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Abstract

Diverse methods have been employed recently to characterise the structure of biological networks. In particular, the concept of network motif and the related concept of coloured motif have proven to be useful to model the notion of a functional/evolutionary building block. However, algorithms that enumerate all the motifs of a network may have a very large output and methods to decide which motifs should be selected for downstream analysis are needed. A widely used method is to assess if the motif is exceptional, that is, over- or under- represented with respect to a null hypothesis. Unlike existing methods, we propose here a method to assess the exceptionality of coloured motifs which does not require simulations. We establish analytical formulas for the mean and the variance of the count of a coloured motif in an Erdös-Rényi random graph model. Using simulations, we further show that a Pólya-Aeppli distribution models well the distribution of the motif count. Altogether, these results now enable to derive a p-value for a coloured motif, without spending time on simulations.

1 Introduction

Describing the structure of a biological network has two main purposes. On the one hand, it enables to address questions related to the evolution of the network, that is, how such a complex structure has been set up in the course of evolution. On the other hand, structural analysis can be seen as a first necessary step previous to dynamical analysis which in turn enables to simulate networks and study their response to perturbation. Usually, three main classes of biological networks are considered (Alm and Arkin (2003)): protein interaction networks, gene regulatory networks and metabolic networks. When analysing their structure, these networks are usually modelled as graphs where nodes represent molecules (metabolites, genes, proteins) and edges represent interactions (direct or indirect) between these molecules. For instance, in the case of a gene regulatory network, nodes correspond to genes and there is an edge between a gene coding for a transcription factor and every gene that this transcription factor regulates.

The structure of a biological network may be apprehended using a variety of measures, such as node degree (Jeong *et al.* (2000)), degree correlation (Maslov and Sneppen (2002)) or average shortest path length (Wagner and Fell (2001)).

In this paper, we focus on the concept of motif. A network motif has been initially defined as a pattern of interconnections which occurs unexpectedly often in a network (Milo *et al.* (2002), Shen-Orr *et al.* (2002)). The assumption generally made is that subnetworks sharing the same topology will be functionally similar. Over- (or under-) represented subnetworks may therefore correspond to conserved (avoided) and thus important (vital/detrimental) cellular functions. In the context of regulatory networks, simple patterns such as loops may be interpreted as logical circuits controlling the dynamic behaviour of a network.

A limitation of the notion of topological motif is that in many cases, the same subgraph may in fact correspond to different functions, depending on the nature of the nodes that compose it. Moreover, in some situations, as for example in the case of protein interaction networks, the topology of the network is not fully known. Indeed, high-throughput experiments used to obtained large-scale protein interaction data are notoriously noisy, that is, they may detect interactions when there is none (false positive) and they may miss existing interactions (false negative). In this context, it may be unadequate to look for exact repetition of a pattern. Therefore, an alternative definition has been proposed, where a motif is defined using the labels of its nodes and not the topology of the induced subgraph (Lacroix *et al.* (2006)).

A coloured motif is defined as a multiset of colours (vertex labels) and an occurrence of a motif is defined as a connected subgraph whose labels match the motif.

The enumeration of coloured motifs is a non-trivial task which has been the subject of several works (Lacroix *et al.* (2006), Hermelin *et al.* (2007)) which enabled to establish the complexity of the problem and provide algorithms to efficiently detect all the occurrences of a motif in a graph. In practice, current methods now enable to enumerate all the motifs of size 7 of a graph representing the metabolic network of a bacterium in less than two hours. Beyond the time complexity of the task, a major challenge that remains open is to make sense of the potentially very large output of such enumeration procedure, especially when the focus is not on a single motif but on all motifs of a given size.

Ideally, one would need a method to rank the motifs according to their biological relevance in order to prioritize a small number of motifs for downstream analysis. However, the notion of biological relevance is generally ill-defined, and a first approximation to it which is classically used is its statistical exceptionality.

The exceptionality of a motif, that is the over- or under- representation of the motif with respect to a null model, can be assessed by comparing the observed count of occurrences of a motif to the expected count of the same motif under a null hypothesis.

Up to now, this procedure was performed in MOTUS (Lacroix *et al.* (2008), `http://pbil.univ-lyon1.fr/software/motus/`) using simulations, that is, a large number of random graphs were generated and the motif of interest was sought in each one, generating a distribution of motif count, to which the observed count could be compared in order to derive a z-score and a p-value.

The main limit to this procedure is that it adds a multiplicative factor to the time complexity of the search algorithm. Moreover, it is not trivial to choose what is the optimal number of simulations to perform in order to get a satisfying estimation of the

p-value. As a rule of thumb, in order to estimate quite accurately a p-value of 1 over 10^i, 10^{i+2} simulations should at least be performed.

In this paper, we propose a new approach for assessing the exceptionality of coloured motifs which does not require simulations and therefore ables to circumvent the previously mentionned limitations.

We were able to establish exact analytical formulas for the mean and the variance of the count of a coloured motif in an Erdös-Rényi (ER) random graph model. Using these results, one can already derive a z-score for each motif and therefore rank them according to their exceptionality.

We then worked on modelling the complete distribution of the count of a coloured motif in an ER random graph model. For this purpose, we performed a large number of simulations, using different colour frequencies for the motif and different number of nodes and edges for the graph. We could establish that the Pólya-Aeppli distribution was a better approximation than the commonly used Gaussian distribution.

These results can in turn be used to derive a p-value for each motif, and therefore introduce a cut-off to decide which motifs should be selected for downstream analysis.

To our knowledge, there has been no previous work on the enumeration of coloured motif in random graphs and this is the reason why we focused on the more general random graph model that is available. We are aware that this may not be the most suitable model to describe the structure of a biological network. However, we argue that this work provides a first necessary basis which can later be extended to richer models, such as a mixture of Erdös-Rényi models as proposed by Daudin *et al.* (2008).

2 Definition and notations

Coloured random graph model. We consider a random graph G with n vertices $\{V_1, \ldots, V_n\}$. We assume that random edges are independent and distributed according to a Bernoulli distribution with parameter $p \in]0,1]$ (so-called Erdös-Rényi model). Moreover, vertices are randomly and independently coloured as follows. Let $\mathcal{C}$ be a finite set of r different colours and f a probability measure on $\mathcal{C}$: $f(c)$ is then the probability for a vertex to be coloured with $c \in \mathcal{C}$.

In metabolic networks, colours of reaction nodes can represent the class of the catalyzing enzymes; In regulation networks, colours of gene nodes can represent the functional class of the genes.

Coloured motif. We consider motifs as introduced in Lacroix *et al.* (2006): a (coloured) motif $\mathbf{m}$ of size k is a set of k colours $\{m_1, \ldots, m_k\} \in \mathcal{C}^k$. Colours from a motif may not be different, i.e. one may have $m_i = m_j$ for some $1 \leq i, j \leq k$; We then denote by $s_{\mathbf{m}}(c)$ the multiplicity of the colour c in $\mathbf{m}$. When there is no ambiguity, $s_{\mathbf{m}}(c)$ will simply be denoted by $s(c)$.

