



Analyse statistique de réseaux biologiques

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Statistical analysis of biological networks.

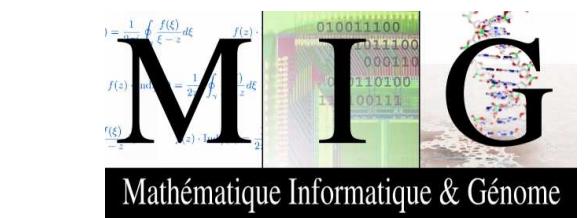
Assessing the exceptionality of network motifs

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<http://genome.jouy.inra.fr/ssb/>



The network revolution

- **Nature of the data:**
 - n individuals (n large),
 - but also n^2 couples.
- **Many scientific fields:**

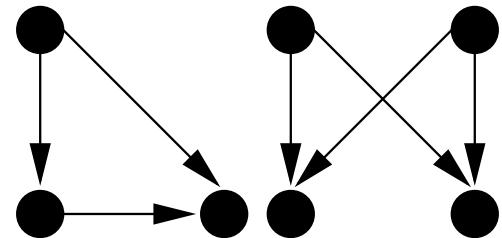
sociology, physics, "internet", biology.
- **Biological networks :**

protein-protein interaction networks, regulatory networks, metabolic networks.
- **Statistical aspects:**
 - network inference,
 - statistical properties of given networks (degrees, diameter, clustering coefficient, modules, motifs etc.),
 - random graph models.

Looking for local structures

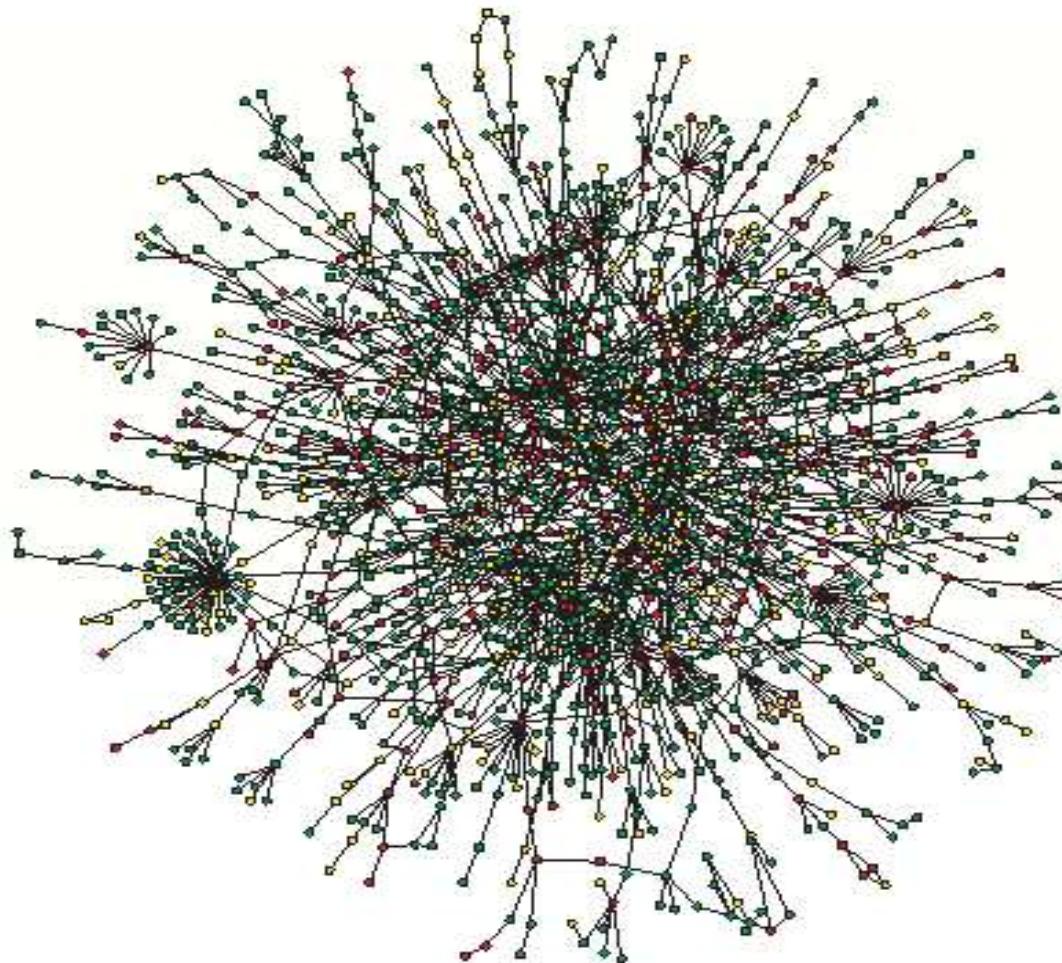
- Breaking-down complex networks into functional modules or **basic building blocks**: [Shen-Orr et al. (02)]
→ patterns of interconnection, **topological motifs**.
- **Focus on exceptional motifs** = motifs appearing more frequently than **expected**. [Milo et al. (02), Shen-Orr et al. (02), Zhang et al. (05)]
- **Interpretation:**
 - they are thought to reflect functional units which combine to regulate the cellular behavior as a whole,
 - mathematical analysis of their dynamics are required. [Mangan and Alon (03), Prill et al. (05)]

- **Transcriptional regulatory networks:**
particular regulatory units (e.g. feed-forward loop, bi-fan).



Other kind of motifs

If the nodes are colored (e.g. GO term, EC number etc.):

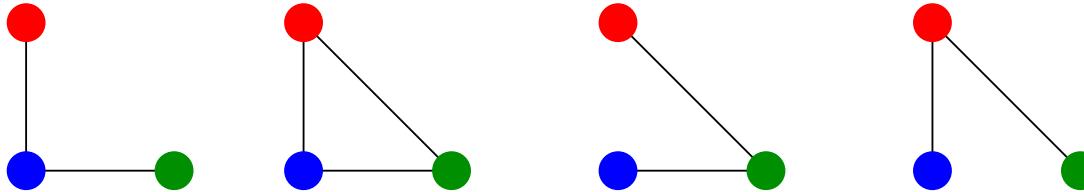


From Barabasi et al.(2004)

Other kind of motifs

If the nodes are colored (e.g. GO term, EC number etc.):

- **Colored motifs** [Lacroix et al. (05, 06)]
 - no topological constraint
 - only a connectedness constraint



- **Topological colored motifs** [Lee et al. (07), Taylor et al. (07)]

How to assess the exceptionality of a motif?

Step 1 To count the observed number of occurrences $N_{\text{obs}}(\mathbf{m})$ of a given motif \mathbf{m} (out of my scope)

Its significance is assessed with the p -value $\mathbb{P}\{N(\mathbf{m}) \geq N_{\text{obs}}(\mathbf{m})\}$
(the probability to get as much occurrences at random)

Step 2 To choose an appropriate **random graph model**

Step 3 To get the **distribution** of the count $N(\mathbf{m})$ under this model

State of the art (1/2)

Analytical approaches:

- The most popular random graph model is the **Erdős-Rényi model** (nodes are connected independently with proba p)
- Some theoretical works exist on Poisson and Gaussian approximations of topological motif count distribution [Janson et al. (00)]
BUT
 - only for particular motifs,
 - the Erdős-Rényi model is not a good model for biological networks (e.g. it does not fit the degrees).

State of the art (2/2)

Simulated approaches:

- Random networks are generated by edge swapping, (degrees are preserved)
- Empirical distributions for motif counts are obtained leading either to p -values or to z -scores

BUT

- huge number of simulations required to estimate tiny p -values,
- z -scores are compared to $\mathcal{N}(0, 1)$ which is not always appropriate,
- Edge swapping does not define a probabilistic random graph model.

