n)$, respectively. The former corresponds to $k$-noncrossing diagrams without isolated points and the latter to $k$-noncrossing diagrams with arc-length $\geq \lambda$.

Furthermore, let $T_k^{[\lambda]}(n, \ell)$ denote the number of $k$-noncrossing RNA structures with arc-length $\geq \lambda$ having exactly $\ell$ isolated points and $M_k(n)$ denotes the number of partial matchings, or equivalently the number of $k$-noncrossing diagrams over $[n]$ (i.e. with isolated points and minimum arc-length 1). Pfriemgheim’s Theorem \cite{23} guarantees the existence of a positive real, dominant singularity of $\sum_{n \geq 0} M_k(n) z^n$ which we denote by $\mu_k$. In order to get some intuition about the various types of diagrams involved, see Figure 2.

2.1. $k$-noncrossing matchings. Our main objective is to discuss some basic properties of $f_k(2n)$ and to give an asymptotic formula. Let us recall that a power series $u(x)$ is called $D$-finite over the function field $K(x)$ if $\dim \langle u, u', \ldots \rangle_{K(x)} < \infty$ \cite{22}. The generating function of $k$-noncrossing matchings satisfies the following identity due to Grabiner et al. \cite{9}

\begin{equation}
\sum_{n \geq 0} f_k(2n) \cdot \frac{z^{2n}}{(2n)!} = \det [I_{i-j}(2z) - I_{i+j}(2z)]_{i,j=1}^{k-1},
\end{equation}
where

\begin{equation}
I_r(2z) = \sum_{j \geq 0} \frac{z^{2j+r}}{j!(r+j)!}
\end{equation}

denotes the hyperbolic Bessel function of the first kind of order \( r \). Eq. (2.1) allows to conclude that

\begin{equation}
F_k(z) = \sum_{n \geq 0} f_k(2n)z^{2n}
\end{equation}
is \( D \)-finite. Indeed, the hyperbolic Bessel function \([9]\) itself is \( D \)-finite and \( D \)-finite functions form an algebra closed under taking Hadamard products \([22]\). Therefore \( D \)-finiteness of \( F_k(z) \) follows from eq. (2.1). However, beyond the cases \( k = 2 \) and \( k = 3 \), eq. (2.1) does not give directly explicit formulas for \( f_k(2n) \) or \( F_k(z) \). For small \( k \)-values asymptotic formulas can be obtained using the approximation of the Bessel function

\begin{equation}
I_m(z) = \frac{e^z}{\sqrt{2\pi z}} \left( \sum_{h=0}^{H-1} \frac{(-1)^h}{h!8^h} \prod_{t=1}^h (4m^2 - (2t-1)^2)z^{-h} + O(|z|^{-H}) \right)
\end{equation}
which holds for \(-\frac{\pi}{2} < \arg(z) < \frac{\pi}{2}\) \([1]\). For arbitrary \( k \), systematic analysis of the determinant \( \det[I_{i-j}(2x) - I_{i+j}(2x)]_{i,j=1}^{k-1} \) by Jin et al. \([13]\) shows for arbitrary \( k \)

\begin{equation}
f_k(2n) \sim c_k n^{-(k-1)^2+(k-1)/2} (2(k-1))^{2n}, \quad c_k > 0.
\end{equation}

In the following we shall denote the dominant singularity of \( F_k(z) \) by \( \rho_k = \frac{1}{2(k-1)} \).
2.2. \textit{k-noncrossing RNA structures}. \textit{k}-noncrossing RNA structures are \textit{k}-noncrossing diagrams satisfying specific arc-length conditions. The latter induce asymmetries (for instance 1-arcs are not preserved) which prohibit enumeration using Gessel and Zeilberger’s reflection-principle \cite{Gessel:1988} directly (the reflection principle implies eq. (2.1)). For any \(k \geq 2\) the numbers of \textit{k}-noncrossing RNA structures with minimum arc-length \(\geq 2\) are given by \cite{Gessel:1988}

\begin{equation}
T^{[2]}_k(n) = \sum_{b=0}^{|n/2|} (-1)^b \binom{n-b}{b} M_k(n-2b)
\end{equation}

and we have \cite{Gessel:1988}

\begin{equation}
T^{[2]}_k(n) \sim c^{[2]}_k n^{-(k-1)^2+(k-1)/2} (\gamma^{[2]}_k)^{-n}, \quad c^{[2]}_k > 0,
\end{equation}

where \(\gamma^{[2]}_k\) is the unique, solution of minimal modulus of \(\frac{z}{z^3-z+1} = \rho_k\). For \textit{k}-noncrossing RNA structures with arc-length \(\geq 3\) we have according to \cite{Gessel:1988}

\begin{equation}
\forall k > 2; \quad T^{[3]}_k(n) = \sum_{b \leq \lfloor n/2 \rfloor} (-1)^b \lambda(n, b) M_k(n-2b),
\end{equation}

