

A MODEL FOR BIOLOGICAL DYNAMIC NETWORKS

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ABSTRACT. The main aim of this paper is to introduce a mathematical framework to study stochastically evolving networks. More precisely, we provide a common language and suitable tools to study systematically the probability distribution of topological characteristics, which, in turn, play a key role in applications, especially for biological networks. The latter is possible via suitable definition of a random network process and new results for graph isomorphism, which, under suitable generic assumptions, can be stated in terms of the graph walk matrix and computed in polynomial time.

1. Introduction. Dynamics of networks attracted the attention of researchers from different domains, [2, 3, 14, 17]. The main reason for this success is the wide applicability of network science, ranging from data networks as internet, to social networks and biological ones.

The classical approach to random graphs, by Erdos and Reny [10], provides a suitable framework to deal with networks with uncertainties and to compute the relative probabilities for typical topological properties, such as the distribution of number of arcs per node. However, using simple rules to add a node or an arc to a given graph with assigned probability, one often obtains time evolving networks whose probability distribution typically does not match with random graph theory. Moreover, such networks are encountered in many situations as internet, social networks, biological networks and others [1, 2, 15, 17].

For applications to biological networks, in particular cells signaling networks, the theory of time evolving networks, representing dynamics of genes over successive generations (large time scale), must be combined with dynamics on networks of given quantities, such as proteins and transcription factors concentrations, within a cell life (small time scale). In this setting, various results were obtained also by the control community, see for instance [5, 8, 11, 16]. For both time scales, it plays a key role the the concept of network motifs, see [1]. The latter are topologies of subnetworks which appear very frequently in real biological networks, opposed to

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their low probabilities in random networks in the sense of Erdos-Renyi. For instance, focusing on simple subnetworks with three nodes, the Feed-Forward-Loop (FFL) is more frequent than all other possible subnetworks with three nodes, see [1]. The FFL motif is linked to specific signaling effects such as sign-sensitive accelerators or sign sensitive delays, see [13].

Taking the large time scale point of view, we aim at introducing a mathematically sound framework to deal with stochastically evolving networks. The aim of the latter is to provide a common language and suitable tools to study systematically the probability distribution of topological characteristics, which, in turn, play key roles in applications.

We first introduce integer valued distances for list representation of graphs and define them over quotient spaces for isomorphism equivalence. Then, we introduce our definition of random network process (the counterpart of a stochastic process) and, in particular, of a Brownian network process (briefly BNP). The latter corresponds to equiprobable evolution over graphs at distance one, starting from a single node. The properties of such process are studied (up to isomorphism equivalence), showing the lack of symmetry after few steps. More precisely, at third step of the process, we obtain that the network with four vertices representing a path of length three is the most probable (with probability equal to $\frac{1}{2}$). On the other side, the other two networks, the triangle and the star, have probability $\frac{1}{4}$. Such phenomenon rapidly gets more involved: at step four the most probable network, a the triangle with an edge attached to a vertex, has still probability $\frac{1}{2}$, while the other network have smaller probabilities, with the smallest one equal to $\frac{1}{28}$ and corresponding to the star with five nodes.

Notice that our process differs from preferential attachment models in that our probabilities of generating a new node or a new arc depends on the graph itself. In case of constant probabilities, many results on the degree distribution are available, see for instance [4, 6, 9].

The main difficulty in computing the probability distribution function of BNP, after several steps, lies in the fact that many isomorphic graphs will appear in the stochastic evolution. Then we deal with graph isomorphisms, introducing a new framework to find necessary and sufficient conditions. The main idea is that of a decomposition of \mathbb{R}^n in terms of eigenspaces of the adjacency matrix, which allows, under suitable assumptions, a statement of isomorphism conditions in terms of the walk matrix, see Theorem 1. More precisely, we consider main eigenspaces of the adjacency matrix (that are those not orthogonal to the vector with all entries equal to 1). Then an adjacency matrix has a *simple* decomposition if there is at most one not main eigenspace and all other eigenvalues are simple (or at most one not simple if there is no not main eigenpace.) Our main result states that cospectral graphs with *simple* eigenspace decompositions are isomorphic if and only if they have the same walk matrix up to permutations.

Since conditions in Theorem 1 are generic and can be translated easily in an algorithm (with polynomial complexity in terms of number of vertices of the graph), we can write a program and automatically compute the probabilities of BNP (up to isomorphisms).

Going back to biological networks, we show how the probability of having a triangular subnetwork, which is the base for the FFL motif, rapidly increases during the stochastic evolution. Since the number of nodes may vary for graphs obtained at a same step of the BNP, it is not immediate a comparison with Erdos-Renyi theory.

However, we are able to argue that such probabilities are above those for random networks, taking into account the average connectivity of graphs produced by BNP. This represents a first step towards studying systematically network motifs with our model. We finally point out that a satisfactory theory for biological networks will necessary include the case of directed graphs and probably connectivity rules more complex than that of BNP.

2. Basic notations and definitions. For future convenience we introduce the following notations. We denote by $\mathbf{e}_i, i = 1, \dots, n$, the canonical vectors of \mathbb{R}^n , by I_n the identity $n \times n$ matrix, by $\mathbf{1}$ the vector of \mathbb{R}^n filled with 1's, and by $J = \mathbf{1}\mathbf{1}^T$ the $n \times n$ matrix filled with 1's.

A graph consists of a set $V = \{v_1, \dots, v_n\}$ of n vertices and a set $E = \{e_1, \dots, e_m\}$ of m edges where, for $j = 1, \dots, m$, the edge e_j linking some vertex v_{j_1} to some vertex v_{j_2} , is denoted by (v_{j_1}, v_{j_2}) . Different data structures for the representation of graphs in a computer system are used in practice. We mainly distinguish them among list and matrix structures. Lists are mainly used to represent and store large (sparse) graphs while matrices are more suitable for the analysis of graphs' properties.

2.1. Representation by lists. Among lists we mention

- **Adjacency list.** An adjacency list is an array of type

$$((1, \{1_1, \dots, 1_{k_1}\}), \dots, (n, \{n_1, \dots, n_{k_n}\}))$$

where, for each $i = 1, \dots, n$, $(i, \{i_1, \dots, i_{k_i}\})$ means that there is an edge from v_i to v_{i_j} , for all $j = 1, \dots, k_i$. Thus, node v_i has k_i adjacent nodes.

- **Incidence list.** An incident list is an array containing pairs (ordered if directed) of vertices (that the edge connects) and possibly weight and other data.

2.2. Representation by matrices.

- **Incidence Matrix.** The graph is represented by a matrix of size $n \times m$ where the entry i, j is 1 if edge e_j starts from vertex v_i , -1 if e_j ends in vertex v_i and 0 otherwise. If the graph is not directed then entry i, j is either equal to 1, if e_j is incident in v_i , or to 0, otherwise.
- **Adjacency Matrix.** The graph is represented by a matrix of size $n \times n$ where the entry i, j is 1 if (v_i, v_j) is an edge of the graph and 0 otherwise. If there are k edges from v_i to v_j than the entry i, j is k .
- **Laplacian Matrix.** The graph is represented by a matrix $D - A$ where A is the adjacency matrix and D is the diagonal degree matrix. The diagonal matrix D has entry i equal to the degree d_i of the vertex v_i : $d_i = \mathbf{e}_i^T A \mathbf{1}$.

In this paper we only consider connected undirected simple graphs, i.e. an undirected graph that has no loops or multiple edges. A graph is simple if there exist neither self-loops nor multiple edges. The adjacency matrix A of a simple graph is then a 0, 1-matrix with 0's on the diagonal. If in addition the graph is undirected its adjacency matrix A is symmetric. A graph is connected if for every two vertices there exists a path connecting them.

We call degree of a vertex the number of edges adjacent to it. The degree vector of a graph G with adjacency matrix A is given by $A\mathbf{1}$. The ij -th component of A^k , $A^k(i, j)$, corresponds to the number of paths of length k connecting vertex i to

vertex j and $A^k \mathbb{1}$ is the vector whose i -th component corresponds to the number of paths of length k starting from vertex i .

