On the Complexity of two Problems on Orientations of Mixed Graphs

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Abstract *Interactions between biomolecules within the cell can be modeled by biological networks, i.e. graphs whose vertices are the biomolecules (proteins, genes, metabolites etc.) and whose edges represent their functional relationships. Depending on their nature, the interactions can be undirected (e.g. protein-protein interactions, PPIs) or directed (e.g. protein-DNA interactions, PDIs). A physical network is a network formed by both PPIs and PDIs, and is thus modeled by a mixed graph. External cellular events are transmitted into the nucleus via cascades of activation/deactivation of proteins, that correspond to paths (called* signaling pathways*) in the physical network from a source protein (cause) to a target protein (effect). There exists experimental methods to identify the cause-effect pairs, but such methods do not provide the signaling pathways. A key challenge is to infer such pathways based on the cause-effect informations. In terms of graph theory, this problem, called* MAXIMUM GRAPH ORIENTATION *(*MGO*), is defined as follows: given a mixed graph G and a set $\mathcal{P}$ of source-target pairs, find an orientation of G that replaces each (undirected) edge by a single (directed) arc in such a way that there exists a directed path, from s to t, for a maximum number of pairs $(s,t) \in \mathcal{P}$. In this work, we consider a variant of* MGO*, called* S-GO*, in which we ask whether* all *the pairs in $\mathcal{P}$ can be connected by a directed path. We also introduce a minimization problem, called* MIN-DB-GO*, in which* all *the pairs in $\mathcal{P}$ must be connected by a directed path, while we allow some edges of G to be doubly oriented (i.e. replaced by two arcs in opposite directions). We investigate the complexity of* S-GO *and* MIN-DB-GO *by considering some restrictions on the input instances (such as the maximum degree of G or the cardinality of $\mathcal{P}$). We provide several polynomial-time algorithms, hardness and inapproximability results that together give an extensive picture of tractable and intractable instances for both problems.*

Keywords Biological networks, computational biology, graph orientation, NP-completeness, APX-hardness.

1 Introduction

A *physical network* [16] is a biological network formed by protein-protein interactions (PPIs) and protein-DNA interactions (PDIs). While PPIs are undirected [5], PDIs are directed from the transcription factors to their target genes [8]. Thus, a physical network can be modeled by a mixed graph whose vertices are proteins, and edges (resp. arcs) are PPIs (resp. PDIs). Such a network is helpful to understand the processes that occur between a cell and its external environment, notably when an external stimulus is to be propagated into the nucleus. Indeed, this propagation is realized via cascades of activation/deactivation of proteins, and these cascades correspond to paths - in the physical network - from a source protein (cause) to a target protein (effect) [16]. The cause-effect pairs can be identified experimentally, for instance by the measure of transcription changes in response to a gene knock-out [16]. However, experimental methods do not provide the paths going from the source to the target proteins. A key problem in biology is to infer these paths by combining causal information on cellular events [10]. This question leads to the well-studied MAXIMUM GRAPH ORIENTATION problem (MGO) [3,4,6,10,14]: given a mixed graph G and a set $\mathcal{P}$ of source-target (cause-effect) pairs of vertices, replace each (undirected) edge (u,v) by a single (directed) arc (either uv or vu), so that in the new graph, there exists a directed path for a maximum number of source-target pairs. In this work, we focus on a variant of MGO, called S-GO, in which we ask whether *all* the pairs in $\mathcal{P}$ can be connected by a directed path [1,7]. We also introduce a minimization problem, called MIN-DB-GO, in which we allow some edges of G to be *doubly* *oriented* (i.e. replaced by two arcs in opposite directions), in such a way that all pairs of $\mathcal{P}$ are satisfied (i.e., can be connected by a directed path). In the context of biology, a doubly oriented edge reflects the presence of a reversible reaction. Furthermore, in a dynamic biological system, most reactions tend to be irreversible [9]. For this reason, MIN-DB-GO asks that the number of doubly oriented edges be minimized.