where \(\lambda(n, b)\) denotes the number of way selecting \(b\) arcs of length \(\leq 2\) over \(n\) vertices. The nonexplicit terms \(\lambda(n, b)\) vanish in the functional equation

\begin{equation}
\sum_{n \geq 0} T^{[3]}_k(n) z^n = \frac{1}{1 - z + z^2 + z^3 - z^4} \sum_{n \geq 0} f_k(2n) \left(\frac{z - z^3}{1 - z + z^2 + z^3 - z^4}\right)^{2n}.
\end{equation}
Singularity analysis based on eq. (2.9) eventually allows to derive the asymptotic formula

\[ T_k^{[3]}(n) \sim c_k^{[3]} n^{-(k-1)^2+(k-1)/2} (\gamma_k^{[3]})^{-n}, \quad c_k^{[3]} > 0, \]

where \( \gamma_k^{[3]} \) denotes the unique, minimal positive real solution of

\[ \frac{z^3 - z}{1 - z + z^2 + z^3 - z^4} = \rho_k. \]

2.3. Singularity Analysis. Pfringsheim’s Theorem [23] guarantees that each power series with positive coefficients has a positive real dominant singularity. This singularity plays a key role for the asymptotics of the coefficients. In the proof of Theorem 3 it will be important to deduce relations between the coefficients from functional equations of generating functions. The class of theorems that deal with such deductions are called transfer-theorems [7]. One key ingredient in this framework is a specific domain in which the functions in question are analytic, which is “slightly” bigger than their respective radius of convergence. It is tailored for extracting the coefficients via Cauchy’s integral formula. Details on the method can be found in [22, 7]. In case of \( D \)-finite functions we have analytic continuation in any simply-connected domain containing zero [29] and all prerequisites of singularity analysis are met. We use the notation

\[ (2.11) \quad \{ f(z) = O(g(z)) \ \text{as} \ z \to \rho \} \iff \left\{ \frac{f(z)}{g(z)} \ \text{is bounded as} \ z \to \rho \right\} \]

The key result used in Theorem 3 is
Theorem 1. [2] Let \( f(z), g(z) \) be \( D \)-finite functions with unique dominant singularity \( \rho \) and suppose

\[
(2.12) \quad f(z) = O(g(z)) \quad \text{as} \quad z \to \rho.
\]

Then we have

\[
(2.13) \quad [z^n]f(z) = C \left( 1 - O\left(\frac{1}{n}\right) \right) [z^n]g(z)
\]

where \( C \) is a constant and \([z^n]h(z)\) denotes the \( n \)-th coefficient of the power series \( h(z) \) at \( z = 0 \).

3. THE GENERATING FUNCTION

In this Section we compute the generating function of \( \Phi_k^4(n) \), the number of \( k \)-noncrossing RNA structures with arc-length \( \geq 4 \). Our first result is a technical lemma which is instrumental in the proof of Theorem 2 below. The proof of the lemma given below is new and uses integral representations [6] instead of dealing with the combinatorial coefficients directly.

Lemma 1. Let \( z \) be an indeterminate over \( \mathbb{C} \). Then we have the identity of power series

\[
(3.1) \quad \forall |z| < \mu_k; \quad \sum_{n \geq 0} M_k(n) z^n = \left( \frac{1}{1 - z} \right) \sum_{n \geq 0} f_k(2n) \left( \frac{z}{1 - z} \right)^{2n}.
\]
Proof. Expressing the combinatorial terms by contour integrals \[6\] we obtain

\[
(3.2) \binom{n}{2m} = \frac{1}{2\pi i} \oint_{|u|=\alpha} (1+u)^n u^{-2m-1} du \quad f_k(2m) = \frac{1}{2\pi i} \oint_{|v|=\beta} F_k(v)v^{-2m-1} dv
\]

where \(\alpha, \beta\) are arbitrary small positive numbers. We derive

\[
M_k(n) = \frac{1}{(2\pi i)^2} \sum_m \oint_{|u|=\alpha, |v|=\beta} (1+u)^n u^{-2m-1} F_k(v)v^{-2m-1} dudv
\]

and furthermore

\[
M_k(n) = \frac{1}{(2\pi i)^2} \oint_{|v|=\beta} F_k(v)^{-1} \left[ \oint_{|u|=\alpha} \frac{(1+u)^n u}{(u+\frac{1}{v})(u-\frac{1}{v})} du \right] dv.
\]