3. Dynamic of networks. We now go back to representation by lists in order to define dynamic of graphs.

Given a set A , $\#[A]$ indicates the cardinality of A , while Δ is the set theoretic symmetric difference, i.e. $\Delta(A, B) = (A \setminus B) \cup (B \setminus A)$. The symbol $\mathcal{P}(A)$ indicates the set of subsets of A .

Definition 1. A network is a subset N of $\mathbf{N} = \mathbb{N} \times \mathcal{P}(\mathbb{N})$ for which there exists $n \in \mathbb{N}$ such that the following holds. Indicating by Π_1 and Π_2 the projections on the first and the second component of \mathbf{N} we have $\Pi_1(N) = \{1, \dots, n\}$ and $\Pi_2(N) \subset \mathcal{P}(\{1, \dots, n\})$. $n = n(N)$ is called the cardinality of the network. We indicate by $\mathcal{N} \subset \mathcal{P}(\mathbf{N})$ the set of networks.

Given a classical network (V, E) given by a finite set of vertices V and of edges $E \subset V \times V$, we obtain easily the representation $N(V, E)$ as follows. Let n be the cardinality of V then there exists a bijection $s : V \mapsto \{1, \dots, n\}$ (a numbering of vertices). The base $\Pi_1(N)$ is given by $\{1, \dots, n\}$, while for every $i \in \{1, \dots, n\}$ the fiber satisfies $\Pi_{2,i}(N) = \{j : (s^{-1}(i), s^{-1}(j)) \in E\}$ where $\Pi_{2,i}$ is the i -th component of Π_2 . Notice that in this way we can represent both directed or not directed networks.

It is then natural to use the same technique to re-arrange networks. Given a network N of cardinality n and a bijection s of $\{1, \dots, n\}$ we define $s(N)$ to be the network of cardinality n satisfying $\Pi_{2,i}(s(N)) = \{j : (s^{-1}(i), s^{-1}(j)) \in \Pi_{2,i}(N)\}$.

At this point we can define a metric as follows. First for every couple of networks N_1 and N_2 we define the distances:

$$\begin{aligned} \bar{D}(N_1, N_2) &= |n(N_1) - n(N_2)| + \tilde{D}(N_1, N_2), \\ \tilde{D}(N_1, N_2) &= \sum_{i=1}^{\max\{n(N_1), n(N_2)\}} \#[\Delta(\Pi_{2,i}(N_1), \Pi_{2,i}(N_2))]. \end{aligned}$$

Let us now indicate by \mathcal{S}_n the set of permutations over n objects, otherwise stated the set of bijections of $\{1, \dots, n\}$. We define the relation:

Definition 2. We say that N_1 is isomorphic to N_2 and we write $N_1 \equiv N_2$ if there exists $s \in \mathcal{S}_{n(N_1)}$ such that $s(N_1) = N_2$. We indicate by π_{\equiv} the canonical projection from \mathcal{N} to \mathcal{N}/\equiv .

It is easy to verify that \equiv is an equivalence relation and that two isomorphic networks have the same cardinality. We define also a weaker relation:

Definition 3. We say that N_1 is edge-isomorphic to N_2 and we write $N_1 \sim N_2$ if there exists $s \in \mathcal{S}_{\max\{n(N_1), n(N_2)\}}$ such that for every $i \in \{1, \dots, \max\{n(N_1), n(N_2)\}\}$ $\Pi_{2,i}(s(N_1)) = \Pi_{2,i}(N_2)$. We indicate by π_{\sim} the canonical projection from \mathcal{N} to \mathcal{N}/\sim .

It is easy to verify that \sim is an equivalence relation and that two edge-isomorphic networks may have different cardinality. However two edge-isomorphic networks may differ in cardinality only for the presence of vertices not connected to any other vertex.

Define now the functions:

$$\bar{d}(N_1, N_2) = \inf_{s_1 \in \mathcal{S}_{n(N_1)}, s_2 \in \mathcal{S}_{n(N_2)}} \bar{D}(s_1(N_1), s_2(N_2)).$$

$$\tilde{d}(N_1, N_2) = \inf_{s_1 \in \mathcal{S}_{n(N_1)}, s_2 \in \mathcal{S}_{n(N_2)}} \tilde{D}(s_1(N_1), s_2(N_2)).$$

Proposition 1. *The functions $\bar{D} : \mathcal{N} \times \mathcal{N} \mapsto \mathbb{N}$ and $\tilde{D} : \mathcal{N} \times \mathcal{N} \mapsto \mathbb{N}$ are pseudo-metrics on \mathbf{N} . The function \bar{d} is a metric on \mathcal{N}/\equiv and the function \tilde{d} is a metric on \mathcal{N}/\sim .*

Proof. Clearly $\bar{D}(N, N) = \tilde{D}(N, N) = 0$ for every $N \in \mathbf{N}$. Symmetry is obvious, while triangular inequality follows from the general fact:

$$\Delta(A, C) \subset \Delta(A, B) \cup \Delta(B, C).$$

Now if $\tilde{d}(N_1, N_2) = 0$ then there exists $s \in \mathcal{S}_{\max\{n(N_1), n(N_2)\}}$ such that for every $i \in \{1, \dots, \max\{n(N_1), n(N_2)\}\}$ one has $\#\left[\Delta(\Pi_{2,i}(N_1), \Pi_{2,i}(N_2))\right]$. Therefore $N_1 \sim N_2$.

Similarly if $\bar{d}(N_1, N_2) = 0$ then the two networks have the same cardinality and are isomorphic. □

Remark 1. Let us further explain the meaning of the distances \bar{d} and \tilde{d} .

The metric \bar{d} measures the difference in cardinalities of set of vertices plus the maximal distance of representation by lists up to isomorphisms. In particular, two graphs may have distance zero if and only if they are isomorphic in classical sense. Moreover, two graphs with different number of vertices have at least distance one. Such minimal distance is realized for instance by adding an isolated vertex to any graph.

On the other side the metric \tilde{d} computes just the distance of representation by lists without summing the difference in vertices cardinality. As a result, non isomorphic graphs (in classical sense) may still have distance zero, thus coincide in the set \mathcal{N}/\sim . This is the case for a graph G and the one obtained adding to G any number of isolated vertices.

3.1. Random network processes.

Definition 4. Given a probability space (Ω, P, \mathcal{F}) a random network is measurable function $X : \Omega \mapsto \mathcal{N}$ for the discrete topology on \mathcal{N} .

A random network process is a map $X : \mathbb{N} \times \Omega \mapsto \mathcal{N}$ such that, for every $t \in \mathbb{N}$, $X(t, \cdot)$ is a random network.

A Brownian network process is a random network process $B : \mathbb{N} \times \Omega \mapsto \mathcal{N}$ such that:

- $B(0) \equiv \{(1, \emptyset)\} \in \mathcal{N}$;
- $B(t+1, \omega)$ is obtained from $B(t, \omega)$ adding one edge among vertices of $B(t, \omega)$ or adding one edge between the vertex $n(B(t, \omega)) + 1$ and a vertex of $B(t, \omega)$. Clearly $\bar{d}(B(t, \omega), B(t+1, \omega)) = 1$ almost surely.
- the probability $P(B(t+1, \omega) = X)$ is the same for every $X \in B_{\bar{D}}(B(t, \omega))$ (the ball of radius one for the pseudo-metric \tilde{D}).

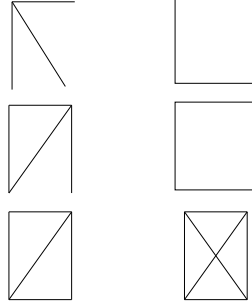
This well defined an almost surely unique process. Moreover, such process satisfies:

$$E \left[\tilde{D}^2(B(n+1), X(n)) \right] = 1.$$

We are interested in networks up to isomorphic equivalence, thus in the process:

$$\bar{B}(t, \omega) = \pi_{\equiv}(B(t, \omega)) = \pi_{\sim}(B(t, \omega)),$$

which we call the equivalence Brownian network process (EBNP) briefly.