Our contributions (1/2)

- To propose probabilistic random graph models
 - adapted for biological networks,
 - allowing probabilistic calculations,
 - with efficient estimation procedures.

Daudin, Picard, Robin (08) *A mixture model for random graphs*. *Statis. Comput.*

Birmelé (07) *A scale-free graph model based on bipartite graphs*. *Disc. Appl. Math.*

Daudin, Picard, Robin (07) *Mixture model for random graphs: a variational approach*, SSB preprint 4

Zanghi, Ambroise, Miele (07) *Fast online graph clustering via Erdős-Rényi mixture*, SSB preprint 8.

Mariadassou, Robin (07) *Uncovering latent structure in valued graphs: a variational approach*, SSB preprint 10.

Our contributions (2/2)

- To provide general analytical results on motif count distribution:
 - mean and variance of the count in a wide class of random graph models,
 - relevant distribution to approximate the count distribution.

Matias, Schbath, Birmelé, Daudin and Robin (06) *Network motifs: mean and variance for the count*, REVSTAT. 4 31–51.

Picard, Daudin, Schbath and Robin (08) *Assessing the exceptionality of network motifs*, J. Comput. Biol.

Schbath, Lacroix and Sagot *Assessing the exceptionality of coloured motifs in networks*, submitted.



Random graph models

Random graphs

- A random graph G is defined by:
 - a set \mathcal{V} of fixed vertices with $|\mathcal{V}| = n$,
 - a set of random edges $\mathbf{X} = \{X_{ij}, (i, j) \in \mathcal{V}^2\}$ such that

$$X_{ij} = \begin{cases} 1 & \text{if } i \text{ and } j \text{ are connected,} \\ 0 & \text{otherwise} \end{cases}$$

- and a distribution on X_{ij} .
- Examples:
 - the Erdős-Rényi model,
 - the Mixture model for random graph (Mixnet/ERMG),
 - the Expected Degree Distribution model.

Example 1: Erdös-Rényi model

- Edges X_{ij} 's are independent ...
- ... and identically distributed according to $\mathcal{B}(p)$

$$\mathbb{P}(X_{ij} = 1) = p$$

- Degrees are Poisson distributed

$$K_i := \sum_{j \neq i} X_{ij} \sim \mathcal{B}(n-1, p) \approx \mathcal{P}((n-1)p)$$

- It does not fit with biological networks.
The main reason is: heterogeneity.

Example 2: Mixture model for random graphs

- Vertices are spread into Q groups.
- Conditionally to the group of vertices, edges are independent and

$$X_{ij} \mid \{i \in q, j \in \ell\} \sim \mathcal{B}(\pi_{q,\ell})$$

$\pi_{q,\ell}$ is the connection probability between groups q and ℓ .

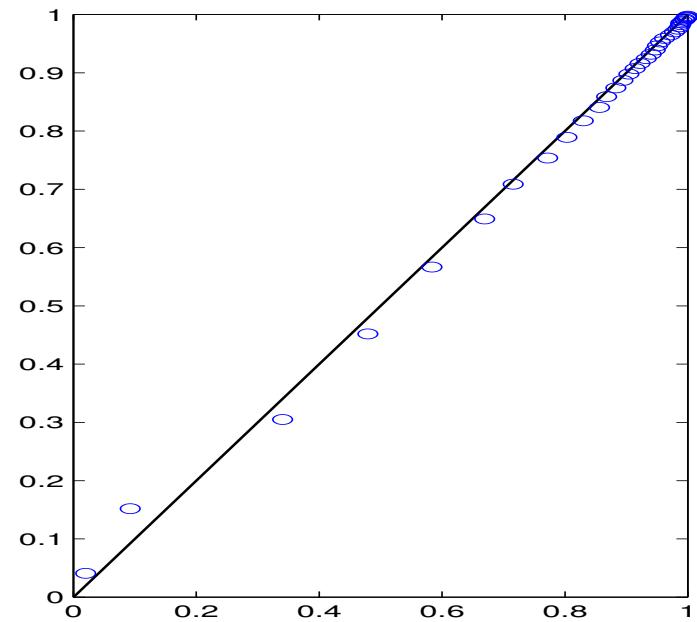
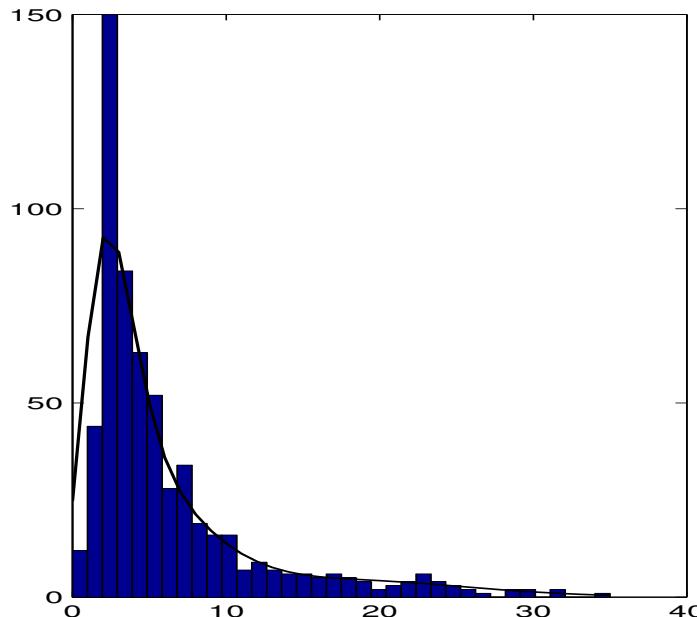
- Degrees are distributed according to a Poisson mixture

$$K_i \sim \sum_q \alpha_q \mathcal{B}(n - 1, \bar{\pi}_q) \text{ with } \bar{\pi}_q = \sum_\ell \alpha_\ell \pi_{q,\ell}$$

- Better fit to biological networks.

Mixnet fit

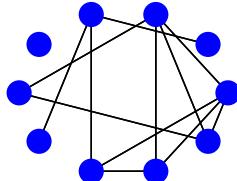
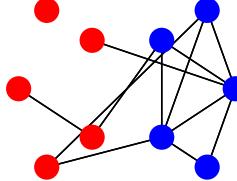
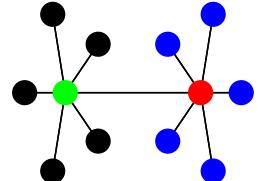
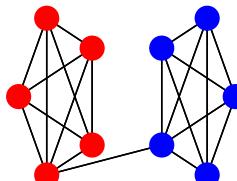
- *E. coli* reaction network: 605 vertices, 1782 edges.
(data curated by V. Lacroix and M.-F. Sagot).
- **Degrees:** Poisson mixture versus empirical distribution
PP-plot



- **Clustering coefficient:**

| Empirical | Mixnet ($Q = 21$) | ER ($Q = 1$) |
|-----------|---------------------|----------------|
| 0.626 | 0.544 | 0.0098 |

Mixnet flexibility

| Examples | Network | Q | π |
|---|--|-----|--|
| Erdös-Rényi |  | 1 | p |
| Independent model (product connectivity) |  | 2 | $\begin{pmatrix} a^2 & ab \\ ab & b^2 \end{pmatrix}$ |
| Stars |  | 4 | $\begin{pmatrix} 0 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 1 & 0 & 0 \end{pmatrix}$ |
| Clusters (affiliation network) |  | 2 | $\begin{pmatrix} 1 & \varepsilon \\ \varepsilon & 1 \end{pmatrix}$ |