Since \(u = \frac{1}{v}\) and \(u = -\frac{1}{v}\) are the only singularities (poles) enclosed by the particular contour, eq. (3.1) implies

\[
\oint_{|u|=\alpha} \frac{(1+u)^n u}{(u+\frac{1}{v})(u-\frac{1}{v})} du = 2\pi i \left[ \frac{(1+u)^n u}{u-\frac{1}{v}} \bigg|_{u=-\frac{1}{v}} + \frac{(1+u)^n u}{u+\frac{1}{v}} \bigg|_{u=\frac{1}{v}} \right]
\]

\[
= \pi i \left( \left[ 1 - \frac{1}{v} \right]^n + \left[ 1 + \frac{1}{v} \right]^n \right).
\]
Therefore, for $|z| < \mu_k$

$$\sum_{n \geq 0} M_k(n)z^n = \frac{1}{4\pi i} \sum_{n \geq 0} \oint_{|v| = \beta} F_k(v)v^{-1} \left( \left[ 1 - \frac{1}{v} \right]^n + \left[ 1 + \frac{1}{v} \right]^n \right) z^n dv$$

$$= \frac{1}{4\pi i} \oint_{|v| = \beta} F_k(v) \frac{1}{v - (v - 1)z} dv + \frac{1}{4\pi i} \oint_{|v| = \beta} F_k(v) \frac{1}{v - (v + 1)z} dv .$$

The first integrand has its unique pole at $v = -\frac{z}{1-z}$ and the second at $v = \frac{z}{1-z}$, respectively:

$$\frac{1}{v - (v - 1)z} = \frac{1}{v + \frac{z}{1-z}} \frac{1}{1-z} \quad \text{and} \quad \frac{1}{v - (v + 1)z} = \frac{1}{v - \frac{z}{1-z}} \frac{1}{1-z} .$$

In view of $F_k(z) = F_k(-z)$ we derive

$$\sum_{n \geq 0} M_k(n)z^n = \frac{1}{1-z} \left[ \frac{1}{2} F_k \left( -\frac{z}{1-z} \right) + \frac{1}{2} F_k \left( \frac{z}{1-z} \right) \right] = \frac{1}{1-z} F_k \left( \frac{z}{1-z} \right) ,$$

whence the lemma. \qed

Before we state the main result of this section, let us introduce some notation. We set

\begin{align}
(3.3) \quad u(z) &= \sqrt{1 + 4z - 4z^2 - 6z^3 + 4z^4 + z^6} \\
(3.4) \quad f_j(z) &= -\frac{2z^2 + z^3 - 1 + (-1)^j u(z)}{2(1 - 2z - z^2 + z^4)} .
\end{align}
Note that $f_j(z)$ is an algebraic function over the function field $K(z)$, i.e. there exists a polynomial with coefficients being polynomials in $z$ for which $f_j(z)$ is a root. This fact will be important when computing the subexponential factors of the asymptotic formula for $T_k^{[4]}(n)$.

**Theorem 2.** Let $k$ be a positive integer, $k > 3$ and $f_1(z)$ and $f_2(z)$ be given by eq. (3.4). Then we have the functional equation

$$
\sum_{n \geq 0} T_k^{[4]}(n) z^n = \frac{F_1(-z^2)}{1 - zf_1(-z^2)} \sum_{n \geq 0} f_k(2n) \left( \frac{z f_1(-z^2)}{1 - zf_1(-z^2)} \right)^{2n} + \frac{F_2(-z^2)}{1 - zf_2(-z^2)} \sum_{n \geq 0} f_k(2n) \left( \frac{z f_2(-z^2)}{1 - zf_2(-z^2)} \right)^{2n}.
$$

**Proof.** Claim 1. Let $\lambda(n, b)$ denote the number of ways to place $b$ arcs of length $\leq 4$ over $[n]$. Then we have

$$
T_k^{[4]}(n) = \sum_{b \leq \lfloor \frac{n}{2} \rfloor} (-1)^b \lambda(n, b) M_k(n - 2b)
$$

and $\lambda(n, b)$ satisfies the recursion
\( \lambda(n + 2b, b) = \)

\[ \lambda(n + 2b - 1, b) + \lambda(n + 2b - 4, b - 2) + \lambda(n + 2b - 5, b - 2) + \lambda(n + 2b - 6, b - 3) \]

\[ + \sum_{i=1}^{b} [\lambda(n + 2b - 2i, b - i) + 2\lambda(n + 2b - 2i - 1, b - i) + \lambda(n + 2b - 2i - 2, b - i)] \]

\[ - \lambda(n + 2b - 3, b - 1) , \]

where \( \lambda(n, 0) = 1, \lambda(n, 1) = 3n - 6 \) and \( n \geq 2b \). The proof of Claim 1 is analogous to the proof of Theorem 5 in [14]. In order to keep the paper self-contained we present it in Section 5.