FIGURE 1. Representation of \mathcal{N}_4^* .

4. Probability computation of dynamic networks. We now address the problem of computing probabilities of graphs generated by a Brownian network process.

4.1. The set \mathcal{N}/ \equiv and the process \bar{B} . Let us now study the set \mathcal{N}/ \equiv . More precisely we start studying the following set $\mathcal{N}_i^* = \{N \in \mathcal{N}/ \equiv: n(N) = i, N \text{ connected, } N \text{ has no self-loop}\}$. Notice that at step i a EBNP takes values in $\cup_{j \leq i} \mathcal{N}_i^*$, thus the characterization of \mathcal{N}_i^* gives information on EBNP. Also for applications to biological, data and social networks this is the interesting case.

Let us start characterizing \mathcal{N}_i^* for small values of i .

i=1. $N = \{(1, \emptyset)\}$, thus $\#(\mathcal{N}_1^*) = 1$.

i=2. $N = \{(1, \{2\}), (2, \{1\})\}$ thus $\#(\mathcal{N}_2^*) = 1$.

i=3. $N = \{(1, \{2\}), (2, \{1, 3\}), (3, \{2\})\}$ or N is fully connected (i.e. has all possible edges), thus $\#(\mathcal{N}_3^*) = 2$.

i=4. See Figure 1, thus $\#(\mathcal{N}_4^*) = 6$.

Notice that we can proceed by induction adding one vertex and edges to elements of \mathcal{N}_n^* to obtain elements of \mathcal{N}_{n+1}^* . Now EBNP adds one edge at each step so in fact it is convenient to classify subclasses of \mathcal{N}_n^* having the same number of edges. In fact different elements of the same equivalence class for \equiv must have the same number of edges, therefore we define:

$$\mathcal{N}_{i,m}^* = \{N \in \mathcal{N}_i^* : N \text{ has } m \text{ edges}\}.$$

From the connectivity property we have $\mathcal{N}_{i,m}^*$ is empty for every $m < i - 1$. On the other side the maximum number of edges is $i - 1 + (i - 2) + \dots + 1 = i(i - 1)/2 = M(i)$.

i=3. $M(3) = 3$. $\mathcal{N}_{3,2}^*$ has the only element $\{(1, \{2\}), (2, \{1, 3\}), (3, \{2\})\}$ while $\mathcal{N}_{3,3}^*$ has only the fully connected element.

i=4. $M(4) = 6$. Each $\mathcal{N}_{4,m}^*$ for $m = 3, 4$ has two elements, respectively those of the first and second row of Figure 1. While $\mathcal{N}_{4,m}^*$ for $m = 5, 6$ has a unique element, respectively that on the left and right of last row of Figure 1.

Let us now go back to EBNP. At time $t = 3$ EBNP takes values in:

$$\mathcal{N}_{3,2}^* \cup \mathcal{N}_{4,3}^*.$$

Is it equidistributed? The answer is no. To understand this let us explicitly construct $B(t)$ and $\bar{B}(t)$ for $t = 0, 1, 2, 3$. We have:

$$\begin{aligned} P(B(1) = \{(1, \{2\}), (2, \{1\})\}) &= \\ P(\bar{B}(1) = \{(1, \{2\}), (2, \{1\})\}) &= 1, \\ P(B(2) = \{(1, \{2\}), (2, \{1, 3\}), (3, \{2\})\}) &= \\ P(\bar{B}(2) = \{(1, \{2, 3\}), (2, \{1\}), (3, \{1\})\}) &= \frac{1}{2}, \\ P(B(2) = \{(1, \{2, 3\}), (2, \{1, 3\}), (3, \{2\})\}) &= 1. \end{aligned}$$

Now we have to construct $B(3)$ by adding one edge to one of the two possible networks, namely $\{(1, \{2\}), (2, \{1, 3\}), (3, \{2\})\}$ and $\{(1, \{2, 3\}), (2, \{1\}), (3, \{1\})\}$, giving equal probability to all cases. Starting from $\{(1, \{2\}), (2, \{1, 3\}), (3, \{2\})\}$ we get:

$$\begin{aligned} P(B(3) = \{(1, \{2, 3\}), (2, \{1, 3\}), (3, \{1, 2\})\}) &= \frac{1}{8}, \\ P(B(3) = \{(1, \{2, 4\}), (2, \{1, 3\}), (3, \{2\}), (4, \{1\})\}) &= \frac{1}{8}, \\ P(B(3) = \{(1, \{2\}), (2, \{1, 3, 4\}), (3, \{2\}), (4, \{2\})\}) &= \frac{1}{8}, \\ P(B(3) = \{(1, \{2\}), (2, \{1, 3\}), (3, \{2, 4\}), (4, \{3\})\}) &= \frac{1}{8}. \end{aligned}$$

While starting from $\{(1, \{2, 3\}), (2, \{1\}), (3, \{1\})\}$ we get:

$$\begin{aligned} P(B(3) = \{(1, \{2, 3\}), (2, \{1, 3\}), (3, \{1, 2\})\}) &= \frac{1}{8}, \\ P(B(3) = \{(1, \{2, 3\}), (2, \{1\}), (3, \{1, 4\}), (4, \{3\})\}) &= \frac{1}{8}, \\ P(B(3) = \{(1, \{2, 3, 4\}), (2, \{1\}), (3, \{1\}), (4, \{1\})\}) &= \frac{1}{8}, \\ P(B(3) = \{(1, \{2, 3\}), (2, \{1, 4\}), (3, \{1\}), (4, \{2\})\}) &= \frac{1}{8}. \end{aligned}$$

From which we easily obtain:

$$\begin{aligned} P(\bar{B}(3) = \{(1, \{2, 3\}), (2, \{1, 3\}), (3, \{1, 2\})\}) &= \frac{1}{4}, \\ P(\bar{B}(3) = \{(1, \{2\}), (2, \{1, 3\}), (3, \{2, 4\}), (4, \{3\})\}) &= \frac{1}{2}, \\ P(\bar{B}(3) = \{(1, \{2, 3, 4\}), (2, \{1\}), (3, \{1\}), (4, \{1\})\}) &= \frac{1}{4}. \end{aligned}$$

The process seems like a diffusion with a peak on a specific graph and then other graphs with less probability in a symmetric situation. However, if we continue with this analysis we get the following (after straightforward computations) the following probability table for $\bar{B}(4)$:

$$\begin{aligned} \{(1, \{2, 3\}), (2, \{1, 3\}), (3, \{1, 2, 4\}), (4, \{3\})\} &P = \frac{1}{2}, \\ \{(1, \{2, 3, 4\}), (2, \{1, 5\}), (3, \{1\}), (4, \{1\}), (5, \{2\})\} &P = \frac{1}{4}, \\ \{(1, \{2\}), (2, \{1, 3\}), (3, \{2, 4\}), (4, \{3, 5\}), (5, \{4\})\} &P = \frac{1}{7}, \\ \{(1, \{2, 4\}), (2, \{1, 3\}), (3, \{2, 4\}), (4, \{1, 3\})\} &P = \frac{1}{14}, \\ \{(1, \{2, 3, 4, 5\}), (2, \{1\}), (3, \{1\}), (4, \{1\}), (5, \{1\})\} &P = \frac{1}{28}, \end{aligned}$$

and now symmetry is completely destroyed!

Finally, after lengthy but straightforward computations we get that $\bar{B}(5)$ is distributed over 12 different graphs and the most probable graph is

$$\{(1, \{2\}), (2, \{1, 3, 4\}), (3, \{2, 4\}), (4, \{2, 3, 5\}), (5, \{4\})\}$$

with probability $52/231 \sim 0,225$.

It remains the main open question:

Q Is it possible to compute the probability distribution of $\bar{B}(t)$?