Mixnet: estimation procedure

- The aim is to maximize the log-likelihood $\mathcal{L}(\mathbf{X})$,
- ... but $\mathcal{L}(\mathbf{X})$ is not calculable because of hidden groups (\mathbf{Z} , Z_i is the group of node i).
- EM algorithm is classical to fit mixture models,
- ... but cannot be used because $\mathbb{P}(\mathbf{Z} \mid \mathbf{X})$ is not computable (all vertices are potentially connected, no local dependence)
- Strategy = **variational approach**
 - maximization of $\mathcal{L}(\mathbf{X}) - KL(\mathbb{P}(\mathbf{Z} \mid \mathbf{X}), Q_R(\mathbf{Z}))$ where Q_R is the best approximation of $\mathbb{P}(\mathbf{Z} \mid \mathbf{X})$ within a class of 'nice' distributions. \Rightarrow estimator of $\mathbb{P}(Z_i = q \mid \mathbf{X})$.
 - iterative algorithm
- Heuristic penalized likelihood criterion inspired from BIC (ICL)

[Daudin, Picard and Robin (07)]

Example 3: Expected Degree Distribution model

- Let f be a given distribution and D_i 's i.i.d. $D_i \sim f$.
- Conditionally to the D_i 's, edges X_{ij} 's are independent and

$$\mathbb{P}(X_{ij} = 1 \mid D_i, D_j) = \gamma D_i D_j$$

- A suitable value for γ ensures that $\mathbb{E}(K_i | D_i) = D_i$.
- This model generates graphs whose degrees follow a given distribution.

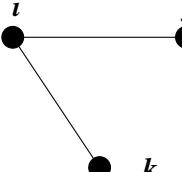
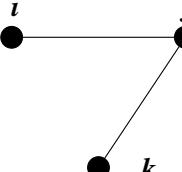
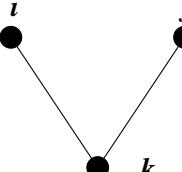


Occurrences of topological motifs

Topological motifs

Let \mathbf{m} be a motif of size k (connected graph with k vertices, $k \ll n$).

- \mathbf{m} is defined by its adjacency matrix (also denoted by \mathbf{m}):
 $\mathbf{m}_{uv} = 1$ iff nodes $u \leftrightarrow v$ ($\mathbf{m}_{uv} = 0$ otherwise).
- Let $\mathcal{R}(\mathbf{m})$ be the set of non redundant permutations of \mathbf{m} (so-called “versions”).
- Ex: 3 versions of the V motif at a **fixed** position (i, j, k) .

| \mathbf{m} | \mathbf{m}' | \mathbf{m}'' |
|---|--|---|
| $\begin{bmatrix} 0 & 1 & 1 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \end{bmatrix}$  | $\begin{bmatrix} 0 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & 1 & 0 \end{bmatrix}$  | $\begin{bmatrix} 0 & 0 & 1 \\ 0 & 0 & 1 \\ 1 & 1 & 0 \end{bmatrix}$  |

Occurrences of a motif

- Let $\alpha = (i_1, \dots, i_k) \in I_k$ be a possible position of \mathbf{m} in G .
 G_α denotes the subgraph $(V_{i_1}, \dots, V_{i_k})$.
- Non strict occurrences:

\mathbf{m} occurs at position $\alpha \Leftrightarrow \mathbf{m} \subseteq G_\alpha$

- Random indicator of occurrence: $Y_\alpha(\mathbf{m})$

$$Y_\alpha(\mathbf{m}) = \mathbf{1}\{\mathbf{m} \text{ occurs at position } \alpha\} = \prod_{1 \leq u, v \leq k} X_{i_u i_v}^{m_{uv}}.$$

- The total count $N(\mathbf{m})$ of motif \mathbf{m} is then:

$$N(\mathbf{m}) = \sum_{\alpha \in I_k} \sum_{\mathbf{m}' \in \mathcal{R}(\mathbf{m})} Y_\alpha(\mathbf{m}')$$

- Warning: $N(\mathbf{m}) \neq$ number of induced subgraphs (“ $\mathbf{m} = G_\alpha$ ”).

Expected count of a motif

Recall that $N(\mathbf{m}) = \sum_{\alpha \in I_k} \sum_{\mathbf{m}' \in \mathcal{R}(\mathbf{m})} Y_\alpha(\mathbf{m}')$

- Under “stationarity” assumption on the random graph model, the distribution of $Y_\alpha(\mathbf{m})$ does not depend on α and let us define

$$\mu(\mathbf{m}) := \mathbb{E}Y_\alpha(\mathbf{m}'), \quad \forall \alpha, \forall \mathbf{m}' \in \mathcal{R}(\mathbf{m}).$$

- The expectation of $N(\mathbf{m})$ is then:

$$\mathbb{E}N(\mathbf{m}) = \binom{n}{k} |\mathcal{R}(\mathbf{m})| \mu(\mathbf{m}).$$

Variance for the count

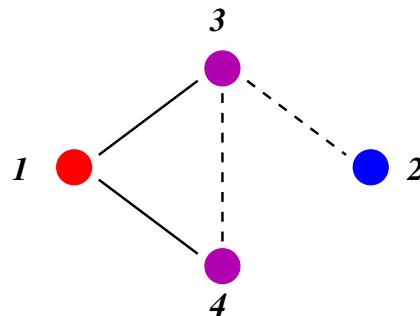
By definition $\text{Var}N(\mathbf{m}) = \mathbb{E}N^2(\mathbf{m}) - [\mathbb{E}N(\mathbf{m})]^2$. We then calculate

$$\begin{aligned}\mathbb{E}N^2(\mathbf{m}) &= \mathbb{E} \left(\sum_{\alpha, \beta \in I_k} \sum_{\mathbf{m}', \mathbf{m}'' \in \mathcal{R}(\mathbf{m})} Y_\alpha(\mathbf{m}') Y_\beta(\mathbf{m}'') \right), \\ &= \mathbb{E} \left(\sum_{s=0}^k \sum_{|\alpha \cap \beta|=s} \sum_{\mathbf{m}', \mathbf{m}'' \in \mathcal{R}(\mathbf{m})} Y_{\alpha \cup \beta}(\mathbf{m}' \underset{s}{\Omega} \mathbf{m}'') \right) \\ &= \sum_{s=0}^k C(n, k, s) \sum_{\mathbf{m}' \underset{s}{\Omega} \mathbf{m}''} \mu(\mathbf{m}' \underset{s}{\Omega} \mathbf{m}''),\end{aligned}$$

where $\mathbf{m}' \underset{s}{\Omega} \mathbf{m}''$ is a **super-motif** composed of the union of two overlapping occurrences of \mathbf{m}' and \mathbf{m}'' sharing s common vertices.

Super-motifs

- Example for the V motif:



- \mathbf{m} occurs at $\alpha = (1, 3, 4)$, \mathbf{m}' occurs at $\beta = (2, 3, 4)$,
- in this case $\alpha \cap \beta = (3, 4)$ and $s = 2$.
- The adjacency matrix of the super-motifs $\mathbf{m}' \underset{s}{\Omega} \mathbf{m}''$ can be easily derived from the adjacency matrices of \mathbf{m}' and \mathbf{m}'' [Picard et al. (07)].