2 Problem Formulation

All along this paper, $G = (V, E, A)$ denotes a mixed graph without loops and with simple edges and arcs, where $V(G)$ (resp. $E(G), A(G)$) is the vertex set (resp. edge set, arc set) of G. The *underlying* graph of G, denoted G^*, is defined as follows: $V(G^*) = V(G)$ and $E(G^*) = E(G) \cup \{(u, v) : uv \in A(G)\}$. Finally, $\Delta(G^*)$ is the maximum degree over all vertices in G^*.

A *path* P in $G = (V, E, A)$ from vertex v_1 to vertex v_m is a sequence $P = v_1, v_2, \ldots v_{m-1}, v_m$ of vertices $v_i \in V$ such that for all $1 \leq i \leq m-1$, $(v_i, v_{i+1}) \in E$ or $v_i v_{i+1} \in A$. A *cycle* C in G is a path $v_1, v_2, \ldots v_{m-1}, v_m$ such that $v_1 = v_m$. A *circuit* in G is a special case of cycle $v_1, v_2, \ldots v_{m-1}, v_1$ where $v_i v_{i+1} \in A$ for all $1 \leq i \leq m-1$. A *Mixed Acyclic Graph* [4] (or *MAG*) is a mixed graph that contains no cycle (and therefore no circuit).

An *orientation* G' of G is a directed graph G' obtained from G by replacing each edge $(u, v) \in E$ by an arc uv, or an arc vu, or by uv and vu simultaneously. An edge (u, v) replaced by both arcs uv and vu is called a *doubly oriented* edge. Any orientation G' of G that contains no doubly oriented edge will be called a *simple orientation*. A pair of vertices $(u, v) \in V \times V$ is said to be *satisfied* by the orientation G' of G if there is a (directed) path from u to v in G'. Let $P = v_1, v_2, \ldots v_{m-1}, v_m$ be a path in G. In the following, we will often write *the orientation of P from v_1 towards v_m* to refer to the orientation that replaces every edge of the form (v_i, v_{i+1}), $1 \leq i \leq m-1$, by the arc $v_i v_{i+1}$.

DEFINITION 2.1. *[1] Let $G = (V, E, A)$ be a mixed graph and let $\mathcal{P} \subseteq V \times V$ be a set of source-target pairs of vertices. The graph G is said to be $\mathcal{P}$-*connected *if for all $(u, v) \in \mathcal{P}$, there is a path in G from u to v.*

DEFINITION 2.2. *[1] Let $G = (V, E, A)$ be a mixed graph and let $\mathcal{P} \subseteq V \times V$ s.t. G is $\mathcal{P}$-connected. A* $\mathcal{P}$-orientation *G' of G is a simple orientation of G that satisfies all pairs in $\mathcal{P}$.*

We call S-GO the problem of deciding whether a graph G admits a $\mathcal{P}$-orientation.

> S-GO [1,7]
> **Instance** : A mixed graph $G = (V, E, A)$ and $\mathcal{P} \subseteq V \times V$ s.t. G is $\mathcal{P}$-connected.
> **Question**: Does G admit a $\mathcal{P}$-orientation ?

Analogously to a $\mathcal{P}$-orientation, we define a *$(\mathcal{P}, k)$-DB-orientation* as follows.

DEFINITION 2.3. *Let $G = (V, E, A)$ be a mixed graph and let $\mathcal{P} \subseteq V \times V$ s.t. G is $\mathcal{P}$-connected. Let $k \geq 0$ be an integer. A $(\mathcal{P}, k)$-DB-orientation G' of G satisfies the two following conditions: (i) G' is an orientation of G satisfying all the pairs in $\mathcal{P}$ and (ii) G' contains exactly k doubly oriented edges.*

We are now able to formulate the problem MIN-DB-GO (an illustration of such a problem is provided in Fig. 1).

> MIN-DB-GO
> **Instance** : A mixed graph $G = (V, E, A)$, $\mathcal{P} \subseteq V \times V$ s.t. G is $\mathcal{P}$-connected.
> **Question**: Find a $(\mathcal{P}, k)$-DB-orientation of G that minimizes k.