5. Decomposition by eigenspaces. We first recall some known facts from linear algebra.

Consider a $n \times n$ symmetric matrix A with real entries. Then it has real eigenvalues, the algebraic multiplicity is equal to the geometric multiplicity of each eigenvalue and eigenspaces relative to different eigenvalues are orthogonal. Let us denote by $\lambda_1 > \dots > \lambda_d$ the distinct eigenvalues of A with multiplicity μ_1, \dots, μ_d , by $\mathcal{E}(\lambda_i)$ the eigenspace of dimension μ_i , relative to the eigenvalue λ_i . If an eigenspace $\mathcal{E}(\lambda)$ has $\{\mathbf{x}_1, \dots, \mathbf{x}_\mu\}$ as an orthonormal basis then

$$P(\lambda) = \mathbf{x}_1 \mathbf{x}_1^T + \dots + \mathbf{x}_\mu \mathbf{x}_\mu^T$$

represents the orthogonal projection of \mathbb{R}^n onto $\mathcal{E}(\lambda)$ with respect to the canonical orthonormal basis of \mathbb{R}^n . Alternatively one can write

$$P(\lambda) = E(\lambda)E(\lambda)^T,$$

where $E(\lambda)$ is the $n \times \mu$ matrix whose j -th column is given by the j -th vector, \mathbf{x}_j , of the basis of $\mathcal{E}(\lambda)$. Shortly we will say that $E(\lambda)$ is the matrix corresponding to the subspace $\mathcal{E}(\lambda)$. Notice that for another choice of orthonormal basis $\{\mathbf{x}'_1, \dots, \mathbf{x}'_\mu\}$, with corresponding matrix $E'(\lambda)$, we have $E(\lambda) = E'(\lambda)Q$, for some orthogonal matrix Q of dimension $\mu \times \mu$ and

$$P(\lambda) = E(\lambda)E(\lambda)^T = E'(\lambda)Q Q^T E'(\lambda)^T = E'(\lambda)E'(\lambda)^T.$$

Hence $P(\lambda)$ is invariant by orthogonal change of basis. Moreover $P(\lambda)^2 = P(\lambda) = P(\lambda)^T$ and $P(\lambda_i)P(\lambda_j) = 0$ for two eigenvalues $\lambda_i \neq \lambda_j$. The spectral decomposition of A is given by

$$A = \lambda_1 P(\lambda_1) + \dots + \lambda_d P(\lambda_d).$$

For the spectral decomposition, since, $P(\lambda_i)P(\lambda_j) = 0$ for $\lambda_i \neq \lambda_j$, it holds:

$$A^i = \lambda_1^i P(\lambda_1) + \dots + \lambda_d^i P(\lambda_d). \quad (1)$$

A permutation matrix π of order n is a $n \times n$ matrix obtained by permuting the rows of an identity matrix according to some permutation σ of the numbers 1 to n . Every row and column therefore contains precisely a single 1 with 0's everywhere else. In particular if $j = \sigma(i)$ then $\pi_{i,j} = 1$. To any permutation σ there corresponds to unique permutation matrix π . A permutation matrix is nonsingular, and the determinant is always ± 1 . In addition, a permutation matrix satisfies $\pi \pi^T = I$.

Let G_1 and G_2 be two graphs, with set of vertices V_1 and V_2 of cardinality n , set of edges E_1 and E_2 of cardinality m . We also denote by A_1 and A_2 the adjacency matrices of G_1 and G_2 respectively. G_1 and G_2 are said to be cospectral if their adjacency matrices have the same spectra. G_1 and G_2 are isomorphic if there exists a permutation σ of the vertices such that $(i, j) \in E_2$ if and only if $(\sigma(i), \sigma(j)) \in E_1$. Then G_1 and G_2 are isomorphic if and only if there exists π , permutation matrix, such that $A_1 = \pi^T A_2 \pi$.

5.1. Eigenspace decomposition of \mathbb{R}^n .

Definition 5. An eigenspace is called *main* if it is not orthogonal to the vector $\mathbb{1}$, otherwise we call it *not main*.

A main eigenspace $\mathcal{E}(\lambda)$ with corresponding $P(\lambda)$ is characterized by the following condition:

$$P(\lambda)\mathbb{1} \neq 0.$$

Proposition 2. For a main eigenspace $\mathcal{E}(\lambda)$ of dimension $\mu > 1$, we can choose an orthonormal basis given by $\mathbf{y}, \mathbf{x}_1, \dots, \mathbf{x}_{\mu-1}$ with $\mathbf{y}^T \mathbf{1} = \|P(\lambda)\mathbf{1}\|$ and $\mathbf{x}_i^T \mathbf{1} = 0$ for all $i = 1, \dots, \mu - 1$.

Proof. Let $E(\lambda)$ be a matrix corresponding to an orthonormal basis for $\mathcal{E}(\lambda)$. Let

$$\alpha = \frac{E(\lambda)^T \mathbf{1}}{\|E(\lambda)^T \mathbf{1}\|},$$

$$\mathbf{y} = E(\lambda)\alpha$$

and $\mathbf{x}_j = E(\lambda)\beta_j, j = 1, \dots, \mu-1$, for some $\beta_1, \dots, \beta_{\mu-1} \in \mathbb{R}^\mu$ such that $\{\mathbf{y}, \mathbf{x}_1, \dots, \mathbf{x}_{\mu-1}\}$ is an orthonormal basis for $\mathcal{E}(\lambda)$. Now

$$\mathbf{y}^T \mathbf{1} = \alpha^T E(\lambda)^T \mathbf{1} = \frac{\mathbf{1}^T E(\lambda) E(\lambda)^T \mathbf{1}}{\|E(\lambda)^T \mathbf{1}\|} = \|E(\lambda)^T \mathbf{1}\|.$$

Since $\|E(\lambda)^T \mathbf{1}\|^2 = \mathbf{1}^T E(\lambda) E(\lambda)^T \mathbf{1} = \mathbf{1}^T P(\lambda) \mathbf{1} = \mathbf{1}^T P(\lambda)^2 \mathbf{1} = \|P(\lambda)\mathbf{1}\|^2$, we get

$$\mathbf{y}^T \mathbf{1} = \|E(\lambda)^T \mathbf{1}\| = \|P(\lambda)\mathbf{1}\|.$$

Moreover, by construction,

$$0 = \mathbf{x}_j^T \mathbf{y} = \mathbf{x}_j^T E(\lambda)\alpha = \mathbf{x}_j^T E(\lambda) \frac{E(\lambda)^T \mathbf{1}}{\|E(\lambda)^T \mathbf{1}\|} = \frac{1}{\|E(\lambda)^T \mathbf{1}\|} \mathbf{x}_j^T P(\lambda)\mathbf{1}.$$

On the other hand

$$P(\lambda)\mathbf{x}_j = E(\lambda)E(\lambda)^T E(\lambda)\beta_j = E(\lambda)\beta_j = \mathbf{x}_j.$$

Then

$$0 = \mathbf{x}_j^T \mathbf{y} = \frac{1}{\|E(\lambda)^T \mathbf{1}\|} \mathbf{x}_j^T P(\lambda)\mathbf{1} = \frac{1}{\|E(\lambda)^T \mathbf{1}\|} \mathbf{x}_j^T \mathbf{1},$$

that is $\mathbf{x}_j^T \mathbf{1} = 0$ for all $j = 1, \dots, \mu - 1$. □

Each not main eigenspace $\mathcal{E}(\lambda)$ has a basis of μ orthonormal vectors which are orthogonal to $\mathbf{1}$. Each main eigenspace $\mathcal{E}(\lambda)$ has a basis of μ orthonormal vectors of which all but one are orthogonal to $\mathbf{1}$.

Definition 6. Consider a $n \times n$ symmetric matrix A with real entries and let $\lambda_1 > \dots > \lambda_d$ be the distinct eigenvalues of A with multiplicity μ_1, \dots, μ_d . The largest eigenvalue λ_1 is called the index of G . By the Perron-Frobenius theorem, there exists a corresponding eigenvector whose entries are all non-negative. The index is a simple eigenvalue ($\mu_1 = 1$) if and only if G is connected. The unique positive unit eigenvector corresponding to the index of a connected graph is called the principal eigenvector.