Motif occurrences. We will now define an occurrence of such coloured motif. For this purpose, we introduce the following notations. If $i_1, i_2, \ldots, i_\ell$ are ℓ different indexes from $\{1, \ldots, n\}$, then $G(i_1, i_2, \ldots, i_\ell)$ represents the subgraph of G induced by the vertices $\{V_{i_1}, \ldots, V_{i_\ell}\}$. Let I_k be the set of all the subsets of size k from $\{1, \ldots, n\}$. We say that a motif $\mathbf{m} = \{m_1, \ldots, m_k\}$ occurs at position $\alpha = \{i_1, \ldots, i_k\} \in I_k$ if and only if $G(\alpha)$ is connected and the colours of $G(\alpha)$, denoted by $C(\alpha)$ are exactly $\{m_1, \ldots, m_k\}$. I_k corresponds then to the set of possible positions for the occurrence of a motif of size k.

Number of occurrences. We introduce the random indicator variable $Y_\alpha(\mathbf{m})$ which equals one if motif $\mathbf{m}$ occcurs at position $\alpha \in I_k$ in G and zero otherwise:

$$Y_\alpha(\mathbf{m}) = \mathbb{I}\{\mathbf{m} \text{ occurs at position } \alpha\}.$$

$Y_\alpha(\mathbf{m})$ is then a Bernoulli random variable whose expectation will be denoted by $\mu(\mathbf{m})$:

$$\mu(\mathbf{m}) = \mathbb{E}Y_\alpha(\mathbf{m}) = \mathbb{P}(\mathbf{m} \text{ occurs at position } \alpha).$$

The probability $\mu(\mathbf{m})$ for $\mathbf{m}$ to occur at position α will be given in Section 3.1.

The number of occurrences of the motif $\mathbf{m}$ in the graph G, denoted by $N(\mathbf{m})$ is defined by:

$$N(\mathbf{m}) = \sum_{\alpha \in I_k} Y_\alpha(\mathbf{m}). \tag{1}$$

3 Mean and variance for the count

This section will provide analytical formulas for the mean and the variance of the number of occurrences of a motif in a random graph. It will involve the computation of the occurrence probability $\mu(\mathbf{m})$ and some probabilities of connectedness.

3.1 Mean number of occurrences

The mean number of occurrences of the motif $\mathbf{m}$ in the graph G simply follows from the count expression (1):

$$\mathbb{E}N(\mathbf{m}) = \sum_{\alpha \in I_k} \mathbb{E}Y_\alpha(\mathbf{m}) = \binom{n}{k} \mu(\mathbf{m})$$

where $\mu(\mathbf{m})$ is the occurrence probability of the motif and is given below by equation (3).

Occurrence probability. The probability $\mu(\mathbf{m})$ for $\mathbf{m}$ to occur at position α is equal to the product of two probabilities: the probability that $G(\alpha)$ is connected and the probability to assign colours $\{m_1, \ldots, m_k\}$ to vertices $\{V_{i_1}, \ldots, V_{i_k}\}$. If we denote the latter by $\gamma(\mathbf{m})$, we then have

$$\gamma(\mathbf{m}) = \frac{k!}{\prod_{c \in \mathcal{C}} s(c)!} \prod_{i=1}^{k} f(m_i) \tag{2}$$

and

$$\mu(\mathbf{m}) = g(k,p) \times \gamma(\mathbf{m}) \tag{3}$$

where $g(k,p)$ denotes the probability for a random graph (Erdös-Rényi model) with k vertices and edge probability p to be connected (put $0! = 1$).

Connectivity probability The probability $g(k,p)$ can be calculated by recursion (Gilbert (1959)) as follows:

$$g(k,p) = 1 - \sum_{i=1}^{k-1} \binom{k-1}{i-1} g(i,p)(1-p)^{i(k-i)} \tag{4}$$

where $g(1,p) = 1$. For instance, for $2 \leq k \leq 5$, which is typically the range for the motif size in practice, we have:

$$\begin{aligned}
g(2,p) &= p, \\
g(3,p) &= 3p^2 - 2p^3, \\
g(4,p) &= 16p^3 - 33p^4 + 24p^5 - 6p^6, \\
g(5,p) &= 125p^4 - 528p^5 + 970p^6 - 980p^7 + 570p^8 - 180p^9 + 24p^{10}.
\end{aligned}$$

3.2 Variance of the number of occurrences

To get the variance, we use that $\mathrm{Var}N(\mathbf{m}) = \mathbb{E}N^2(\mathbf{m}) - (\mathbb{E}N(\mathbf{m}))^2$ and we then compute the moment of order two:

$$\mathbb{E}N^2(\mathbf{m}) = \sum_{\alpha \in I_k} \sum_{\beta \in I_k} \mathbb{E}[Y_\alpha(\mathbf{m}) Y_\beta(\mathbf{m})].$$

First, the sums over α and β will be done according to the number ℓ of vertices shared by the subgraphs $G(\alpha)$ and $G(\beta)$:

$$\mathbb{E}N^2(\mathbf{m}) = \sum_{\ell=0}^{k} \sum_{|\alpha \cap \beta| = \ell} \mathbb{E}[Y_\alpha(\mathbf{m}) Y_\beta(\mathbf{m})].$$

Second, we use that $Y_\alpha(\mathbf{m})$ and $Y_\beta(\mathbf{m})$ are indicator variables which leads to $\mathbb{E}[Y_\alpha(\mathbf{m})Y_\beta(\mathbf{m})] = \mathbb{P}(Y_\alpha(\mathbf{m}) = 1 \text{ and } Y_\beta(\mathbf{m}) = 1)$. These random variables are not independent but the above probability can be writen like

$$\mathbb{E}[Y_\alpha(\mathbf{m}) Y_\beta(\mathbf{m})] = K(\alpha,\beta) \times Q_{\mathbf{m}}(\alpha,\beta) \tag{5}$$

with

$$\begin{aligned}
K(\alpha,\beta) &= \mathbb{P}(G(\alpha) \text{ and } G(\beta) \text{ are connected}) \\
Q_{\mathbf{m}}(\alpha,\beta) &= \mathbb{P}(C(\alpha) = C(\beta) = \{m_1, \ldots, m_k\}).
\end{aligned}$$

Terms $K(\alpha,\beta)$ and $Q_{\mathbf{m}}(\alpha,\beta)$ will now be separately calculated.

Computation of $Q_{\mathbf{m}}(\alpha,\beta)$ Let $\ell = |\alpha \cap \beta|$; Subgraphs $G(\alpha)$ and $G(\beta)$ have thus ℓ vertices in common, with $0 \leq \ell \leq k$. Let $\mathbf{m}^* \subset \mathbf{m}$ such that $|\mathbf{m}^*| = \ell$ and denote $\mathbf{m}^- = \mathbf{m} \backslash \mathbf{m}^*$; $\mathbf{m}^*$ represents the colours of the ℓ vertices shared by $G(\alpha)$ and $G(\beta)$. The multiplicity of colour $c \in \mathcal{C}$ in $\mathbf{m}^*$ (respectively in $\mathbf{m}^-$) is denoted by $s^*(c)$ (resp. $s^-(c)$). To calculate $\mathbb{P}(C(\alpha) = C(\beta) = \mathbf{m})$, we start by choosing the ℓ colours $\mathbf{m}^*$ of $G(\alpha) \cap G(\beta)$ and the $(k - \ell)$ remaining colours $\mathbf{m}^-$ are spread over both $G(\alpha) \backslash (G(\alpha) \cap G(\beta))$ and $G(\beta) \backslash (G(\alpha) \cap G(\beta))$. It leads to

$$Q_{\mathbf{m}}(\alpha,\beta) = \sum_{\mathbf{m}^* \subset \mathbf{m}} \frac{\gamma(\mathbf{m}^*)[\gamma(\mathbf{m}^-)]^2}{s(\mathbf{m}^*)} \tag{6}$$

where $s(\mathbf{m}^*)$ is the multiplicity of $\mathbf{m}^*$ in $\mathbf{m}$.