The idea is now to relate \( \sum_{n \geq 0} T_{k}^{[4]}(n) z^n \) to the power series \( \sum_{n \geq 0} M_{k}(n) z^n \). For this purpose we compute

\[ \sum_{n \geq 0} T_{k}^{[4]}(n) z^n = \sum_{n \geq 0} (-1)^b \lambda(n, b) \sum_{m=2b}^{n} \binom{n - 2b}{m - 2b} f_k(m - 2b, 0) z^n \]

\[ = \sum_{b \geq 0} (-1)^b z^{2b} \sum_{n \geq 2b} \lambda(n, b) M_{k}(n - 2b) z^{n - 2b} \]

\[ = \sum_{b \geq 0} (-1)^b z^{2b} \sum_{n \geq 0} \lambda(n + 2b, b) M_{k}(n) z^n . \]

Interchanging the summations w.r.t. \( b \) and \( n \) we arrive at

\[ \sum_{n \geq 0} T_{k}^{[4]}(n) z^n = \sum_{n \geq 0} \left[ \sum_{b \geq 0} (-1)^b z^{2b} \lambda(n + 2b, b) \right] M_{k}(n) z^n . \]
Now we use the recursion formula for $\lambda(n, b)$. Let

$$\varphi_n(z) = \sum_{b \geq 0} \lambda(n + 2b, b) z^b.$$  

Multiplying in eq. (3.6) with $z^b$ and taking the summation over all $b$ ranging from 0 to $\lfloor n/2 \rfloor$ implies for $\varphi_n(z)$, $n = 1, 2, \ldots$

$$\left(1 - z^2 - z^3 - \frac{z}{1 - z}\right) \varphi_n(z) = \left(z^2 + \frac{z^2 + 1}{1 - z}\right) \varphi_{n-1}(z) + \left(\frac{z}{1 - z}\right) \varphi_{n-2}(z).$$

We make the Ansatz

$$f(x, y) = \sum_{n \geq 0} \sum_{j \leq \frac{n}{2}} \lambda(n, j) x^j \frac{y^n}{n!} = \sum_{n \geq 0} \varphi_n(x) \frac{y^n}{n!}.$$  

Multiplying in eq. (3.9) with $\frac{y^n}{n!}$ and taking the summation over all $n \geq 0$ leads to the partial differential equation

$$\left(1 - x^2 - x^3 - \frac{x}{1 - x}\right) \frac{\partial^2 f(x, y)}{\partial y^2} = \left(x^2 + \frac{x^2 + 1}{1 - x}\right) \frac{\partial f(x, y)}{\partial y} + \left(\frac{x}{1 - x}\right) f(x, y).$$

The general solution of eq. (3.11) can be computed by MAPLE and is given by

$$f(x, y) = F_1(x) \exp(f_1(x) \cdot y) + F_2(x) \exp(f_2(x) \cdot y)$$

$$= \sum_{n \geq 0} \left[F_1(x) f_1(x)^n + F_2(x) f_2(x)^n\right] \frac{y^n}{n!},$$
where $F_1(x), F_2(x)$ are arbitrary functions and

$$f_1(x) = \frac{2x^2 - x^3 + 1 + u(x)}{2(1 - 2x - x^2 + x^4)}, \quad f_2(x) = \frac{2x^2 - x^3 + 1 - u(x)}{2(1 - 2x - x^2 + x^4)}.$$  

By definition we have $f(x, y) = \sum_{n \geq 0} \varphi_n(x) \cdot \frac{x^n}{n!}$ and

$$\varphi_n(x) = F_1(x)(f_1(x))^n + F_2(x)(f_2(x))^n.$$  

In order to solve eq. (3.13) it remains to compute $F_1(x)$ and $F_2(x)$. The key information lies in the initial conditions for $f(x, y)$ and $\varphi_n(x)$. Explicitly we have $f(x, 0) = 1$ and $\varphi_1(x) = \lambda(1, 0) x^0 = 1$, which implies

$$F_1(x) + F_2(x) = 1$$
$$F_1(x)f_1(x) + F_2(x)f_2(x) = 1.$$  

Accordingly we obtain

$$F_1(x) = \frac{f_2(x) - 1}{f_2(x) - f_1(x)} \quad \text{and} \quad F_2(x) = \frac{f_1(x) - 1}{f_1(x) - f_2(x)}.$$  

In view of $\varphi_n(-z^2) = \sum_{b \geq 0} \lambda(n + 2b, b)(-1)^b z^{2b}$ we can express $\sum_{n \geq 0} T_k^n(n) z^n$ as follows:

$$\sum_{n \geq 0} T_k^n(n) z^n = \sum_{n \geq 0} \varphi_n(-z^2) M_k(n) z^n$$
$$= F_1(-z^2) \sum_{n \geq 0} M_k(n) \left(f_1(-z^2)z\right)^n + F_2(-z^2) \sum_{n \geq 0} M_k(n) \left(f_2(-z^2)z\right)^n.$$  