Occurrence probability for mean and variance

The following expressions for the mean and variance of $N(\mathbf{m})$ are valid under any stationary random graph model:

$$\begin{aligned}\mathbb{E}N(\mathbf{m}) &= \binom{n}{k} |\mathcal{R}(\mathbf{m})| \mu(\mathbf{m}) \\ \mathbb{V}\text{ar}N(\mathbf{m}) &= \sum_{s=0}^k C(n, k, s) \sum_{\substack{\mathbf{m}' \Omega \mathbf{m}'' \\ s}} \mu(\mathbf{m}' \Omega \mathbf{m}'') - [\mathbb{E}N(\mathbf{m})]^2.\end{aligned}$$

The final point is now the calculation of the occurrence probability $\mu(\cdot)$ given the adjacency matrix of a motif.

Calculating $\mu(\mathbf{m})$

- The probability of occurrence of a given motif depends on the distribution of the X_{ij} 's.
- Stationary assumption: $\mu(\mathbf{m})$ does not depend on the position of the motif
- In the **Erdős-Rényi model**: $\mu(\mathbf{m}) = \pi^{v(\mathbf{m})}$, with $v(\mathbf{m})$ the number of edges in \mathbf{m} .
- In the **Mixnet** model with Q groups with proportion $\alpha_1, \dots, \alpha_Q$:

$$\mu(\mathbf{m}) = \sum_{c_1=1}^Q \dots \sum_{c_k=1}^Q \alpha_{c_1} \dots \alpha_{c_k} \prod_{1 \leq u < v \leq k} \pi_{c_u, c_v}^{m_{uv}}.$$

- In the **EDD** model ($D \sim f$): $\mu(\mathbf{m}) = \gamma^{m_{++}/2} \prod_{u=1}^k \mathbb{E} D^{m_{u+}}$

Motif count distribution

- Exact distribution unknown.
- Several approximations exist (or are used) in the literature:
 - Gaussian distribution
 - Poisson distribution

Motif count distribution

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BUT not adapted for rare motifs
 - Poisson distribution
BUT mean \neq variance

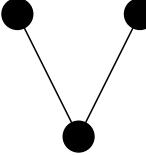
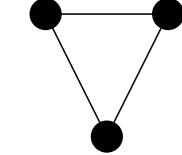
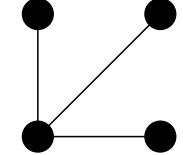
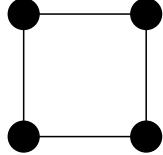
Motif count distribution

- Exact distribution unknown.
- Several approximations exist (or are used) in the literature:
 - Gaussian distribution
BUT not adapted for rare motifs
 - Poisson distribution
BUT mean \neq variance
 - \Rightarrow Compound Poisson distribution?

Compound Poisson distribution

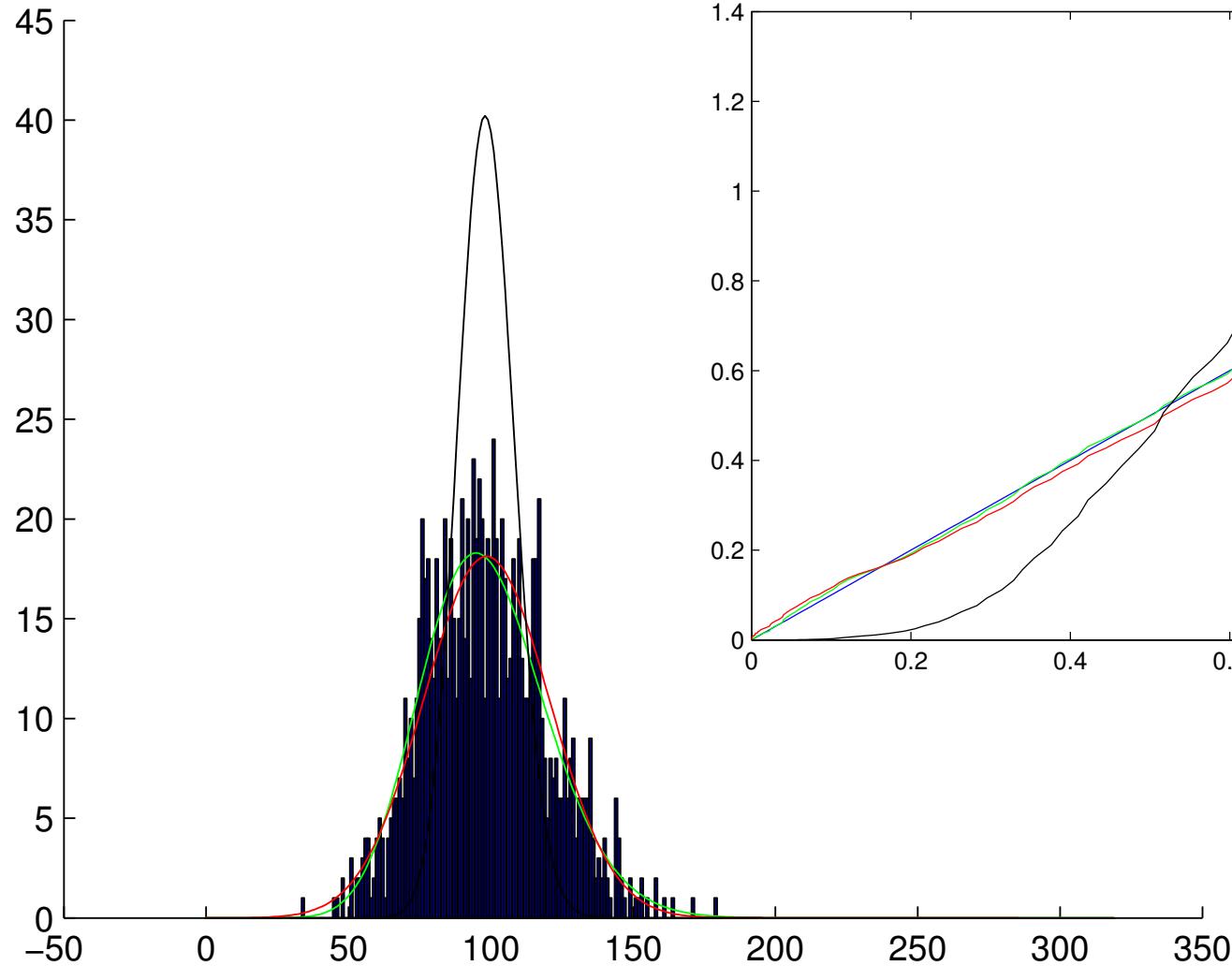
- Distribution of $\sum_{i=1}^Z T_i$ when $Z \sim \mathcal{P}(\lambda)$ and T_i 's iid.
- Particularly adapted for the count of clumping events: Z is the number of clumps and T_i is the size of the i -th clump.
- All network motifs are overlapping: they occur in clumps.
- We proposed to use a **Geometric-Poisson** (λ, a) distribution, i.e. when $T_i \approx \mathcal{G}(1 - a)$
 - analogy with sequence motifs [Schbath (95)],
 - (λ, a) can be calculated according to $\mathbb{E}N(\mathbf{m})$ and $\text{Var}N(\mathbf{m})$.

Simulation study

- Aim: to compare the Gaussian, Poisson and Geometric-Poisson approximations for the motif count distribution.
- Random graph model: Mixnet with 2 groups.
- Simulation design:
 - the number of vertices $n = 20, 200$
 - the mean connectivity $\bar{\pi} = 1/n, 2/n$
 - the within/between group connectivity $\gamma = 0.1, 0.5, 0.9$
 - the proportion of the groups $\alpha = 0.1, 0.9$
- 4 motifs:
 -  V
 -  triangle
 -  4-star
 -  square
- We cover a large range for $\mathbb{E}N(\mathbf{m})$ (from 0.07 to 1075.5).