Computation of $K(\alpha,\beta)$ Let again $\ell = |\alpha \cap \beta|$. If $\ell = 0$ ($G(\alpha)$ and $G(\beta)$ are disjoint) or $\ell = 1$ ($G(\alpha)$ and $G(\beta)$ have a unique vertex in common) then the events $\{G(\alpha) \text{ is connected}\}$ and $\{G(\beta) \text{ is connected}\}$ are independent leading to

$$K(\alpha,\beta) = g^2(k,p), \quad \text{if } \ell = 0 \text{ or } 1.$$

Another easy case is when $\ell = k$: $\beta = \alpha$ and $K(\alpha,\beta) = g(k,p)$.
For the other cases, no general formulas have been found so far but, for small values of k, one can automatically enumerate all the solutions thanks to the edge binary tree. The idea is to work conditionnally to the subgraph $G(\alpha) \cap G(\beta)$ of size $2 \leq \ell \leq k-1$. This method is presented in the supplementary material and here are the results for $k = 3$ and $k = 4$ ($k = 2$ can be processed with the above formulas):

$$\begin{aligned}
k = 3 \text{ and } \ell = 2 &\ : \ K(\alpha,\beta) = 4p^3 - 3p^4 \\
k = 4 \text{ and } \ell = 2 &\ : \ K(\alpha,\beta) = 64p^5 - 160p^6 + 100p^7 + 77p^8 - 136p^9 + 68p^{10} - 12p^{11} \\
k = 4 \text{ and } \ell = 3 &\ : \ K(\alpha,\beta) = 27p^4 - 60p^5 + 46p^6 - 12p^7.
\end{aligned}$$

4 Occurrences of multiple motifs

In some cases, the motif of interest may not be restricted to a single set of colours but can correspond to several sets of colours. This is typically the case when one allows some colours to be equivalent at some point. For instance, if $\mathcal{C} = \{\text{red, green, dark blue, light blue}\}$, then one could be interested to look for the occurrences of the "degenerated" motif $\{\text{red, blue}\} = \{\text{red, dark blue}\} \cup \{\text{red, light blue}\}$. Such motif is then the union of several "single" motifs.

Formally, denote by $\mathcal{M}$ a set of coloured motifs. The number of occurrences of $\mathcal{M}$ in the graph G is then the sum of the counts $N(\mathbf{m})$ for $m \in \mathcal{M}$. Consequently, the expected count $\mathbb{E}N(\mathcal{M})$ is also the sum of the expected counts $\mathbb{E}N(\mathbf{m})$, $m \in \mathcal{M}$. The novelty only appears for the variance because it requires covariance terms:

$$\text{Var}N(\mathcal{M}) = \sum_{\mathbf{m} \in \mathcal{M}} \text{Var}(N(\mathbf{m})) + \sum_{\mathbf{m} \neq \mathbf{m}' \in \mathcal{M}} \text{Cov}(N(\mathbf{m}), N(\mathbf{m}')).$$

In other words, one has to calculate $\mathbb{P}(Y_\alpha(\mathbf{m}) = 1 \text{ and } Y_\beta(\mathbf{m}') = 1)$ for $\alpha, \beta \in I_k$ and $\mathbf{m} \neq \mathbf{m}' \in \mathcal{M}$. Similarly to equation (5), this probability is equal to $K(\alpha,\beta) \times Q_{\mathbf{m},\mathbf{m}'}(\alpha,\beta)$ where $K(\alpha,\beta)$ has been previously introduced and $Q_{\mathbf{m},\mathbf{m}'}(\alpha,\beta) = \mathbb{P}(C(\alpha) = \mathbf{m}, C(\beta) = \mathbf{m}')$. The latter quantity is null when $\ell = |\alpha \cap \beta| > |\mathbf{m} \cap \mathbf{m}'|$. When $\ell \leq |\mathbf{m} \cap \mathbf{m}'|$, $Q_{\mathbf{m},\mathbf{m}'}(\alpha,\beta)$ is calculated like $Q_{\mathbf{m}}(\alpha,\beta)$ (see eq. (6)) and we get:

$$Q_{\mathbf{m},\mathbf{m}'}(\alpha,\beta) = \sum_{\mathbf{m}^* \subset \{\mathbf{m} \cap \mathbf{m}'\}, |\mathbf{m}^*| = \ell} \frac{\gamma(\mathbf{m}^*)\gamma(\mathbf{m}^-)\gamma(\mathbf{m}'^-)}{s(\mathbf{m}^*)}$$

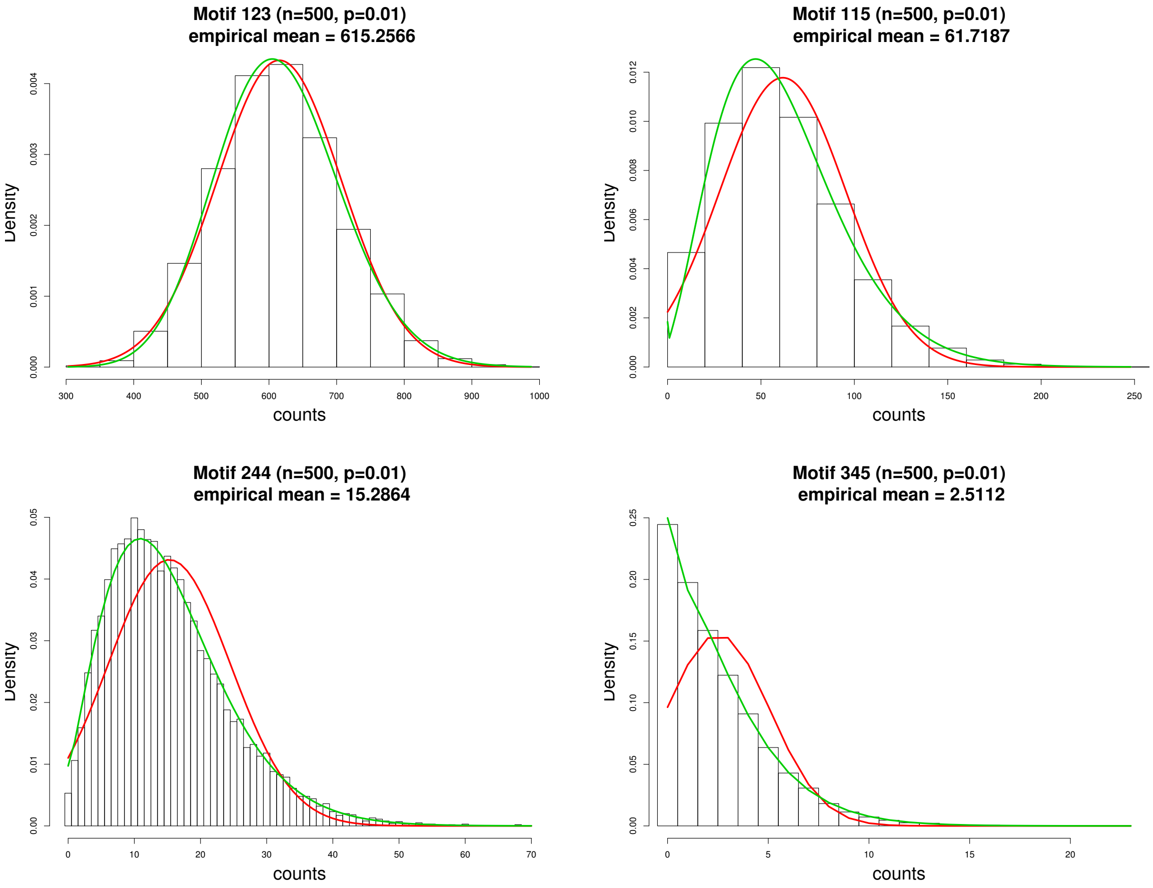
where $\mathbf{m}^*$ is still the colour of the ℓ common vertices and $\mathbf{m}^-$ and $\mathbf{m}'^-$ are the remaining colours from $\mathbf{m}$ and $\mathbf{m}'$.