Now we use Lemma 1:

$$\sum_{n \geq 0} M_k(n) z^n = \left( \frac{1}{1-z} \right) \sum_{n \geq 0} f_k(2n) \left( \frac{z}{1-z} \right)^{2n},$$

which allows to express $\sum_{n \geq 0} T_k^4(n) z^n$ via $\sum_{n \geq 0} f_k(2n) z^{2n}$

$$\sum_{n \geq 0} T_k^4(n) z^n = \frac{F_1(-z^2)}{1 - z f_1(-z^2)} \sum_{n \geq 0} f_k(2n) \left( \frac{z f_1(-z^2)}{1 - z f_1(-z^2)} \right)^{2n} + \frac{F_2(-z^2)}{1 - z f_2(-z^2)} \sum_{n \geq 0} f_k(2n) \left( \frac{z f_2(-z^2)}{1 - z f_2(-z^2)} \right)^{2n}.$$ 

\[\square\]

4. Asymptotics of RNA pseudoknot structures with arc-length $\geq 4$

We set

\begin{align*}
\vartheta_1(z) & = \frac{z f_1(-z^2)}{1 - z f_1(-z^2)}, \\
\vartheta_2(z) & = \frac{z f_2(-z^2)}{1 - z f_2(-z^2)}.
\end{align*}

Note that $\vartheta_1(z)$ and $\vartheta_2(z)$ are algebraic functions over the function field $K(z)$.

**Theorem 3.** Let $k > 3$ be a positive integer and $\rho_k, \gamma_k$ denote the positive real singularities of $F_k(z) = \sum_{n \geq 0} f_k(2n) z^{2n}$ and $\sum_{n \geq 0} T_k^4(n) z^n$, respectively. Then the number of $k$-noncrossing RNA structures with arc-length $\geq 4$ is for $k \leq 9$
asymptotically given by

\[ T_k^{[4]}(n) \sim c_k n^{-((k-1)^2+(k-1)/2)} (\gamma_k^{-1})^n, \]

where \( \gamma_k \) is the unique positive, real solution of the equation \( \vartheta_1(z) = \rho_k \).

Proof. According to Theorem 2 we have the functional equation

\[
\sum_{n \geq 0} T_k^{[4]}(n) z^n = \frac{F_1(-z^2)}{1-z f_1(-z^2)} \sum_{n \geq 0} f_k(2n) \left( \frac{z f_1(-z^2)}{1-z f_1(-z^2)} \right)^{2n} + \frac{F_2(-z^2)}{1-z f_2(-z^2)} \sum_{n \geq 0} f_k(2n) \left( \frac{z f_2(-z^2)}{1-z f_2(-z^2)} \right)^{2n}.
\]

We consider the functions \( \vartheta_1(z), \vartheta_2(z) \) given by eq. (4.1) and eq. (4.2). The mappings \( x \mapsto \vartheta_1(x) \) and \( x \mapsto \vartheta_2(x) \) are strictly monotone and \( \vartheta_1(x) > \vartheta_2(x) \) for \( \vartheta_1(x) \in ]0, \frac{1}{5}[ \). Furthermore we have \( \rho_k < \rho_4 = \frac{4}{5} \), for \( k > 4 \). We can conclude from this that the real, positive dominant singularity, \( \gamma_k \), of \( \sum_{n \geq 0} T_k^{[4]}(n) z^n \), whose existence is guaranteed by Pfringsheim’s Theorem \cite{23}, satisfies

\[ \vartheta_1(\gamma_k) = \rho_k. \]

Being a determinant of Bessel functions \cite{9}, \( F_k(z) \) is \( D \)-finite. Moreover \( \vartheta_1(z) \) and \( \vartheta_2(z) \) are algebraic over \( K(z) \), analytic for \( |z| < \delta \), where \( \gamma_k < \delta \) and satisfy \( \vartheta_1(0) = \vartheta_2(0) = 0 \). Therefore the composition \( F_k(\vartheta_i(z)), i = 1, 2 \), is \( D \)-finite \cite{22} and
F_k(\vartheta_1(z)) \text{ and } F_k(\vartheta_2(z)) \text{ have singular expansions, respectively. We further observe that neither } F_k(-z^2) \text{ nor } F_k(-z^2) \text{ have a singularity } \zeta \text{ with } |\zeta| \leq \gamma_k. \text{ Hence if } \zeta \text{ is a dominant singularity of } \sum_n T_k[n] z^n \text{ then it is necessarily a singularity of } F_k(\vartheta_1(z)) \text{ or } F_k(\vartheta_2(z)). \text{ As for singularities of } F_k(\vartheta_1(z)) \text{ and } F_k(\vartheta_2(z)), \text{ we consider for } k \leq 9 \text{ the ODE satisfied by } F_k(z):}