Definition 7. Let $\mathcal{E}(\lambda_i)$ be the eigenspace of dimension μ_i relative to the eigenvalue λ_i . We denote by J the set of indices $j \in \{1, \dots, m\}$ such that $\mathcal{E}(\lambda_j)$ is main and by K the set of indices $k \in \{1, \dots, m\}$ such that $\mathcal{E}(\lambda_k)$ is not main. Clearly $J \cup K = \{1, \dots, m\}$. Let \mathcal{Y} be the space spanned by the set of vectors $\{\mathbf{y}(\lambda_j), j \in J\}$, one for each main eigenspace, not orthogonal to $\mathbf{1}$. For all $j \in J$ we call $\mathbf{y}(\lambda_j)$ the main eigenvector.

With definition 7 we have decomposed \mathbb{R}^n in the direct sum

$$\mathbb{R}^n = \bigoplus_{j \in J} \mathcal{E}(\lambda_j) \oplus \bigoplus_{k \in K} \mathcal{E}(\lambda_k) \tag{2}$$

For each $j \in J$ we choose a orthonormal basis for $\mathcal{E}(\lambda_j)$ as in proposition 2 and denote by $E(\lambda_j)$ the corresponding matrix and by $P_j = E(\lambda_j)E(\lambda_j)^T$. Analogously, for each $k \in K$ we choose a orthonormal basis for $\mathcal{E}(\lambda_k)$ and denote by $E(\lambda_k)$ the corresponding matrix and by $P_k = E(\lambda_k)E(\lambda_k)^T$. With this notation, the spectral decomposition of A can be rewritten as:

$$A = \sum_{j \in J} \lambda_j P_j + \sum_{k \in K} \lambda_k P_k$$

and, analogously to equation (1), we have:

$$A^i = \sum_{j \in J} \lambda_j^i P_j + \sum_{k \in K} \lambda_k^i P_k. \quad (3)$$

Remark. The above spectral decomposition of A does not depend on the choice of orthonormal basis for $\mathcal{E}(\lambda_j)$ and $\mathcal{E}(\lambda_k)$ but only on the decomposition of \mathbb{R}^n given in (2).

5.2. The walk matrix.

Definition 8. The *walk matrix* of a graph G with adjacency matrix A is the matrix

$$W(A) = [\mathbf{1}|A\mathbf{1}|A^2\mathbf{1}|\dots|A^{n-1}\mathbf{1}]$$

whose i -th column is given by $A^{i-1}\mathbf{1}$.

$W(A)$ is called walk matrix because its (i, j) -th component describes the number of paths of length $j - 1$ starting from vertex v_i . Next proposition restates a known result (see e.g. [12])

Proposition 3. *The rank of $W(A)$ is given by the cardinality $|J|$ of J and the space spanned coincides with \mathcal{Y} .*

Proof. Let $J = \{j_1, \dots, j_{|J|}\} \subset \{1, \dots, d\}$, $m_j = \mathbf{y}(\lambda_j)^T \mathbf{1} = \|P(\lambda_j)\mathbf{1}\|$, for $j \in J$, D the diagonal matrix with diagonal elements $D_{ii} = m_{j_i}$, \mathbb{V} the Vandermonde matrix

$$\mathbb{V} = \begin{bmatrix} 1 & \lambda_{j_1} & \dots & \lambda_{j_1}^{n-1} \\ 1 & \lambda_{j_2} & \dots & \lambda_{j_2}^{n-1} \\ \vdots & \vdots & & \vdots \\ 1 & \lambda_{j_{|J|}} & \dots & \lambda_{j_{|J|}}^{n-1} \end{bmatrix}.$$

of dimension $|J| \times n$ and

$$Y = [\mathbf{y}(\lambda_{j_1})|\dots|\mathbf{y}(\lambda_{j_{|J|}})]$$

the matrix whose i -th column is given by the main eigenvector $\mathbf{y}(\lambda_{j_i}) \in \mathcal{Y}$. Notice that, \mathbb{V} is full row rank, i.e. equal to $|J|$, because $\lambda_j, j \in J$ are all distinct. We show that

$$W(A) = YD\mathbb{V}.$$

The i -th column of $YD\mathbb{V}$ is given by multiplying

$$YD = [m_{j_1}\mathbf{y}(\lambda_{j_1})|\dots|m_{j_{|J|}}\mathbf{y}(\lambda_{j_{|J|}})]$$

by the i -th column of \mathbb{V} . Hence for $i = 1, \dots, n$, the i -th column of $YD\mathbb{V}$ is

$$\sum_{j \in J} m_j \mathbf{y}(\lambda_j) \lambda_j^{i-1},$$

and for $i = 1$, i -th column of $YD\mathbb{V}$ is

$$\sum_{j \in J} m_j \mathbf{y}(\lambda_j).$$

On the other hand by equation (3), for $i = 1, \dots, n - 1$, we have

$$A^i \mathbf{1} = \sum_{j \in J} \lambda_j^i P_j \mathbf{1} + \sum_{k \in K} \lambda_k^i P_k \mathbf{1}$$

and, since $P_k \mathbf{1} = E(\lambda_k)E(\lambda_k)^T \mathbf{1} = 0$ and $P_j \mathbf{1} = \mathbf{y}(\lambda_j)\mathbf{y}(\lambda_j)^T \mathbf{1} = m_j \mathbf{y}(\lambda_j)$,

$$A^i \mathbf{1} = \sum_{j \in J} \lambda_j^i P_j \mathbf{1} = \sum_{j \in J} \lambda_j^i m_j \mathbf{y}(\lambda_j).$$

Then the $i + 1$ -th column of $W(A)$ coincides with the $i + 1$ -th column of $YD\mathbb{V}$, for all $i = 1, \dots, n - 1$.

It remains to show that the first column of $YD\mathbb{V}$ is equal to the first column of $W(A)$, that is

$$YD\mathbf{1} = \sum_{j \in J} m_j \mathbf{y}(\lambda_j) = \mathbf{1}$$

Now $\mathbf{1} \in \mathcal{Y}$, because $\mathcal{E}_k, k \in K$, is orthogonal to $\mathbf{1}$. Then we can write $\mathbf{1} = \sum_{l \in J} \alpha_l \mathbf{y}(\lambda_l)$ for some coefficients $\alpha_1, \dots, \alpha_{|J|}$. Moreover, $y(\lambda_{j_1})^T y(\lambda_{j_2}) = 0$ for all $\lambda_{j_1} \neq \lambda_{j_2}$ and $y(\lambda_j)^T y(\lambda_j) = 1$. Hence

$$\begin{aligned} \sum_{j \in J} m_j \mathbf{y}(\lambda_j) &= \sum_{j \in J} \mathbf{y}(\lambda_j)\mathbf{y}(\lambda_j)^T \mathbf{1} = \\ \sum_{j \in J} \mathbf{y}(\lambda_j)\mathbf{y}(\lambda_j)^T \sum_{l \in J} \alpha_l \mathbf{y}(\lambda_l) &= \\ \sum_{j \in J} \alpha_j \mathbf{y}(\lambda_j) &= \mathbf{1}. \end{aligned}$$

Finally, $\mathbf{1} = YD\mathbf{1}$, thus

$$W(A) = YD\mathbb{V}.$$

From this expression we get that $\text{rank}(W(A)) = \text{rank}(Y) = |J|$. Consider now a $x \in \mathbb{R}^n$. Then $x^T W(A) = 0$ if and only if $x^T YD\mathbb{V} = 0$. Since $D\mathbb{V}$ is full row rank, we have that $x^T W(A) = 0$ if and only if $x^T Y = 0$. Since the left null space is the orthogonal complement to the column space, we have that the column space of $W(A)$ coincide with the column space of Y . \square

6. Isomorphism problem.

Definition 9. Let G_1 and G_2 be two cospectral graphs with adjacency matrices A_1 and A_2 and walk matrices $W(A_1)$ and $W(A_2)$ respectively. For $i = 1, 2$, let the eigenspaces of G_i be $\mathcal{E}_i(\lambda_j)$ and $\mathcal{E}_i(\lambda_k)$, for $j \in J_i, k \in K_i$ and $h \in H_i$. Consider the following:

H One of the following is satisfied

H.1: $K_1 = K_2 = \emptyset$ $\mu_j = 1$ for all $j \in J$.