5 Towards the motif count distribution: a simulated approach

Aim No theoretical results exist so far on the distribution of coloured motifs in random graphs. In this paper, we propose an approximation for this distribution. Thanks to simulations, we first studied the quality of the normal approximation which is classically employed, especially when using z-scores. By analogy with motifs in sequences (Schbath (1995)), we also considered a Pólya-Aeppli approximation as suggested by Picard *et al.* (2008) for topological motifs (*i.e.* the motif has no colours but a fixed topology) in random graphs. The idea is that a normal distribution is not adapted for the count of rare events, whereas compound Poisson distributions are relevant for the count of rare and clumping events; And network motif occurrences will tend to overlap in networks. The Pólya-Aeppli distribution (denoted by $\mathcal{PA}$) with parameters (λ, a) is the distribution of $\sum_{c=1}^{C} K_c$ where the number of clumps C is Poisson distributed ($C \sim \mathcal{P}(\lambda)$) and the size of the clumps K_c is geometrically distributed ($\mathbb{P}(K_c = k) = (1-a)a^k$). Its mean is equal to $\lambda/(1-a)$ and its variance equals $\lambda(1+a)/(1-a)^2$. We did not investigate the Poisson approximation because, as we can see on Table 1, the variance of the count (whatever the coloured motif) is quite different from the mean count.

Simulation design We have simulated 10,000 Erdös-Rényi random graphs with n nodes ($n \in \{100, 500, 1000\}$) and edge probability $p \in \{0.05, 0.01, 0.005\}$. Nodes have been randomly coloured with 5 colours ($\mathcal{C} = \{1,2,3,4,5\}$) and according to the following colour frequencies: $f = (50, 25, 10, 5, 1)/91$. These choices for n, p and f allow to get coloured motifs of size 3 with a wide range of expected counts. We have then selected 14 motifs of size 3 to cover both this variety of counts and different multiplicity pattern: $\{1,1,1\}$, $\{1,2,2\}$, $\{1,2,3\}$, $\{1,1,4\}$, $\{1,3,4\}$, $\{1,1,5\}$, $\{2,4,4\}$, $\{4,4,4\}$, $\{2,4,5\}$, $\{3,4,5\}$, $\{1,5,5\}$, $\{3,5,5\}$, $\{4,5,5\}$ and $\{5,5,5\}$.

For each motif and each couple (n,p), we then obtained an empirical distribution which has been compared with both the normal distribution $\mathcal{N}(\widehat{\mathbb{E}}N(\mathbf{m}), \widehat{\text{Var}}N(\mathbf{m}))$ and the


Motif 123 (n=500, p=0.01)
empirical mean = 615.2566

Motif 115 (n=500, p=0.01)
empirical mean = 61.7187

Motif 244 (n=500, p=0.01)
empirical mean = 15.2864

Motif 345 (n=500, p=0.01)
empirical mean = 2.5112

Figure 1: Empirical distributions for the count of motifs $\{1,2,3\}$, $\{1,1,5\}$, $\{2,4,4\}$ and $\{3,4,5\}$ in random graphs with $n = 500$ and $p = 0.01$. The empirical means are respectively 615, 61, 15 and 2. The red (respectively green) curves correspond to the ad-hoc normal distributions (resp. Pólya-Aeppli distributions).

Pólya-Aeppli distribution $\mathcal{PA}(\widehat{\lambda},\widehat{a})$ with $\widehat{\lambda} = (1-a)\widehat{\mathbb{E}}N(\mathbf{m})$ and $\widehat{a} = [\widehat{\mathrm{Var}}N(\mathbf{m}) - \widehat{\mathbb{E}}N(\mathbf{m})]/[\widehat{\mathrm{Var}}N(\mathbf{m}) + \widehat{\mathbb{E}}N(\mathbf{m})]$ (see Figure 1).

Quality of approximation To measure this quality we took two criteria: (1) the Kolmogorov-Smirnov distance which measures the maximal difference between the empirical cumulative distribution function (cdf) $\widehat{F}$ and the cdf of the normal or the Pólya-Aeppli distribution. Closer to 0 the KS distance, better the approximation. (2) 1 minus the empirical cdf calculated at the 99% and 99.9% quantiles of the normal or the Pólya-Aeppli distribution. Closer these values from 1% and 0.1%, better the approximation.

Results Results for different values of n and p are very similar. We only present here the ones corresponding to $n = 500$ and $p = 0.01$ because these values are very close to real cases such as the metabolic network of *Escherichia coli* as considered in Lacroix *et al.* (2006). Nevertheless all results are presented in the supplementary material.

We can first notice just by eyes (see Figure 1) that the normal distribution seems satisfactory for frequent motifs but becomes as bader as the motif becomes rare. The Pólya-Aeppli distribution seems to fit quite correctly the count distribution whatever the motif. These points are emphasized when we look at the Kolmogorov-Smirnov distances (see Table 1): the ones for the Pólya-Aeppli distribution are always smaller than for the normal distribution and sometimes strongly smaller. In fact, the distance to the normal distribution is terribly large for very rare motifs (typically when $\mathbb{E}N(\mathbf{m}) \leq 10$). If we now look at the distribution tails thanks to the empirical probabilities to exceed the 99% or 99.9% quantiles $q_{\mathcal{N}}$ and $q_{\mathcal{PA}}$, we can also notice that they are closer to 1% or 0.1% for the Pólya-Aeppli distribution than for the normal distribution. The "look-so-bad performance" of the Pólya-Aeppli distribution for very rare motifs are artefact due to the fact that the $\mathcal{PA}$ and the count distributions are concentrated close to zero and the ambiguity to compute quantiles for discrete distributions is amplified. Moreover, note that most of the time the normal distribution underestimates the quantile (the empirical right tail is overestimated) leading to false positives.

6 Discussion and conclusion

In this paper, we proposed a new way to assess the exceptionality of coloured motifs in networks which does not require to perform simulations. Indeed, we were able to establish analytical formulas for the mean and the variance of the count of a coloured motif in an Erdös-Rényi random graph model. Furthermore, using simulations, we showed that the motif count distribution can be quite accurately approximated with a Polya-Aeppli distribution, and that the Gaussian distribution is not relevant. Altogether, these results now enable to derive a p-value for a coloured motif without performing simulations. Clearly, when several motifs have to be tested, which is the case in the context of motif discovery, one has to control for multiple testing. A conservative strategy that is classically used and that we would recommend is then to use a Bonferroni correction.

In this work, we did not investigate the case of long motifs, but we can anticipate that motifs containing submotifs which are exceptional, will tend to be exceptional themselves. This type of phenomenon is also observed for motifs in sequences and a classical way to deal with it is to control for the number of sequence motifs of size $k-1$ (by using a Markov model of order $k-2$), when assessing the exceptionality of motifs of size k. However, in the case of networks, the problem is far from trivial and it is unclear, even for small values of k if the space of random graphs verifying these constraints will not be too small. In the worst case, this space may even be reduced to the observed graph itself.