\begin{equation}
q_{0,k}(z) \frac{d^e}{dz^e} F_k(z) + q_{1,k}(z) \frac{d^{e-1}}{dz^{e-1}} F_k(z) + \cdots + q_{e,k}(z) F_k(z) = 0,
\end{equation}

where \( q_{j,k}(z) \) are polynomials. The key point is now that any dominant singularity of \( F_k(z) \) is contained in the set of roots of \( q_{0,k}(z) \) \cite{22}. Computing the ODEs for \( 4 \leq k \leq 9 \) we can therefore conclude that \( F_k(z) \) has only the two dominant singularities \( \rho_k \) and \( -\rho_k \). Let \( S = \{ \zeta \mid \vartheta_1(\zeta) = \rho_k \text{ or } \vartheta_2(\zeta) = -\rho_k \} \). Then \( \gamma_k \) is the unique \( S \)-element of minimal modulus. We can draw two conclusions: first

\begin{equation}
[z^n] T_k[n] \sim c_k [z^n] F_k(\vartheta_1(z)) \quad \text{for some } c_k > 0
\end{equation}

and secondly, \( \gamma_k \) is the unique dominant singularity of \( \sum_n T_k[n] z^n \). In view of eq. (4.6) it thus remains to analyze the subexponential factors of the singular expansion of \( F_k(\vartheta_1(z)) \) at \( z = \gamma_k \). Since \( \vartheta_1(z) \) is regular at \( \gamma_k \) we are given the supercritical case of singularity analysis \cite{7}. In the supercritical case the subexponential factors of the compositum, \( F_k(\vartheta_1(z)) \) coincide with those of the outer function, \( F_k(z) \). According to \cite{13} we have for arbitrary \( k \)

\begin{equation}
f_k(2n) \sim n^{-((k-1)^2 + \frac{k-1}{2})} (\rho_k^{-1})^{2n}
\end{equation}
and therefore the subexponential factors of $F_k(z) = \sum_{n \geq 0} f_k(2n)z^{2n}$ coincide with those of $F_k(\vartheta_1(z))$, i.e. we have

\[(4.8)\quad T_k^4(n) \sim c_k n^{-((k-1)2+\frac{k-1}{2})} (\gamma_k^{-1})^n\]

proving the theorem. \hfill \Box

5. Proof of Claim 1

We recall that the numbers of $k$-noncrossing matchings and RNA structures with arc-length $\geq \lambda$ are denoted by $f_k(2n)$ and $T_k^{[\lambda]}(n)$, respectively. Furthermore, $T_k^{[\lambda]}(n, \ell)$ denotes the number of $k$-noncrossing RNA structures with arc-length $\geq \lambda$ having exactly $\ell$ isolated points, and let $f_k(m, \ell)$ denote the number of $k$-noncrossing diagrams with $\ell$ isolated points over $m$ vertices. Let $G_{n,k}(\ell, j_1, j_2, j_3)$ be the set of all $k$-noncrossing diagrams having exactly $\ell$ isolated points and exactly $j_1$ 1-arcs, $j_2$ 2-arcs and $j_3$ 3-arcs. We set $G_k(n, \ell, j_1, j_2, j_3) = |G_{n,k}(\ell, j_1, j_2, j_3)|$. In particular, we have $G_k(n, \ell, 0, 0, 0) = T_k^{[4]}(n, \ell)$. We observe that Claim 1 is implied (taking the sum over all $\ell$) by

\[(5.1)\quad T_k^{[4]}(n, \ell) = \sum_{b \leq \lfloor \frac{n}{2} \rfloor} (-1)^b \lambda(n, b) f_k(n - 2b, \ell),\]
where $\lambda(n, b)$ satisfies the recursion

$$\lambda(n, b) = \lambda(n - 1, b) + \lambda(n - 4, b - 2) + \lambda(n - 5, b - 2) + \lambda(n - 6, b - 3)$$

$$+ \sum_{i=1}^{b} [\lambda(n - 2i, b - i) + 2\lambda(n - 2i - 1, b - i) + \lambda(n - 2i - 2, b - i)]$$

$$- \lambda(n - 3, b - 1)$$

(5.2)

with the initial conditions $\lambda(n, 0) = 1$, $\lambda(n, 1) = 3n - 6$ and $n \geq 2b$.

We shall proceed by proving eq. (5.1). For this purpose, let $\lambda(n, b_1, b_2, b_3)$ denote the number of ways to select exactly $b_1$ 1-arcs, $b_2$ 2-arcs and $b_3$ 3-arcs over 1, \ldots, $n$ vertices.