H.2: $K_1 = K_2 = \emptyset$ $\mu_j = 1$ for all but one $j \in J$.

H.3: $K_1 = K_2 = K$ with cardinality $|K| = 1$ and $\mu_j = 1$ for all $j \in J$.

If the pair of graphs G_1 and G_2 satisfy **H** then we say that G_1, G_2 have simple equidimensional eigenspace decomposition.

Notice that if **H.1** holds then all eigenspaces are main. In addition G_1 and G_2 have n different eigenvalues with multiplicity 1. If **H.2** holds then all eigenspaces are main. In addition G_1 and G_2 have $|J|$ different eigenvalues of which $|J| - 1$ with multiplicity 1 and one with multiplicity $n - |J| + 1$. If finally **H.3** holds then all

but one eigenspaces are main. The main eigenspaces have dimension 1 and the non main eigenspace has dimension $n - |J|$.

Theorem 1. *Let G_1 and G_2 be two cospectral graphs with adjacency matrices A_1 and A_2 and walk matrices $W(A_1)$ and $W(A_2)$ respectively. For $i = 1, 2$, let the eigenspaces of G_i be $\mathbf{y}_i(\lambda_j), \mathcal{E}_i(\lambda_k), \mathcal{F}_i(\lambda_h)$ for $j \in J_i, k \in K_i$ and $h \in H_i$. Assume that G_1 and G_2 have simple equidimensional eigenspace decomposition. Then G_1 and G_2 are isomorphic with $A_1 = \pi^T A_2 \pi$ if and only if $W(A_1) = \pi^T W(A_2)$.*

Proof. Assume first that G_1 and G_2 are isomorphic. Then, for each $i = 0, \dots, n - 1$, the i -th column of $W(A_1)$ is

$$W(A_1)_i = A_1^{i-1} \mathbf{1} = \pi^T A_2^{i-1} \pi \mathbf{1} = \pi^T A_2^{i-1} \mathbf{1} = \pi^T W(A_2)_i.$$

Hence $W(A_1) = \pi^T W(A_2)$.

Assume now that $W(A_1) = \pi^T W(A_2)$ for some permutation matrix π . Then, for all $i = 1, \dots, n - 1$, $A_1 A_1^{i-1} \mathbf{1} = A_1^i \mathbf{1} = \pi^T A_2^i \mathbf{1} = \pi^T A_2 \pi \pi^T A_2^{i-1} \mathbf{1} = \pi^T A_2 \pi A_1^{i-1} \mathbf{1}$, hence

$$(A_1 - \pi^T A_2 \pi) A_1^{i-1} \mathbf{1} = 0.$$

In matrix form we get

$$(A_1 - \pi^T A_2 \pi) W(A_1) = 0. \tag{4}$$

Now G_1 and G_2 have simple equidimensional eigenspace decomposition. Assume that condition **H.1** is satisfied. It follows that $W(A_1)$ is full rank and, from equation (4),

$$A_1 - \pi^T A_2 \pi = 0,$$

i.e. G_1 and G_2 are isomorphic.

Assume now that condition **H.3** is satisfied. For all $\mathbf{x} \in \mathcal{E}_1(\lambda_k), k \in K$ we have that $\mathbf{x}^T W(A_1) = 0$, i.e. $\mathbf{x} \in \ker(W(A_1)^T)$. On the other hand, since $W(A_1) = \pi^T W(A_2)$, we have:

$$\mathbf{x}^T W(A_1) = \mathbf{x}^T \pi^T W(A_2)$$

Then $\pi \mathbf{x} \in \ker W(A_2)$, i.e

$$\mathbf{x} \in \mathcal{E}_1(\lambda_k) \iff \pi \mathbf{x} \in \mathcal{E}_2(\lambda_k). \tag{5}$$

From $W(A_1) = \pi^T W(A_2)$, we also get

$$Y_1 D_1 \mathbb{V} = W(A_1) = \pi^T W(A_2) = \pi^T Y_2 D_2 \mathbb{V}.$$

Then, since \mathbb{V} is full rank,

$$Y_1 D_1 = \pi^T Y_2 D_2$$

and, being D_1, D_2 diagonal matrices,

$$\mathbf{y}_1(\lambda_j) = \alpha \pi^T \mathbf{y}_2(\lambda_j), \quad j \in J,$$

for some $\alpha \in \mathbb{R}$. For $i = 1, 2$ and $j \in J$, $\|\mathbf{y}_i(\lambda_j)\| = 1$, then it must be $\alpha = \pm 1$, thus

$$\mathbf{y}_1(\lambda_j) = \pm \pi^T \mathbf{y}_2(\lambda_j), \quad j \in J, \tag{6}$$

Recall that, under **H.3**, the spectral decomposition of the adjacency matrix of A_1 is:

$$A_1 = \sum_{j \in J} \lambda_j \mathbf{y}(\lambda_j) \mathbf{y}_1(\lambda_j)^T + \sum_{k \in K} \lambda_k E_1(\lambda_k) E_1(\lambda_k)^T$$

Then, by conditions (6 and 5) we write:

$$\begin{aligned}
 A_1 &= \sum_{j \in J} \lambda_j \pi^T \mathbf{y}_2(\lambda_j) \mathbf{y}_2(\lambda_j)^T \pi + \sum_{k \in K_1} \lambda_k \pi^T E_2(\lambda_k) E_2(\lambda_k)^T \pi = \\
 &= \pi^T \left(\sum_{j \in J} \lambda_j \mathbf{y}_2(\lambda_j) \mathbf{y}_2(\lambda_j)^T + \sum_{k \in K_1} \lambda_k E_2(\lambda_k) E_2(\lambda_k)^T \right) \pi = \\
 &= \pi^T A_2 \pi.
 \end{aligned}$$

If condition **H.2** is satisfied, we let $j_0 \in J$ be the only index of J such that $\mu_{j_0} > 1$. We denote by $\mathcal{E}(\lambda_{j_0})$ the vector space generated by the vectors of $\mathcal{E}(\lambda_{j_0})$ orthogonal to $\mathbf{1}$ (see construction in the proof of proposition 2) and apply the same arguments of case **H.3** with $\mathcal{E}(\lambda_{j_0})$ in place of $\mathcal{E}(\lambda_k)$. \square