Also, in the case of very rare motifs, the expected distribution of the count is essentially concentrated on 0. Therefore, a single occurrence of such a motif will often be sufficient for it to be considered as exceptional. Now if we consider the extreme case of a coloured graph where each node is assigned a different colour, then all possible motifs will be very

									$\alpha = 1\%$				$\alpha = 0.1\%$			
motif $\mathbf{m}$	$\mathbb{E}N(\mathbf{m})$	$\mathrm{Var}N(\mathbf{m})$	$\widehat{\mathbb{E}}N(\mathbf{m})$	$\widehat{\mathrm{Var}}N(\mathbf{m})$	$\widehat{a}$	$\widehat{\lambda}$	$KS_{\mathcal{N}}$	$KS_{\mathcal{PA}}$	$q_{\mathcal{N}}$	$1 - \widehat{F}(q_{\mathcal{N}})$	$q_{\mathcal{PA}}$	$1 - \widehat{F}(q_{\mathcal{PA}})$	$q_{\mathcal{N}}$	$1 - \widehat{F}(q_{\mathcal{N}})$	$q_{\mathcal{PA}}$	$1 - \widehat{F}(q_{\mathcal{PA}})$
							(%)	(%)		(%)		(%)		(%)		(%)
111	1023.65	27462.66	1021.97	27446.53	0.93	73.37	2.40	0.78	1407.4	1.6	1436	1.1	1533.9	0.23	1591	0.12
122	767.74	14941.43	766.05	14660.79	0.90	76.08	2.14	0.65	1047.7	1.5	1068	1.0	1140.2	0.25	1181	0.07
123	614.19	8546.68	615.26	8493.22	0.86	83.12	1.75	0.68	829.6	1.4	845	0.8	900.0	0.18	929	0.08
114	307.09	5729.89	307.77	5807.09	0.90	30.98	3.20	0.71	485.0	1.5	505	0.8	543.3	0.28	583	0.08
134	122.84	1305.02	123.06	1311.64	0.83	21.11	3.43	0.78	207.3	1.8	219	0.9	235.0	0.37	257	0.12
115	61.41	1180.68	61.72	1147.95	0.90	6.30	5.72	0.98	140.5	2.3	160	0.8	166.4	0.57	205	0.06
244	15.35	85.99	15.29	85.57	0.70	4.63	8.73	1.07	36.8	2.4	43	0.8	43.9	0.81	55	0.12
245	6.14	27.76	6.20	28.45	0.64	2.22	12.72	1.27	18.6	2.5	23	0.8	22.7	1.09	32	0.10
345	2.46	6.63	2.51	6.58	0.45	1.39	17.97	0.53	8.5	1.9	11	0.5	10.4	0.77	15	0.09
155	1.23	6.94	1.22	6.74	0.69	0.37	34.23	5.75	7.2	3.3	12	0.6	9.2	1.56	20	0.05
444	1.02	2.46	1.02	2.51	0.42	0.59	27.39	3.80	4.7	2.4	7	0.5	5.9	1.48	10	0.09
355	0.25	0.50	0.25	0.50	0.34	0.16	48.47	0.43	1.9	2.5	3	0.4	2.4	0.96	6	2e-05
455	0.12	0.20	0.13	0.20	0.23	0.09	51.63	0.16	1.2	0.6	2	0.1	1.5	0.65	4	0.03
555	0.008	0.01	0.007	0.008	0.035	0.007	52.61	2e-03	0.2	0.03	0	0.03	0.3	0.03	1	2e-05

Table 1: Quality of approximation of the count distribution for $n = 500$ and $p = 0.01$. The empirical mean $\widehat{\mathbb{E}}N(\mathbf{m})$, variance $\widehat{\mathrm{Var}}N(\mathbf{m})$ and cumulative distribution function $\widehat{F}$ have been obtained thanks to 10,000 random graphs. $(\widehat{a}, \widehat{\lambda})$ are the parameters of the Pólya-Aeppli distribution. $KS_{\mathcal{N}}$ and $KS_{\mathcal{PA}}$ are the Kolmogorov-Smirnov distances. For $\alpha = 1\%$ then 0.1%, $q_{\mathcal{N}}$ is the $1 - \alpha$ quantile of the normal distribution (idem for the Pólya-Aeppli distribution).

rare and therefore, they may all be detected as exceptional. In practical cases, such as for the network representing the metabolic network of the bacterium *Escherichia coli*, the situation is less dramatic but indeed a lot of colours are present only once. This issue may be partially adressed by considering a random graph model where the colours and the topology are not independent anymore. This would enable to discriminate between unfrequent poorly connected colours and unfrequent highly connected colours. Motifs containing the latter type of colours would be expected to have more occurrences and should therefore not be systematically considered as exceptional when they have a single occurrence.

More generally, we considered in this paper a very simple random graph model. Even though we think this work was necessary to establish a framework to assess the exceptionality of coloured motifs, an important step is now to extend these results to other models of random graphs which better model the structure of real networks.

Finally, we think there is still room for improvement about the approximation of the motif count distribution. Indeed, no theoretical evidence has been found so far to use a Poisson distribution for the number of clumps of occurrences and a geometric distribution for their size. Getting the third moment and eventually the fourth moment of the count could certainly allow to investigate other distributions.

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Supplementary material

Connectedness probability for two subgraphs sharing vertices

We describe here how to compute the probability that $G(\alpha)$ and $G(\beta)$ are both connected given that they share $2 \leq \ell < k$ vertices ; Recall that $G(\alpha)$ and $G(\beta)$ have k vertices. The principle is to work conditionnally to the subgraph $G(\alpha) \cap G(\beta)$:

$$\begin{aligned}&\mathbb{P}(G(\alpha) \text{ and } G(\beta) \text{ are connected}) = \\ &\quad \sum_{G'} \mathbb{P}(G(\alpha) \cap G(\beta) = G') \times [\mathbb{P}(G(\alpha) \text{ connected} \mid G(\alpha) \cap G(\beta) = G')]^2 \end{aligned} \tag{7}$$

where G' is any subgraph of ℓ vertices.
Since k is typically small, both probabilities can be computed by enumerating all possible subgraphs G' and $G(\alpha)$. This can be done by traversing the complete edge binary tree associated to the $k(k-1)/2$ potential edges. This tree is composed of $k(k-1)/2$ levels, one for each potential edge and each internal node in this tree has two sons: the left one corresponds to the presence of the corresponding edge in the graph whereas the right one corresponds to its absence. It follows that each path from the root to a leaf corresponds to one of the $2^{k(k-1)/2}$ possible graphs of size k.

Figure 2 gives an example for $k = 3$; Vertices are labelled $\{i, j, u\}$, the higher level corresponds to edge (i, j), the middle one corresponds to edge (i, u) and the lower level corresponds to edge (j, u). Leaves corresponding to connected graphs are drawn with a square. In practice, the connectedness of a graph can be checked by calculating its adjacency matrix to the power $k - 1$. Indeed a graph of size k with adjacency matrix A is connected if and only if A^{k-1} contains no zero (every vertex can be reached from any vertex in at most $k - 1$ step). Additionnally, the binary tree is built such that all pairs of common vertices between $G(\alpha)$ and $G(\beta)$ are at the top levels. Therefore, the probability of each connected graph of size k can be easily calculated when traversing the tree while taking care of the conditional probabilities that should be to the square (cf. Equation (7)).