Expectedly frequent motif count distribution

Gaussian (—), Poisson (—) and Geometric-Poisson (—)



Approximation for expectedly frequent motif



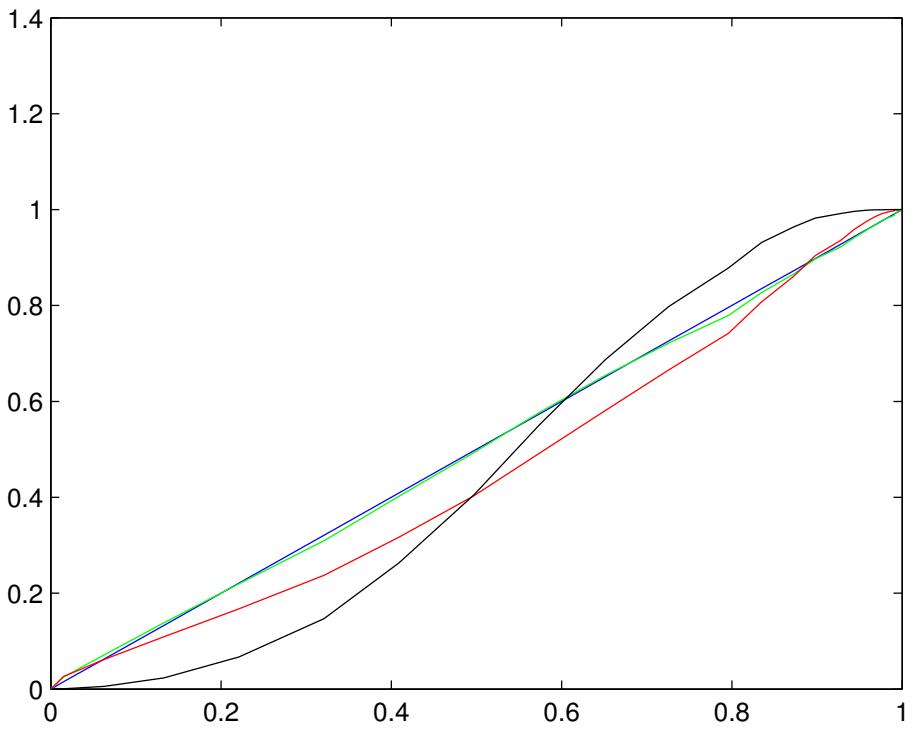
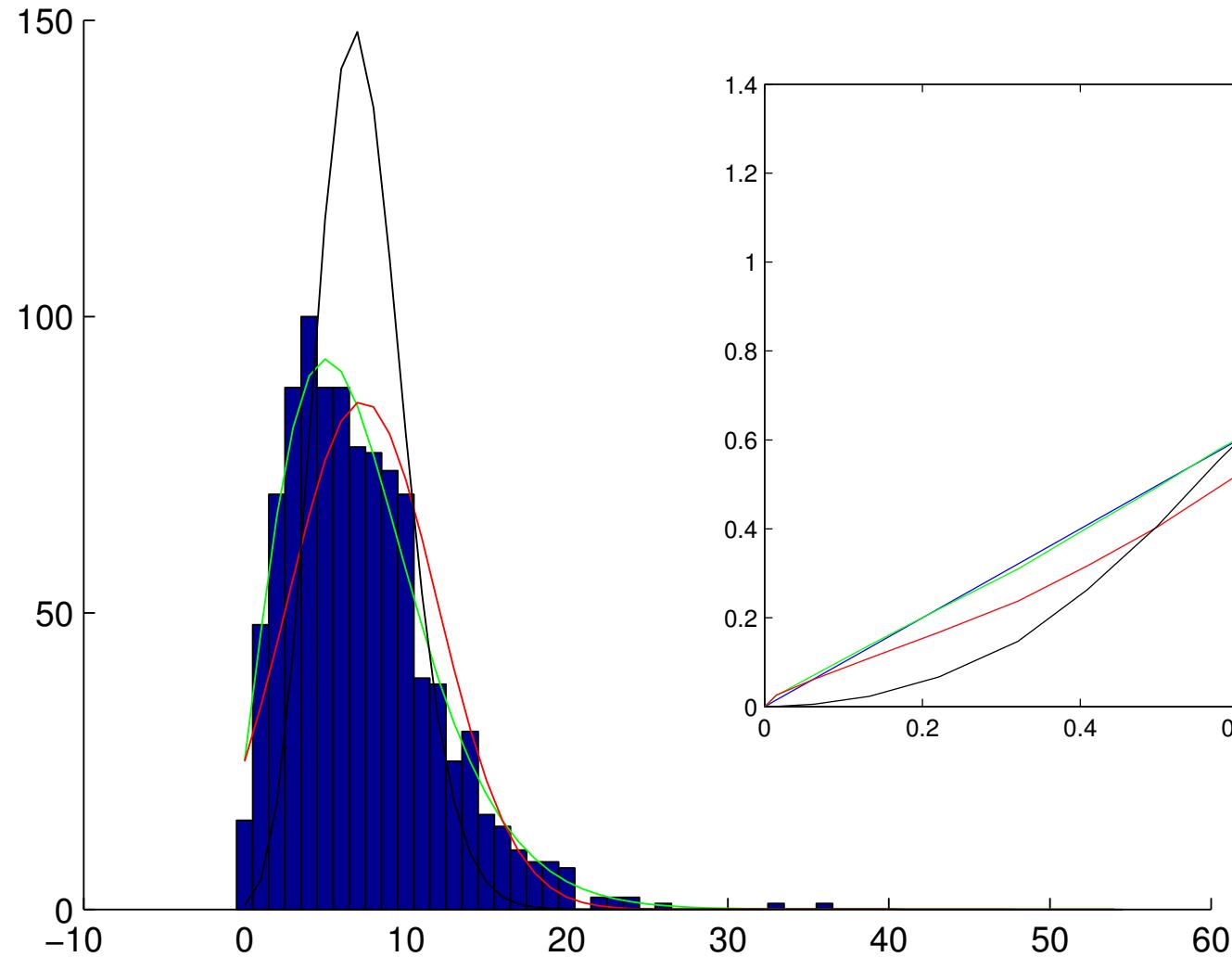
| simulation parameters | | | | motif V | | | | | | | |
|-----------------------|-------------|--------------|--------------|--------------|--------------|-----------|-----------------|-------|----------|-------------|----------------|
| n | $\bar{\pi}$ | α (%) | γ (%) | \mathbb{E} | \mathbb{V} | λ | $\frac{1}{1-a}$ | D_G | D_{GP} | \hat{F}_G | \hat{F}_{GP} |
| 200 | 0.5 | 10 | 10 | 159.5 | 2034.0 | 23.1 | 6.66 | 20.4 | 19.7 | 2.5 | 1.6 |
| 200 | 0.5 | 10 | 90 | 104.9 | 590.5 | 31.6 | 3.33 | 15.2 | 14 | 1.9 | 1.2 |
| 200 | 0.5 | 50 | 10 | 98.5 | 484.0 | 33.3 | 2.27 | 13.1 | 12.6 | 1.1 | 0.7 |
| 200 | 0.5 | 50 | 50 | 98.5 | 484.0 | 33.2 | 2.27 | 14.3 | 13.2 | 1.6 | 1.1 |
| 200 | 0.5 | 50 | 90 | 98.5 | 488.4 | 33.1 | 2.27 | 14.5 | 14.8 | 2.5 | 0.9 |

Criteria to assess the goodness-of-fit:

- D_G (resp. D_{GP}): **total variation distance** between the empirical dist. and the Gaussian (resp. Geometric-Poisson) dist.
- \hat{F}_G (resp. \hat{F}_{GP}): **empirical proba. of exceeding the 0.99 quantile** of the Gaussian (resp. Geometric-Poisson) dist.