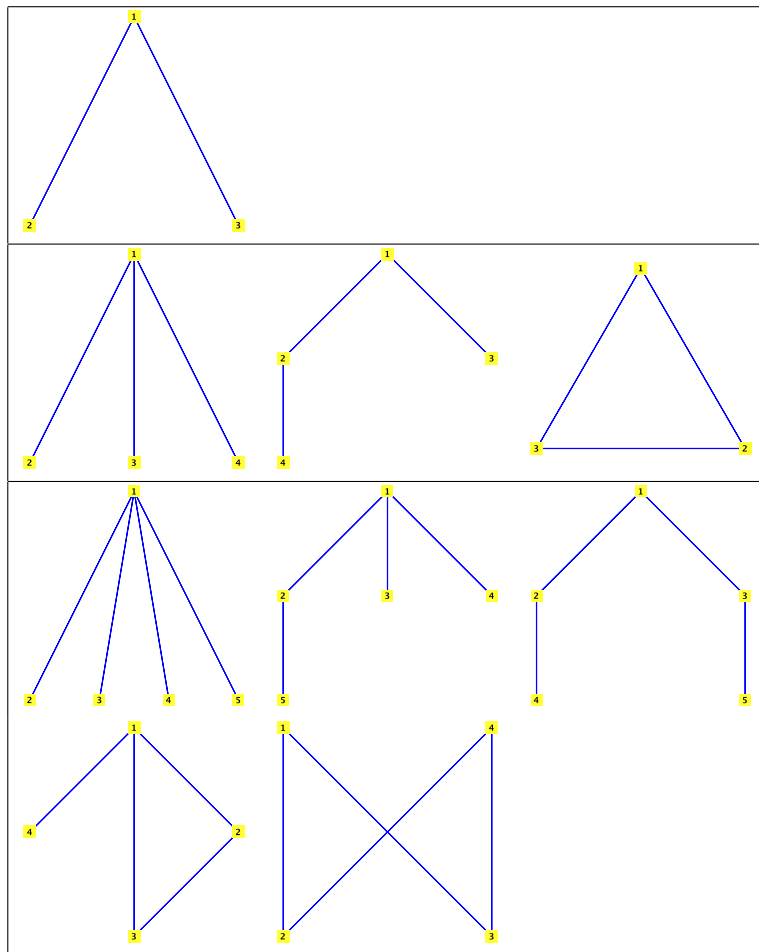


FIGURE 2. EBNP for $n = 1, 2, 3$ and 4 .

7. Average properties of dynamic graphs. Using the results on graph isomorphism from Section 6, we implemented a program to automatically generate the graphs produced by the EBNP and compute the relative probabilities. We report the results for the first steps, namely for $n = 2, 3, 4$ in Figure 2, for $n = 5$ in Figure 3 and for $n = 6$ in Figures 4 and 5.

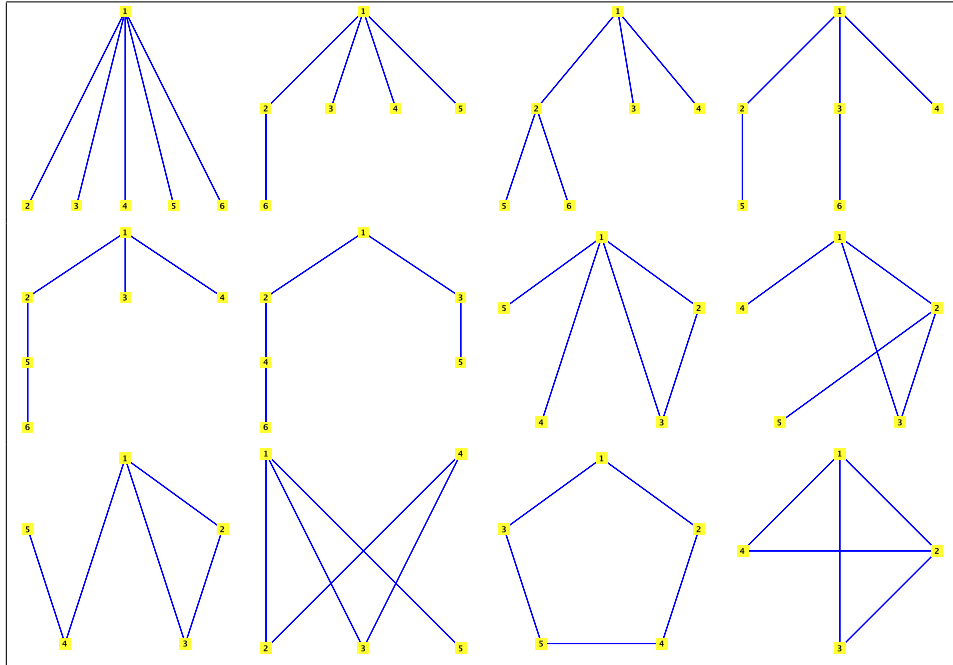


FIGURE 3. EBNP for $n = 5$.

As explained in the Introduction, the emergence of typical network motifs is one of the main phenomena in real biological networks. Focusing on triangular subnetworks, like the FFL motif, we measure the presence of such subnetworks in probability terms for the EBNP. We report below obtained results about the number of edges and probabilities to have a triangular subnetwork.

m=2. We obtain only one graph with $n = 3$ vertices. There are no graphs with triangles.

m=3. We obtain one graph with $n = 3$ vertices (with $p = 0.25$) and two graphs with $n = 4$ vertices (one with $p = 0.25$ and one with $p = 0.50$), for a total of 3 graphs. There is only one graph (with $p = 0.25$) containing one triangle.

m=4. We obtain two graphs with $n = 4$ vertices and three graphs with $n = 5$ vertices. There is only one graph (with $p = 0.5$) containing one triangle.

m=5. We obtain one graph with $n = 4$ vertices, five graphs with $n = 5$ vertices and six graphs with 6 vertices, for a total of twelve graphs. There are four graphs (with total $p = 0.673$) containing at least one triangle.

m=6. We obtain one graph with $n = 4$ vertices, five graphs with $n = 5$ vertices, 13 graphs with 6 vertices and 11 graphs with 7 vertices, for a total of 30 graphs. There are 12 graphs (with total $p = 0.793$) containing at least one triangle.

m=7. We obtain 4 graphs with $n = 5$ vertices, 19 graphs with $n = 6$ vertices, 33

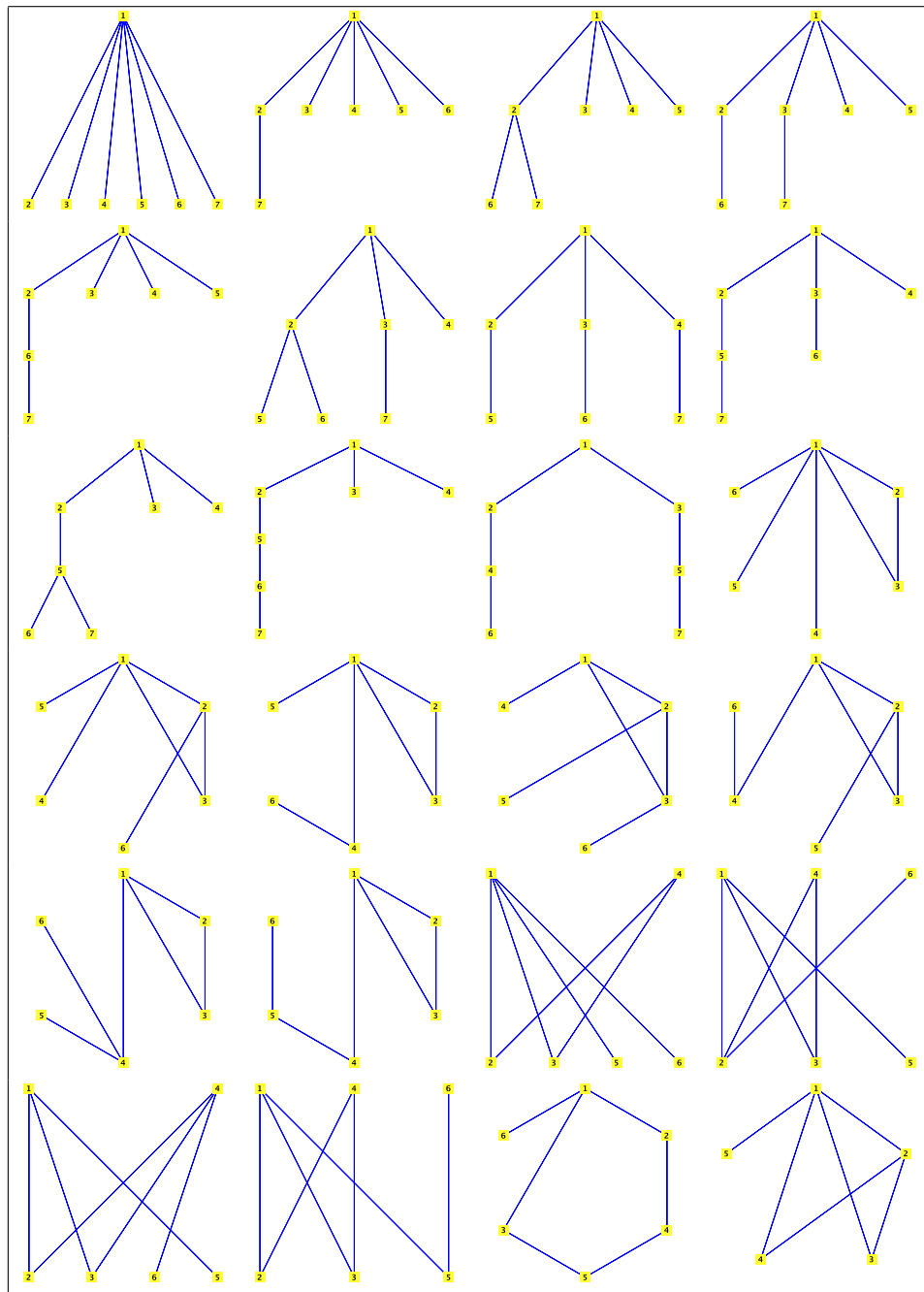
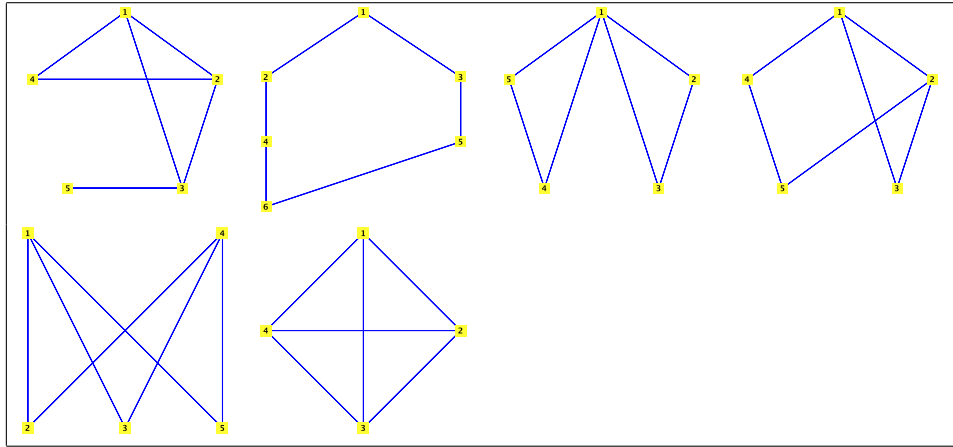