As an illustration, we now detail the computation for $k = 3$ and $\ell = 2$. Let i and j be the two common vertices between $G(\alpha)$ and $G(\beta)$, and let u be the third vertex of $G(\alpha)$ ($\alpha = \{i, j, u\}$). The edge binary tree is given by Figure 2. In this case, there are only two subgraphs G' with $\ell = 2$ vertices: either i and j are connected (probability p) or they are not connected (probability $1-p$). In Fig. 2 we indicate with a dashed horizontal line the separation between edges in G' (the conditioning event) and edges in $G(\alpha)\backslash G'$. Overall, with $k = 3$, there are four possible connected subgraphs: the triangle (labelled 'a') and the three possible 'V' (labelled 'b', 'c', and 'd'). The probability that $G(\alpha)$ is connected given $i \leftrightarrow j$ is obtained from cases 'a' (proba. p^2), 'b' (proba. $p(1-p)$) and 'c' (proba. $p(1-p)$):

$$\mathbb{P}(G(\alpha) \text{ connected} \mid i \leftrightarrow j) = p^2 + 2p(1-p).$$

The probability that $G(\alpha)$ is connected given i is not connected with j is obtained from

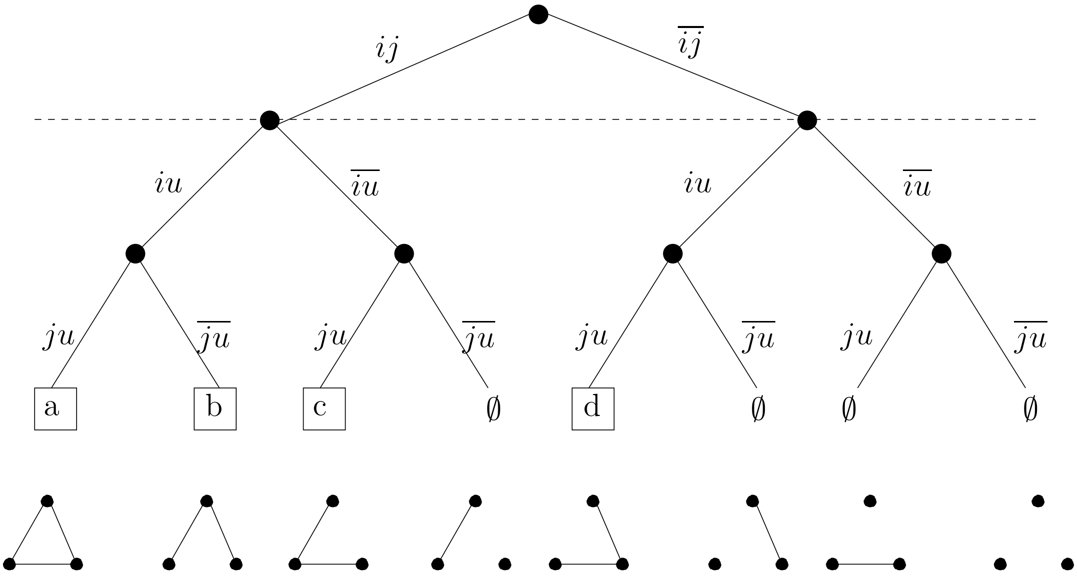

Figure 2: Complete edge binary tree for vertices i, j and u. Branches are labelled according to the presence or absence of edges: label ij for instance means that i and j are connected, whereas $\overline{ij}$ means the opposite. Leafs which correspond to connected subgraphs are represented by a square.

case 'd' (proba. p^2), leading to

$$\begin{aligned}\mathbb{P}(G(\alpha) \text{ and } G(\beta) \text{ are connected}) &= p \times [2p - p^2]^2 + (1-p) \times [p^2]^2 \\ &= 4p^3 - 3p^4.\end{aligned}$$

Approximation quality

Tables 2, 3 and 4 give the results about the approximation quality for $n = 100$ ($p \in \{0.05, 0.01, 0.005\}$), $n = 500$ ($p \in \{0.05, 0.005\}$) and $n = 1000$ ($p \in \{0.05, 0.01, 0.005\}$).

m	$\mathbb{E}N(\mathbf{m})$	Var$N(\mathbf{m})$	$\widehat{\mathbb{E}}N(\mathbf{m})$	$\widehat{\text{Var}N}(\mathbf{m})$	$\widehat{a}$	$\widehat{\lambda}$	$KS_{\mathcal{N}}$	$KS_{\mathcal{PA}}$	$\alpha = 0.1\%$ $q_{\mathcal{N}}$	$1-\widehat{F}(q_{\mathcal{N}})$	$q_{\mathcal{PA}}$	$1-\widehat{F}(q_{\mathcal{PA}})$
							(%)	(%)		(%)		(%)
111	194.46	4868.66	194.42	4827.85	0.92	15.05	5.03	1.23	409.1	0.63	461	0.15
122	145.85	2646.09	145.81	2685.28	0.90	15.02	4.42	0.49	305.9	0.54	344	0.07
123	116.68	1520.30	117.19	1551.07	0.86	16.46	3.68	0.90	238.9	0.28	266	0.07
114	58.34	1023.94	58.29	1030.84	0.90	6.24	6.05	0.49	157.5	0.65	194	0.06
134	23.36	234.83	23.42	241.19	0.82	4.14	8.70	0.66	71.4	0.78	92	0.08
115	11.67	211.46	11.57	208.10	0.89	1.22	19.17	6.76	56.1	1.32	91	0.07
244	2.92	15.63	2.90	15.09	0.68	0.93	20.49	3.94	14.9	1.52	25	0.11
245	1.17	5.08	1.16	5.01	0.62	0.44	33.31	1.06	8.1	1.26	16	0.08
345	0.47	1.22	0.47	1.22	0.44	0.26	43.07	0.39	3.9	1.46	8	0.08
155	0.23	1.28	0.23	1.30	0.69	0.07	49.95	1.28	3.8	2.00	13	0.05
444	0.19	0.46	0.19	0.42	0.38	0.11	49.44	1.11	2.2	0.77	6	0.05
355	0.05	0.09	0.04	0.08	0.28	0.03	53.10	0.04	0.9	0.85	3	0.02
455	0.02	0.04	0.02	0.03	0.16	0.02	53.24	4e-03	0.6	0.33	2	0.01
555	0.002	0.002	0.002	0.002	0.05	0.002	51.40	1e-03	0.1	0.01	1	2e-05
111	8.00	29.43	8.00	29.64	0.57	3.40	11.33	2.02	24.8	0.90	32	0.09
122	6.00	16.99	5.94	16.74	0.48	3.11	11.83	0.53	18.6	0.65	24	0.04
123	4.80	11.77	4.75	11.90	0.43	2.71	13.46	0.78	15.4	0.62	20	0.06
114	2.40	6.87	2.36	6.73	0.48	1.23	19.06	1.62	10.4	0.97	16	0.04
134	0.96	2.02	0.95	1.96	0.35	0.62	28.54	0.44	5.3	0.74	9	0.02
115	0.48	1.36	0.48	1.33	0.47	0.25	43.23	0.40	4.0	0.76	9	0.05
244	0.12	0.19	0.11	0.17	0.20	0.09	51.97	0.30	1.4	0.53	4	0.01
245	0.05	0.07	0.05	0.07	0.20	0.04	53.33	0.02	0.9	0.87	3	0.01
345	0.02	0.02	0.02	0.02	0.10	0.01	53.17	3e-03	0.5	0.16	2	2e-05
155	0.01	0.02	0.008	0.01	0.17	0.006	52.35	0.05	0.3	0.16	2	NA
444	0.008	0.01	0.006	0.007	0.08	0.005	52.27	0.01	0.3	0.03	1	0.01
355	0.002	0.002	0.002	0.002	0.047	0.002	51.51	9e-04	0.1	0.01	1	2e-05
455	0.001	0.001	0.001	0.001	< 0	0.001	51.21	-	0.1	2e-05	-	-
555	6e-05	7e-05	0	0	-	-	-	-	-	-	-	-
111	2.00	4.42	2.01	4.48	0.38	1.243	20.04	2.67	8.5	0.88	13	0.03
122	1.50	2.73	1.49	2.69	0.28	1.07	22.97	0.93	6.6	0.70	10	0.01
123	1.20	2.00	1.17	1.93	0.25	0.89	23.93	0.38	5.4	0.64	8	0.02
114	0.60	1.10	0.59	1.11	0.30	0.41	36.44	1.05	3.9	1.23	7	0.02
134	0.24	0.36	0.24	0.36	0.20	0.19	47.88	0.14	2.1	0.39	4	0.03
115	0.12	0.22	0.13	0.24	0.29	0.09	51.52	0.17	1.6	0.85	4	0.05
244	0.03	0.04	0.027	0.03	0.12	0.02	53.45	0.02	0.6	0.28	2	2e-05
245	0.01	0.01	0.01	0.01	0.08	0.01	52.90	0.02	0.4	0.07	1	0.02
345	0.005	0.005	0.005	0.005	< 0	0.005	52.30	-	0.2	2e-05	-	-
155	0.002	0.003	0.004	0.008	0.30	0.003	51.63	0.01	0.3	0.08	1	0.04
444	0.002	0.002	0.002	0.002	< 0	0.002	51.58	-	0.1	2e-05	-	-
355	0.0005	0.0005	3e-04	0.0003	< 0	0.0003	50.66	-	0.05	2e-05	-	-
455	0.0002	0.0002	4e-04	0.0004	< 0	0.0004	50.76	-	0.06	2e-05	-	-
555	2e-05	2e-05	0	0	-	-	-	-	-	-	-	-