Expectedly rare motif count distribution

Gaussian (—), Poisson (—) and Geometric-Poisson (—)



Approximation for expectedly rare motif



| simulation parameters | | | | motif \square | | | | | | | |
|-----------------------|-------------|--------------|--------------|-----------------|--------------|-----------|-----------------|-------|----------|-------------|----------------|
| n | $\bar{\pi}$ | α (%) | γ (%) | \mathbb{E} | \mathbb{V} | λ | $\frac{1}{1-a}$ | D_G | D_{GP} | \hat{F}_G | \hat{F}_{GP} |
| 200 | 1 | 10 | 10 | 7.31 | 21.72 | 3.68 | 2 | 11.8 | 5.4 | 3.2 | 0.9 |
| 200 | 1 | 10 | 90 | 2.57 | 3.42 | 2.21 | 1.16 | 9.3 | 2.7 | 3.6 | 0.5 |
| 200 | 1 | 50 | 10 | 2.74 | 3.69 | 2.33 | 1.17 | 12.3 | 3.6 | 4.7 | 1.2 |
| 200 | 1 | 50 | 50 | 1.94 | 2.40 | 1.74 | 1.11 | 11.3 | 2.0 | 3.2 | 1.6 |
| 200 | 1 | 50 | 90 | 2.74 | 3.72 | 2.32 | 1.17 | 10.8 | 4.5 | 3.7 | 0.7 |

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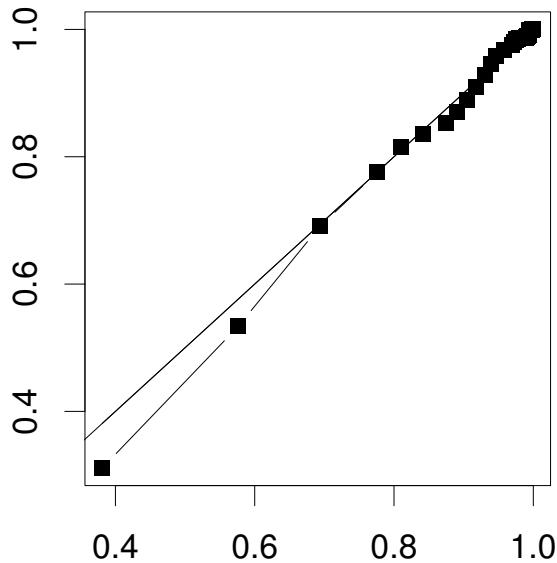
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Conclusions for the simulation study

- Validation of our analytical expressions for $\mathbb{E}N$ and $\text{Var}N$.
- The Poisson approximation is not satisfactory.
- The Geometric-Poisson approximation outperforms the Gaussian approximation for both criteria in all cases, especially for “rare” motifs.
- The 0.99 quantile is underestimated by the Gaussian approximation:
→ false positive results.
- The total variation distance is high for both approximations in some cases, especially for frequent and highly self overlapping motifs.
- The clumps size distribution is probably not geometric . . .

Application to the *H. pylori* PPI network

- Protein-protein interaction network: 706 proteins (nodes) and 1420 interactions (edges).
- Mixnet was fitted to the network and 4 groups of connectivity were selected using a model selection criterion.
- Goodness-of-fit for the degree distribution (PP-plot):

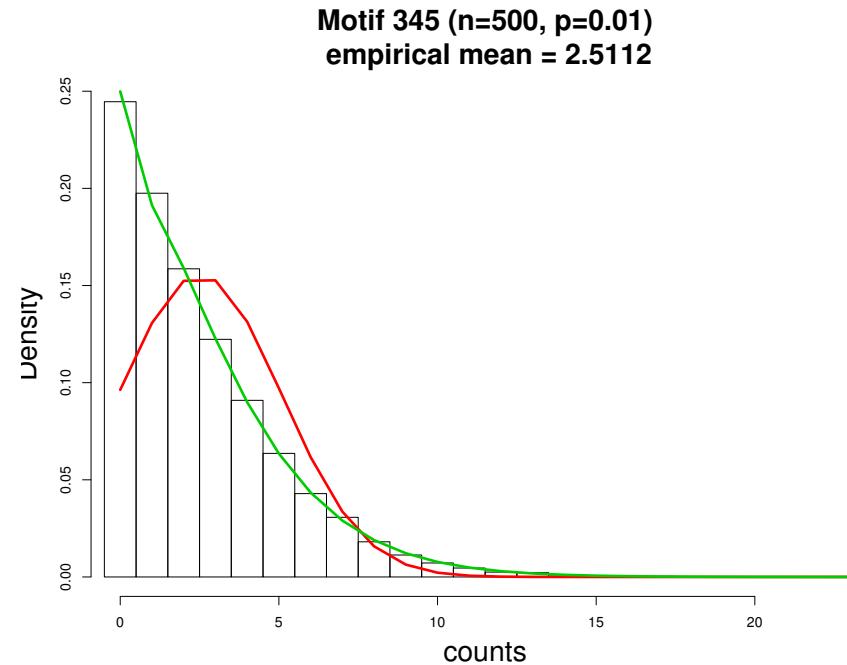
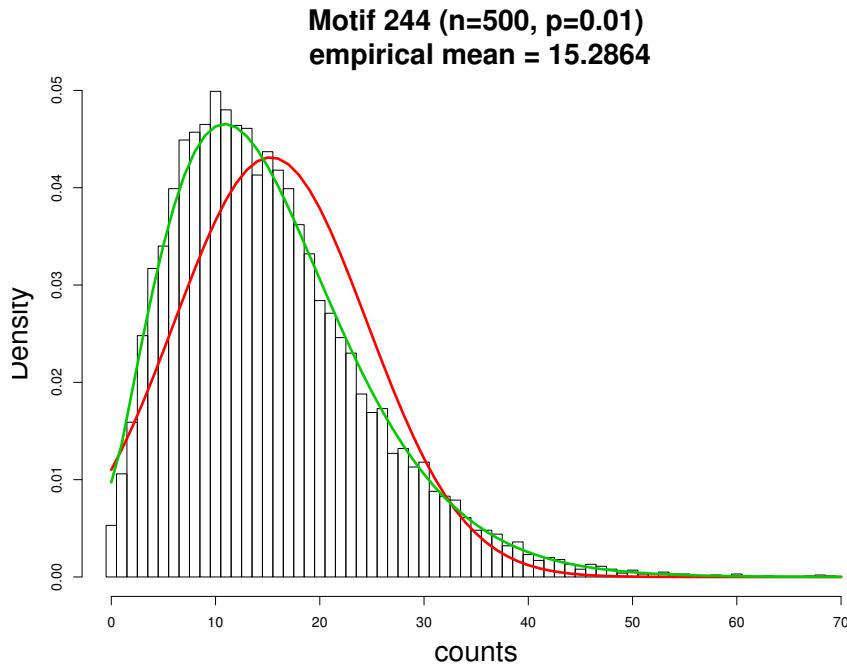


Exceptional motifs of size 3 and 4

| Motif | N_{obs} | $\mathbb{E}_{\text{mixnet}} N$ | $\sigma_{\text{mixnet}}(N)$ | $\mathbb{P}(\mathcal{GP} \leq N_{\text{obs}})$ | $\mathbb{P}(\mathcal{GP} \geq N_{\text{obs}})$ |
|---|------------------|--------------------------------|-----------------------------|--|--|
|  | 14113 | 13602 | 2659 | | $4.06 \cdot 10^{-1}$ |
|  | 75 | 66.9 | 20.4 | | $3.31 \cdot 10^{-1}$ |
|  | 98697 | 94578 | 27039 | | $4.12 \cdot 10^{-1}$ |
|  | 112490 | 93741 | 27257 | | $2.34 \cdot 10^{-1}$ |
|  | 1058 | 516.6 | 208.7 | | $1.33 \cdot 10^{-2}$ |
|  | 3535 | 2897 | 1120 | | $2.63 \cdot 10^{-1}$ |
|  | 79 | 34.8 | 20.0 | | $3.11 \cdot 10^{-2}$ |
|  | 0 | 0.17 | 0.45 | $8.5 \cdot 10^{-1}$ | |

What about colored motifs?