FIGURE 4. EBNP for $n = 6$ part I.

graphs with $n = 7$ vertices and 23 graphs with $n = 8$ vertices, for a total of 79 graphs. There are 38 graphs (with total $p = 0.872$) containing at least one triangle.

FIGURE 5. EBNP for $n = 6$ part II.

Let us now compare such probabilities with random graphs in the sense of Erdos-Renyi. Typically a random graph is defined as an equiprobable graph for fixed numbers of vertices and edges or a graph obtained having assigned the same probability to each possible edge. In particular, the number of vertices is fixed for a random graph.

For the EBNP the number of vertices is not constant at each step. Already at step three the number of vertices is either 3 or 4, while at step seven the number of vertices ranges from 5 to 8. To produce comparable situations, we thus have to define an average number of vertices. In the same way it is interesting measuring an average connectivity. For doing so, we simply set the average of any quantity to be computed according to the probabilities assigned by EBNP. A direct computation gives the following averages: $\bar{B}(1)$ has 2 vertices and connectivity 1, $\bar{B}(2)$ has 3 vertices and connectivity $\frac{2}{3}$, $\bar{B}(3)$ has $\frac{15}{4}$ edges and connectivity $\frac{13}{16}$, while $\bar{B}(4)$ has $\frac{124}{28}$ and connectivity $\frac{64}{70}$. It is easy to see that the connectivity tends to 1 as the number of steps increases.

Now to compare with the case of Erdos-Renyi we proceed as follows. We assume that a random graph has number of edges, vertices and thus connectivity computed according to the probability assigned by EBNP. Then it is possible to compute the probability of having a triangular network using the averaged quantities. For simplicity, we restrict to two cases: for random graphs corresponding to $\bar{B}(4)$ we have a probability of ~ 0.29 of having a triangular network, while for $\bar{B}(7)$ such probability raises to ~ 0.54 . These numbers are definitely below those computed above which are, respectively, $\frac{1}{2}$ for $\bar{B}(4)$ and ~ 0.87 for $\bar{B}(7)$.

8. Conclusion. We introduced a new mathematical framework to model stochastic networks, i.e. graphs which evolve in time according to given probabilistic growth rules. Such processes are encountered in a number of applications such as in biological networks. In particular we defined new metrics for graphs and considered processes which are defined up to isomorphisms of graphs.

The resulting processes are on one side very natural, thus called Brownian network processes, and on the other side fairly complicate, loosing symmetry after few steps. Then new results for graph isomorphisms are provided, which allows to compute

probabilities of such processes. The latter are used for a first comparison with random graphs, in terms of probability of typical subnetworks, called network motifs and playing a key role in biological networks.

REFERENCES

- [1] U. Alon, “An Introduction to Systems Biology: Design Principles of Biological Circuits,” Chapman & Hall/CRC Mathematical and Computational Biology Series, Chapman & Hall/CRC, Boca Raton, FL, 2007.
- [2] A.-L. Barabási and R. Albert, *Emergence of scaling in random networks*, Science, **286** (1999), 509–512.
- [3] A.-L. Barabási and R. E. Crandall, *Linked: The new science of networks*, Am. J. Phys., **71** (2003), 409–410.
- [4] B. Bollobás, C. Borgs, J. Chayes and O. Riordan, *Directed scale-free graphs*, in “Proceedings of the Fourteenth Annual ACM-SIAM Symposium on Discrete Algorithms” (Baltimore, MD, 2003), 132–139, ACM, New York, 2003.
- [5] M. Chaves and E. D. Sontag, *State-estimation for chemical reaction networks of Feinberg-Horn-Jackson zero deficiency type*, Europ. J. of Control, **8** (2002), 343–359.
- [6] C. Cooper and A. Frieze, *A general model of web graphs*, Random Struct. Alg., **22** (2003), 311–335.
- [7] D. M. Cvetković, M. Doob and H. Sachs, “Spectra of Graphs: Theory and Applications,” Third edition, Johann Ambrosius Barth, Heidelberg, 1995.
- [8] D. Del Vecchio, A. J. Ninfa and E. D. Sontag, *Modular cell biology: Retroactivity and insulation*, Mol. Syst. Biology, **4** (2008), Article number 161.
- [9] R. Durrett, “Random Graph Dynamics,” Cambridge Series in Statistical and Probabilistic Mathematics, Cambridge University Press, Cambridge, 2007.
- [10] P. Erdős and A. Rényi, *On random graphs*, Publ. Math. Debrecen, **6** (1959), 290–297.
- [11] M. Farina, R. Findeisen, E. Bullinger, S. Bittanti, F. Allgower and P. Wellstead, *Results towards identifiability properties of biochemical reaction networks*, in “Proceedings of the 45th IEEE Conference on Decision & Control,” San Diego, CA, USA, December 13–15, (2006), 2104–2109.
- [12] E. M. Hagos, *Some results on graph spectra*, Linear Algebra Appl., **356** (2002), 103–111.
- [13] S. Mangan and U. Alon, *Structure and function of the feed-forward loop network motif*, PNAS, **100** (2003), 11980–11985.
- [14] M. E. J. Newman, *The structure and functions of complex networks*, SIAM Review, **45** (2003), 167–256.
- [15] B. O. Palsson, “Systems Biology—Properties of Reconstructed Networks,” Cambridge University Press, Cambridge, 2006.
- [16] E. D. Sontag, *Molecular systems biology and control*, Europ. J. of Control, **11** (2005), 396–435.
- [17] D. J. Watts and S. H. Strogatz, *Collective dynamics of ‘small-world’ networks*, Nature, **393** (1998), 440–442.

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