Table 2: Quality approximation of the count distribution for $n = 100$ and $p = 0.05$ (top), $p = 0.01$ (middle), $p = 0.005$ (bottom). The empirical mean $\widehat{\mathbb{E}}N(\mathbf{m})$, variance $\widehat{\text{Var}N}(\mathbf{m})$ and cumulative distribution function $\widehat{F}$ have been obtained thanks to 10,000 random graphs. $(\widehat{a}, \widehat{\lambda})$ are the parameters of the Pólya-Aeppli distribution. KS are the Kolmogorov-Smirnov distances. For $\alpha = 0.1\%$ $q_{\mathcal{N}}$ is the $1 - \alpha$ quantile of the normal distribution (idem for the Pólya-Aeppli distribution). NA indicates numerical problems to compute the $\mathcal{PA}$ distribution, whereas '$-$' indicates quantities that have not been calculated ($\widehat{a} < 0$ or null empirical mean and variance).

									$\alpha = 0.1\%$			
m	$\mathbb{E}N(\mathbf{m})$	$\mathrm{Var}N(\mathbf{m})$	$\widehat{\mathbb{E}}N(\mathbf{m})$	$\widehat{\mathrm{Var}N}(\mathbf{m})$	$\widehat{a}$	$\widehat{\lambda}$	$KS_{\mathcal{N}}$	$KS_{\mathcal{PA}}$	$q_{\mathcal{N}}$	$1-\widehat{F}(q_{\mathcal{N}})$	$q_{\mathcal{PA}}$	$1-\widehat{F}(q_{\mathcal{PA}})$
							(%)	(%)		(%)		(%)
111	24904.19	10415630	24941.43	10463804	0.99	118.62	2.36	NA	34937.6	0.25	NA	NA
122	18678.15	5778818	18675.54	5816997	0.99	119.53	1.74	NA	26128.7	0.18	NA	NA
123	14942.52	2922292	14914.40	2934663	0.99	150.83	0.40	NA	20208.2	7e-02	NA	NA
114	7471.26	2112934	7479.15	2103159	0.99	53.00	1.75	NA	11960.7	0.25	NA	NA
134	2988.50	429279.6	2982.40	420630.6	0.99	42.00	2.53	NA	4986.6	0.32	NA	NA
115	1494.25	451540.6	1497.61	454673.2	0.99	9.83	3.68	1.68	3581.3	0.44	4208	0.04
244	373.56	23775.19	373.30	23459.00	0.97	11.69	5.22	1.32	846.6	0.63	977	0.16
245	149.42	6427.06	149.36	6412.56	0.95	6.80	5.66	0.56	396.8	0.77	485	0.11
345	59.77	1180.90	59.57	1159.17	0.90	5.82	6.24	0.47	164.8	0.73	205	0.11
155	29.88	1225.46	30.29	1242.37	0.95	1.44	18.73	16.78	139.2	1.63	220	0.10
444	24.90	350.77	24.80	345.33	0.87	3.32	11.04	4.33	82.2	1.25	110	0.22
355	5.98	57.78	5.98	56.56	0.81	1.14	17.66	7.55	29.2	1.40	48	0.10
455	2.99	17.18	3.00	16.90	0.70	0.91	20.63	4.78	15.7	1.58	27	0.13
555	0.20	0.48	0.20	0.49	0.42	0.12	49.01	1.27	2.3	0.87	6	0.10
111	256.77	2619.15	256.74	2596.12	0.82	46.21	3.30	0.99	414.2	0.35	435	0.13
122	192.58	1433.80	192.47	1412.41	0.76	46.17	3.17	0.85	308.6	0.29	324	0.10
123	154.06	890.78	154.35	893.83	0.70	45.46	2.84	0.45	246.7	0.24	259	0.04
114	77.031	564.99	76.36	558.69	0.76	18.36	5.14	1.25	149.4	0.52	165	0.07
134	30.81	141.53	30.57	140.58	0.64	10.92	5.84	0.51	67.2	0.51	77	0.03
115	15.41	114.06	15.36	111.20	0.76	3.73	9.10	0.33	47.9	0.77	63	0.02
244	3.85	10.74	3.80	10.73	0.48	1.98	15.18	1.72	13.9	1.05	19	0.07
245	1.54	3.77	1.55	3.66	0.40	0.92	23.09	0.46	7.5	0.77	12	0.04
345	0.62	1.06	0.61	1.04	0.26	0.45	35.66	0.51	3.8	0.86	7	0.03
155	0.31	0.96	0.30	0.91	0.50	0.15	47.67	1.27	3.2	1.42	8	0.04
444	0.26	0.42	0.25	0.40	0.24	0.19	47.39	0.95	2.2	0.60	5	0.02
355	0.06	0.09	0.06	0.08	0.16	0.05	53.37	0.03	0.9	0.80	3	2e-05
455	0.03	0.04	0.03	0.04	0.10	0.03	53.58	0.03	0.7	0.32	2	0.01
555	0.002	0.002	0.002	0.003	0.13	0.002	51.38	0.01	0.2	0.01	1	0.01

Table 3: Quality approximation of the count distribution for $n = 500$ and $p = 0.05$ (top), $p = 0.005$ (bottom). The empirical mean $\widehat{\mathbb{E}}N(\mathbf{m})$, variance $\widehat{\mathrm{Var}N}(\mathbf{m})$ and cumulative distribution function $\widehat{F}$ have been obtained thanks to 10,000 random graphs. $(\widehat{a}, \widehat{\lambda})$ are the parameters of the Pólya-Aeppli distribution. KS are the Kolmogorov-Smirnov distances. For $\alpha = 0.1\%$ $q_{\mathcal{N}}$ is the $1-\alpha$ quantile of the normal distribution (idem for the Pólya-Aeppli distribution). NA indicates difficulties to compute the $\mathcal{PA}$ distribution (empirical mean greater than 1500).