- Ongoing work : colored Erdös-Rényi model.
- Analytical mean and variance for motifs of size up to 5 (difficulty in the variance: connectivity term).
- Simulations: Geometric-Poisson distribution performs better than the Gaussian one.



Conclusions & future directions

- We have proposed a flexible mixture model to fit biological networks.
- We proposed statistical methods to assess the exceptionality of network motifs *without simulations*.
- The Geometric-Poisson approximation for the count distribution works well (better than the Gaussian) on simulated data.
- For topological motifs:
 - The method to calculate the moments of the count is general and can be applied to any random graph model with stationary distribution.
 - Results can be easily generalized to directed motifs.

Directions:

- Distribution of the clump size.
- For colored motifs:
 - General formula for the variance.
 - Generalization to Mixnet.

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Mixnet: model selection procedure

- Heuristic penalized likelihood criterion inspired from BIC (ICL)
- The completed log-likelihood $\mathcal{L}(\mathbf{X}, \mathbf{Z})$ is the sum

$$\sum_i \sum_q \mathbf{1}\{Z_i = q\} \log \alpha_q + \sum_{i,j > i} \sum_{q,\ell} \mathbf{1}\{Z_i = q\} \mathbf{1}\{Z_j = \ell\} \log b(X_{ij}; \pi_{q,\ell})$$

$(Q - 1)$ independent proportions α_q 's and n terms

$Q(Q + 1)/2$ probabilities $\pi_{q,\ell}$'s and $1)/2$ terms

$n(n -$

- The heuristic criterion is then:

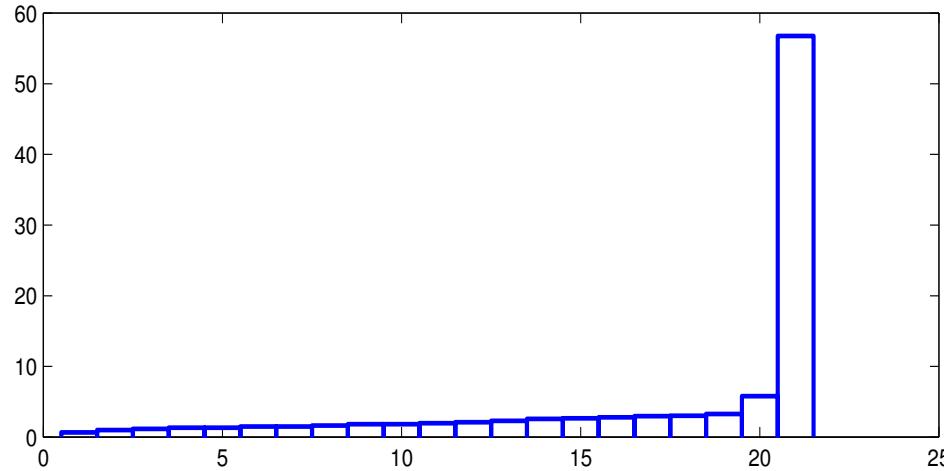
$$-2\widehat{\mathcal{L}}(\mathbf{X}, \mathbf{Z}) + (Q - 1) \log n + \frac{Q(Q + 1)}{2} \log \left[\frac{n(n - 1)}{2} \right].$$

Illustration of Mixnet

The Mixnet has been adjusted to

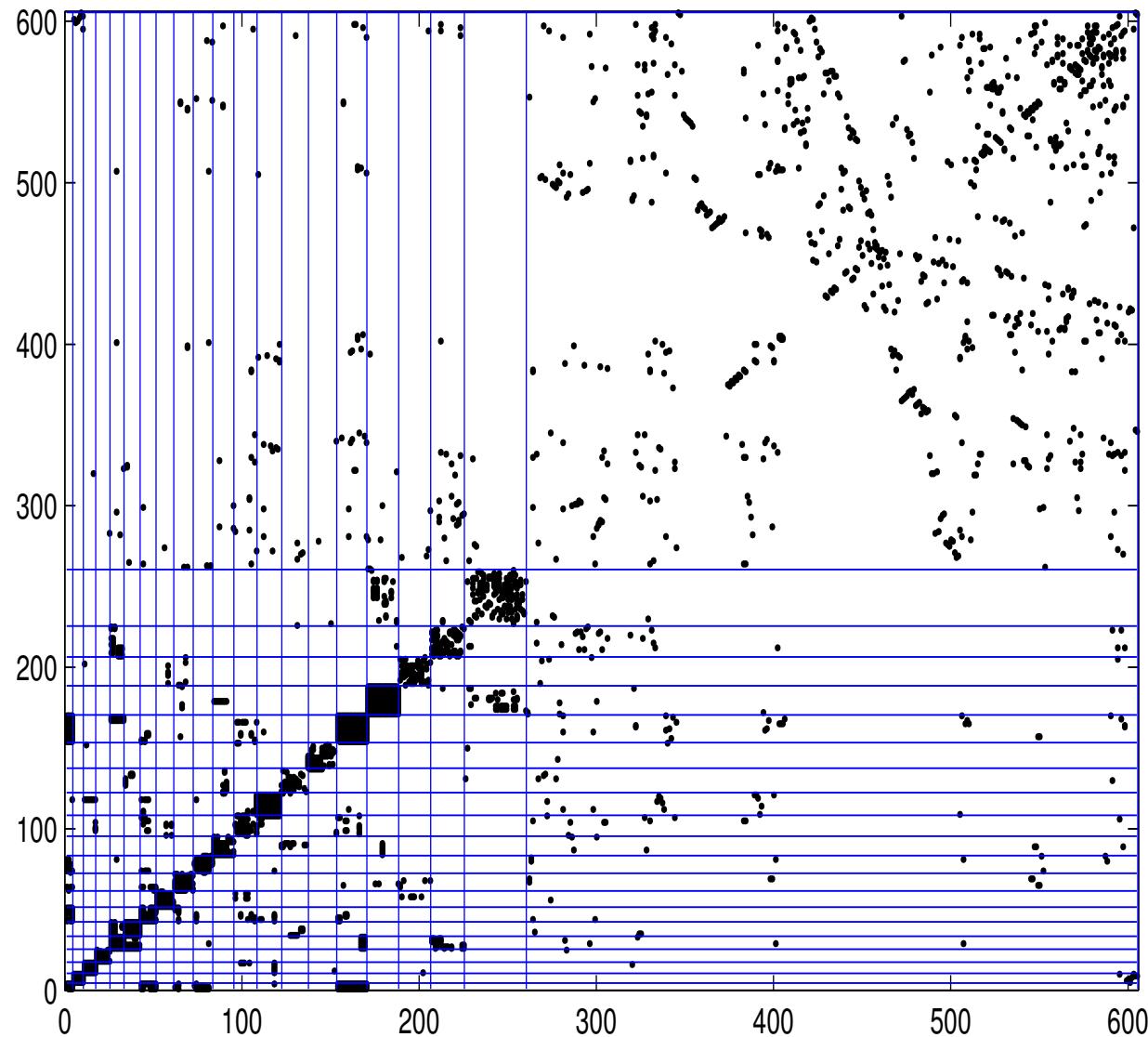
- *E. coli* reaction network: 605 vertices, 1782 edges.
(data curated by V. Lacroix and M.-F. Sagot).
- $Q = 21$ groups selected

Group proportions $\hat{\alpha}_q$ (%).