**Claim A.**

$$\sum_{j_1 \geq b_1, j_2 \geq b_2, j_3 \geq b_3} \binom{j_1}{b_1} \binom{j_2}{b_2} \binom{j_3}{b_3} G_k(n, \ell, j_1, j_2, j_3) = \lambda(n, b_1, b_2, b_3)f_k(n-2(b_1+b_2+b_3), \ell).$$

(5.3)

The idea is to construct a family $\mathcal{F}$ of $G_{n,k}$-diagrams, having $\ell$ isolated points and at least $b_1$ 1-arcs, $b_2$ 2-arcs and $b_3$ 3-arcs, respectively. We then express $|\mathcal{F}|$ via the numbers $G_k(n, \ell, j_1, j_2, j_3)$. We select (a) $b_1$ 1-arcs and $b_2$ 2-arcs and $b_3$ 3-arcs and (b) an arbitrary $k$-noncrossing diagram over the remaining $n-2(b_1+b_2+b_3)$ vertices with exactly $\ell$ isolated points. Let $\mathcal{F}$ be the family of diagrams obtained in this way.
It is straightforward to show that $\lambda(n, b_1, b_2, b_3)$ satisfies the recursion:

$$
\lambda(n, b_1, b_2, b_3) = \\
\lambda(n - 1, b_1, b_2, b_3) + \lambda(n - 2, b_1 - 1, b_2, b_3) + \lambda(n - 4, b_1 - 1, b_2, b_3 - 1) \\
+ \lambda(n - 5, b_1, b_2, b_3 - 2) + \lambda(n - 6, b_1, b_2, b_3 - 3) - \lambda(n - 3, b_1, b_2 - 1, b_3) \\
+ \sum_{i=1}^{b} [2\lambda(n - 2i - 1, b_1, b_2 - 1, b_3 - (i - 1)) + \lambda(n - 2i - 2, b_1, b_2, b_3 - i)] \\
+ \sum_{i=2}^{b} [\lambda(n - 2i, b_1, b_2 - 2, b_3 - (i - 2))] 
$$

with the initial conditions $\lambda(n, 0, 0, 0) = 1$, $\lambda(n, 1, 0, 0) = n - 1$, $\lambda(n, 0, 1, 0) = n - 2$, $\lambda(n, 0, 0, 1) = n - 3$, $n \geq 2b$.

Clearly, each element $\theta \in \mathcal{F}$ is contained in $\mathcal{G}_{n,k}(\ell, j_1, j_2, j_3)$ for some $j_1 \geq b_1$ and $j_2 \geq b_2$ and $j_3 \geq b_3$. Indeed, any 1-arc or 2-arc or 3-arc can only cross at most two other arcs. Therefore 1-arcs and 2-arcs and 3-arcs cannot be contained in a set of more than 3-mutually crossing arcs. As a result, for $k > 3$ the construction generates $k$-noncrossing diagrams. Clearly, $\theta$ has exactly $\ell$ isolated vertices and in step (b) we potentially derive additional 1-arcs and 2-arcs and 3-arcs, whence $j_1 \geq b_1$ and $j_2 \geq b_2$ and $j_3 \geq b_3$, respectively. Next we observe that we have by construction

$$
|\mathcal{F}| = \lambda(n, b_1, b_2, b_3) f_k(n - 2(b_1 + b_2 + b_3), \ell).
$$
Since any of the \( k \)-noncrossing diagrams over \( n - 2(b_1 + b_2 + b_3) \) vertices can generate additional 1-arcs or 2-arcs or 3-arcs, we consider

\[
\mathcal{F}(j_1, j_2, j_3) = \{ \theta \in \mathcal{F} \mid \theta \text{ has exactly } j_1 \text{ 1-arcs, } j_2 \text{ 2-arcs and } j_3 \text{ 3-arcs} \}.
\]

Obviously, we then have the partition \( \mathcal{F} = \bigcup_{j_1 \geq b_1, j_2 \geq b_2, j_3 \geq b_3} \mathcal{F}(j_1, j_2, j_3) \). Suppose \( \theta \in \mathcal{F}(j_1, j_2, j_3) \), then \( \theta \in \mathcal{G}_{n, k}(\ell, j_1, j_2, j_3) \) and furthermore \( \theta \) occurs with multiplicity \( \binom{j_1}{b_1} \binom{j_2}{b_2} \binom{j_3}{b_3} \) in \( \mathcal{F} \) since by construction any \( b_1 \)-element subset of the \( j_1 \) 1-arcs and \( b_2 \)-element subset of the \( j_2 \) 2-arcs and \( b_3 \)-element subset of the \( j_3 \) 3-arcs is counted respectively in \( \mathcal{F} \). Therefore we have

\[
(5.4) \quad |\mathcal{F}(j_1, j_2, j_3)| = \binom{j_1}{b_1} \binom{j_2}{b_2} \binom{j_3}{b_3} G_k(n, \ell, j_1, j_2, j_3)
\]

and

\[
\sum_{j_1 \geq b_1, j_2 \geq b_2, j_3 \geq b_3} |\mathcal{F}(j_1, j_2, j_3)| = \lambda(n, b_1, b_2, b_3) f_k(n - 2(b_1 + b_2 + b_3), \ell)
\]