									$\alpha = 0.1\%$			
$\mathbf{m}$	$\mathbb{E}N(\mathbf{m})$	$\mathrm{Var}N(\mathbf{m})$	$\widehat{\mathbb{E}}N(\mathbf{m})$	$\widehat{\mathrm{Var}}N(\mathbf{m})$	$\widehat{a}$	$\widehat{\lambda}$	$KS_{\mathcal{N}}$	$KS_{\mathcal{PA}}$	$q_{\mathcal{N}}$	$1-\widehat{F}(q_{\mathcal{N}})$	$q_{\mathcal{PA}}$	$1-\widehat{F}(q_{\mathcal{PA}})$
							(%)	(%)		(%)		(%)
111	199833.7	314809999	199562.5	317861578	0.999	250.42	1.17	NA	254657.2	0.31	NA	NA
122	149875.2	175755625	149798.2	179968751	0.998	249.16	1.21	NA	191254.5	0.21	NA	NA
123	119900.2	86883859	120091.4	85519373	0.997	336.81	0.64	NA	148668.9	0.16	NA	NA
114	59950.1	63565443	59924	64198229	0.998	111.76	1.27	NA	84684.1	0.21	NA	NA
134	23980.04	12670746	24019.74	12797890	0.996	89.99	1.62	NA	35074.8	0.23	NA	NA
115	11990.02	13673678	11987.86	13594556	0.998	21.12	2.31	NA	23381.8	0.27	NA	NA
244	2997.50	682659.7	3000.27	697930.4	0.991	25.68	4.18	NA	5581.9	0.51	NA	NA
245	1199.00	176888.0	1201.13	179141.7	0.987	16.00	3.85	0.56	2509.1	0.53	2819	0.05
345	479.60	31096.36	481.62	31496.74	0.970	14.51	3.96	0.46	1030.1	0.54	1166	0.08
155	239.80	29743.89	240.65	29747.06	0.984	3.86	8.55	2.36	773.6	1.19	1024	0.16
444	199.83	8536.03	199.96	8581.79	0.954	9.11	6.80	1.95	486.2	0.87	575	0.19
355	47.96	1300.61	48.33	1323.87	0.929	3.40	9.53	2.86	160.8	1.12	216	0.17
455	23.98	359.80	24.17	368.78	0.877	2.97	10.64	3.34	83.5	1.29	114	0.20
555	1.60	7.15	1.61	7.37	0.641	0.58	27.84	8.08	10.0	1.23	19	0.20
111	8213.85	682747.2	8197.27	683834.4	0.98	194.20	1.58	NA	10752.7	0.23	NA	NA
122	6160.39	374345.9	6164.75	374787.5	0.97	199.52	1.12	NA	8056.6	0.18	NA	NA
123	4928.31	200136	4927.37	204984.5	0.95	231.32	1.05	NA	6326.5	0.11	NA	NA
114	2464.16	139786.6	2460.80	138179.1	0.96	86.11	1.72	NA	3609.5	0.18	NA	NA
134	985.66	29788.37	984.84	29629.79	0.93	63.36	2.19	0.53	1516.8	0.22	1580	0.09
115	492.83	29351.43	494.34	29697.4	0.97	16.19	3.28	0.75	1026.9	0.31	1152	0.07
244	123.21	1772.00	123.54	1739.11	0.87	16.39	4.25	0.65	252.4	0.48	282	0.06
245	49.28	523.43	49.58	530.73	0.83	8.47	5.93	0.68	120.8	0.58	143	0.09
345	19.71	108.05	19.80	108.17	0.69	6.13	7.79	0.65	51.9	0.72	63	0.09
155	9.86	119.19	9.87	117.56	0.84	1.53	18.36	12.03	43.4	1.29	67	0.09
444	8.21	36.60	8.29	36.64	0.63	3.06	12.01	2.69	27.0	1.08	36	0.14
355	1.97	6.83	1.98	6.94	0.55	0.88	23.34	2.74	10.1	0.95	17	0.11
455	0.99	2.35	0.98	2.31	0.40	0.58	28.66	1.21	5.7	1.05	10	0.07
555	0.07	0.10	0.06	0.09	0.17	0.05	53.16	0.18	1.0	0.30	3	2e-05
111	2060.35	55750.96	2058.76	55507.45	0.93	147.26	2.06	NA	2786.8	0.27	NA	NA
122	1545.26	30335.99	1544.53	30678.85	0.90	148.06	1.34	NA	2085.8	0.17	NA	NA
123	1236.21	17343.32	1235.04	17059.00	0.86	166.76	1.36	0.59	1638.6	0.17	1668	0.09
114	618.11	11620.72	617.55	11686.33	0.90	61.99	2.67	0.79	951.6	0.25	991	0.10
134	247.24	2644.45	246.68	2612.29	0.83	42.57	2.99	0.71	404.6	0.33	427	0.11
115	123.62	2393.86	124.32	2378.23	0.90	12.35	4.33	0.49	275.0	0.45	315	0.08
244	30.90	174.02	30.94	174.27	0.70	9.33	6.19	0.52	71.7	0.61	83	0.13
245	12.36	56.14	12.49	55.82	0.63	4.57	9.63	1.02	35.6	0.66	45	0.11
345	4.94	13.38	5.00	13.45	0.46	2.71	12.90	1.18	16.3	0.62	22	0.08
155	2.47	14.03	2.43	13.40	0.69	0.74	27.60	7.84	13.7	1.56	24	0.06
444	2.06	4.97	2.07	4.99	0.41	1.21	20.01	3.06	9.0	1.19	13	0.08
355	0.49	1.02	0.49	0.99	0.34	0.32	40.73	0.63	3.6	0.94	7	0.04
455	0.25	0.40	0.24	0.39	0.22	0.19	47.91	0.11	2.1	0.42	5	2e-05
555	0.02	0.02	0.01	0.02	0.04	0.01	53.22	0.01	0.4	0.05	1	0.01

Table 4: Quality approximation of the count distribution for $n = 1000$ and $p = 0.05$ (top), $p = 0.01$ (middle), $p = 0.005$ (bottom). The empirical mean $\widehat{\mathbb{E}}N(\mathbf{m})$, variance $\widehat{\mathrm{Var}}N(\mathbf{m})$ and cumulative distribution function $\widehat{F}$ have been obtained thanks to 10,000 random graphs. $(\widehat{a}, \widehat{\lambda})$ are the parameters of the Pólya-Aeppli distribution. KS are the Kolmogorov-Smirnov distances. For $\alpha = 0.1\%$ $q_{\mathcal{N}}$ is the $1-\alpha$ quantile of the normal distribution (idem for the Pólya-Aeppli distribution). NA indicates difficulties to compute the $\mathcal{PA}$ distribution (empirical mean greater than 1500).