- Many small groups correspond to cliques or pseudo-cliques.

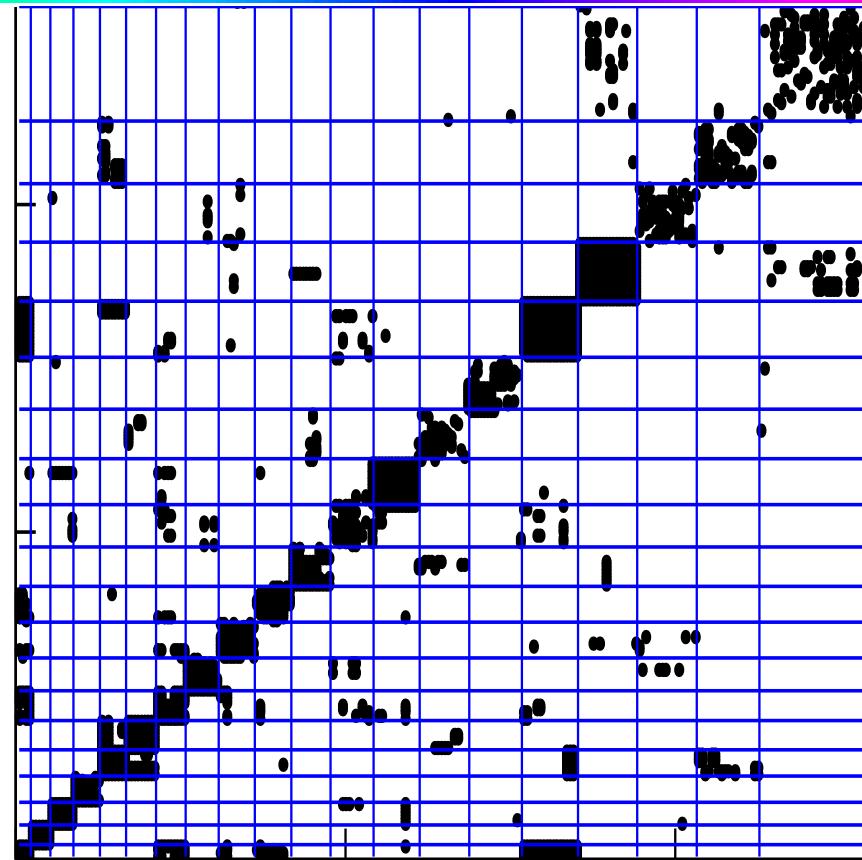
Dot plot representation of the network



Dot plot representation (zoom)

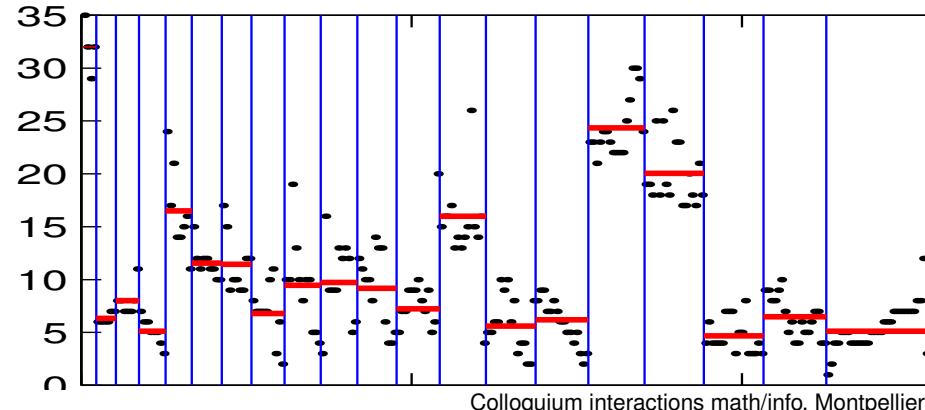
Sub-matrix of π :

| q, ℓ | 1 | 10 | 16 |
|-----------|-----|-----|-----|
| 1 | 1.0 | | |
| 10 | .43 | .67 | |
| 16 | 1.0 | 0 | 1.0 |



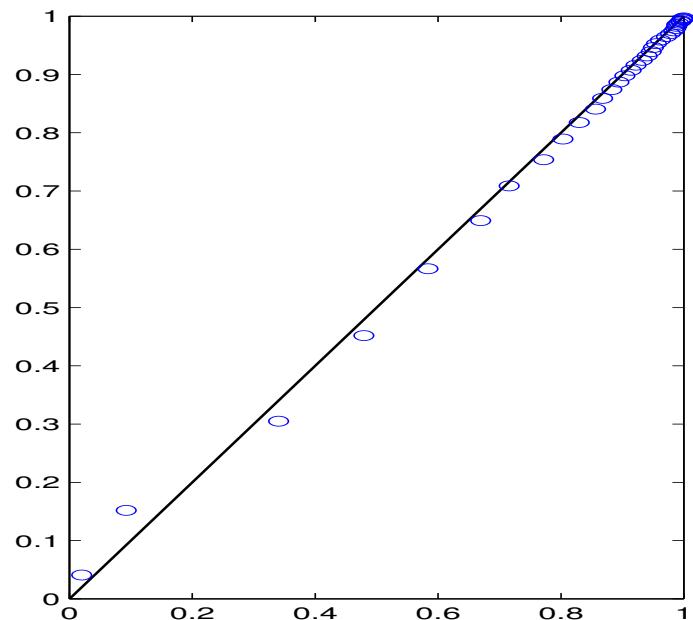
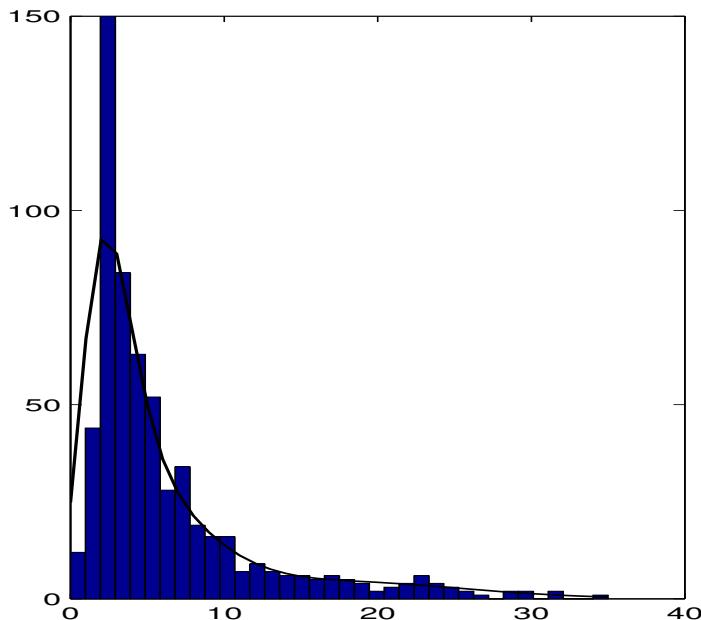
Vertex degrees K_i 's.

Mean degree in the last group: $\bar{K}_{21} = 2.6$



Model fit

- **Degrees:** Poisson mixture versus empirical distribution
PP-plot



- **Clustering coefficient:**

| Empirical | Mixnet ($Q = 21$) | ER ($Q = 1$) |
|-----------|---------------------|----------------|
| 0.626 | 0.544 | 0.0098 |