proving Claim \( A \). We next set

\[
F_k(x, y, z) = \sum_{j_1 \geq 0} \sum_{j_2 \geq 0} \sum_{j_3 \geq 0} G_k(n, \ell, j_1, j_2, j_3) x^{j_1} y^{j_2} z^{j_3}.
\]
Taking derivatives we obtain

\[
\frac{1}{b_1!} \frac{1}{b_2!} \frac{1}{b_3!} F_{k_1, b_2, b_3}(1)
= \sum_{j_1 \geq b_1, j_2 \geq b_2, j_3 \geq b_3} \binom{j_1}{b_1} \binom{j_2}{b_2} \binom{j_3}{b_3} G_{k_1}(n, \ell, j_1, j_2, j_3) 1^{j_1 - b_1} 1^{j_2 - b_2} 1^{j_3 - b_3}
\]

and accordingly

\[
\sum_{j_1 \geq 0, j_2 \geq 0, j_3 \geq 0} G_{k_1}(n, \ell, j_1, j_2, j_3) x^{j_1} y^{j_2} z^{j_3}
= \sum_{b_1 \geq 0, b_2 \geq 0, b_3 \geq 0} \lambda(n, b_1, b_2, b_3) f_k(n - 2(b_1 + b_2 + b_3), \ell) (x - 1)^{b_1} (y - 1)^{b_2} (z - 1)^{b_3}.
\]

By construction \(G(n, \ell, 0, 0, 0)\) is the constant term of the \(F_k(x, y, z)\). That is, the number of \(k\)-noncrossing RNA structures with \(\ell\) isolated vertices and no 1-arcs, 2-arcs and 3-arcs is given by

\[
(5.5) \ G(n, \ell, 0, 0, 0) = \sum_{b_1 \geq 0, b_2 \geq 0, b_3 \geq 0} (-1)^{b_1 + b_2 + b_3} \lambda(n, b_1, b_2, b_3) f_k(n - 2(b_1 + b_2 + b_3), \ell).
\]
We take the sum over all $\ell$ and derive

\[(5.6)\]

\[
T_k^{[4]}(n) = \sum_{b_1 \geq 0, b_2 \geq 0, b_3 \geq 0} (-1)^{b_1 + b_2 + b_3} \lambda(n, b_1, b_2, b_3) \left[ \sum_{\ell=0}^{n-2(b_1 + b_2 + b_3)} f_k(n - 2(b_1 + b_2 + b_3), \ell) \right].
\]

Setting

\[
\lambda(n, b) = \sum_{b_1 + b_2 + b_3 = b} \lambda(n, b_1, b_2, b_3)
\]

we conclude first

\[
T_k^{[4]}(n) = \sum_{b \leq \lfloor \frac{n}{2} \rfloor} (-1)^b \lambda(n, b) M_k(n - 2b)
\]

and second eq. (5.2), completing the proof of Claim 1.

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### Table 1. The first 15 numbers of 4-noncrossing RNA structures with arc-length $\geq 4$

| $T_k^4(n)$ | 1 | 1 | 1 | 1 | 2 | 5 | 15 | 51 | 179 | 647 | 2397 | 9081 | 35181 | 139307 | 563218 |
|---|---|---|---|---|---|---|----|----|----|----|-----|-----|-----|------|------|

### Table 2. Exponential growth rates and asymptotic formulas for $k$-noncrossing RNA structures with minimum arc-length $\geq 4$.

| $\gamma_k^{-1}$ | 6.52900 | 8.64830 | 10.71759 | 12.76349 | 14.79631 |
| $T_k^4(n)$ | $c_4n^{-\frac{24}{5}}(\gamma_4^{-1})^n$ | $c_5n^{-18}(\gamma_5^{-1})^n$ | $c_6n^{-\frac{52}{5}}(\gamma_6^{-1})^n$ | $c_7n^{-39}(\gamma_7^{-1})^n$ | $c_8n^{-\frac{105}{5}}(\gamma_8^{-1})^n$ |
Figure 1. $k$-noncrossing structures: 2-, 3- and 4-noncrossing structures (top to bottom). Maximal sets of mutually crossing arcs are colored red.

Figure 2. Basic diagram types: (a) 3-noncrossing matching (no isolated points), (b) 3-noncrossing partial matching (isolated points 4 and 7), (c) 4-noncrossing RNA structure with arc-length $\geq 3$, (d) 3-noncrossing RNA structure with arc-length $\geq 4$. 
Figure 3. The ratio $r(n) = T_4^{[4]}/(n^{-21/2} \gamma_4^{-n})$ as a function of $n$. The curve shows that the asymptotic approximation is valid as $r(n) \sim c_4 \approx 4.4509 \times 10^7$. 