In Section 3, we show that for both problems, we can always assume, without loss of generality, that G is a Mixed Acyclic Graph (MAG). In Section 4, we give some complexity results for S-GO. We study the complexity of MIN-DB-GO in Section 5. Section 6 is the conclusion, together with several open questions.

3 Reduction to Mixed Acyclic Graphs

It has been shown in [14] that starting with any instance $(G_1, \mathcal{P}_1)$ of problem MGO (defined in Section 1), one can construct an equivalent instance $(G_2, \mathcal{P}_2)$ s.t. G_2 is a MAG.

PROPERTY 1. *[14] Let $G_1 = (V_1, E_1, A_1)$ be a mixed graph and let $\mathcal{P}_1 \subseteq V_1 \times V_1$. One can construct a MAG $G_2 = (V_2, E_2, A_2)$ and a set $\mathcal{P}_2 \subseteq V_2 \times V_2$ with $|\mathcal{P}_2| = |\mathcal{P}_1|$ s.t. for every integer $k \geq 0$, there exists a simple orientation of G_1 satisfying k pairs in $\mathcal{P}_1$ if and only if there exists a simple orientation of G_2 satisfying k pairs in $\mathcal{P}_2$.*

Applying Property 1 with $k = |\mathcal{P}_1|$, we obtain that G_1 admits a $\mathcal{P}_1$-orientation if and only if G_2 admits a $\mathcal{P}_2$-orientation. Hence, in the S-GO problem, without loss of generality we can always consider the input mixed graph to be a MAG. We will show that this property is also valid for the MIN-DB-GO problem. For this, we first show in Property 2 that, for any mixed graph G, we can find a orientation G' such that the edges of any cycle C in G become arcs of a circuit C' in G'. We then show in Property 4 that the vertices of any circuit in G' can be contracted in a single vertex without changing the nature of the problem. This proof closely follows the one in [14].

PROPERTY 2 (ORIENTATION OF CYCLES). *Let $G = (V, E, A)$ be a mixed graph and let $\mathcal{P} \subseteq V \times V$. Let C be a cycle in G. There exists an optimal solution G'' for* MIN-DB-GO*, with inputs G and $\mathcal{P}$, in which C becomes a circuit in G''.*

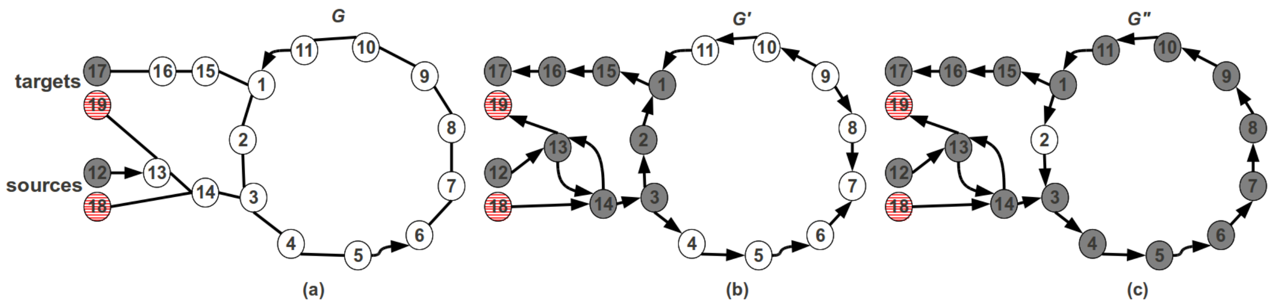

Figure 1. (a) $(G, \mathcal{P})$ is an instance of MIN-DB-GO with $\mathcal{P} = \{(12, 17), (18, 19)\}$, C is a cycle in G with vertex set $\{1, 2, \ldots, 11\}$ (b) G' is an optimal $(\mathcal{P}, 1)$-DB-orientation of G in which the orientation C' of C is not a circuit (c) G'' is an optimal $(\mathcal{P}, 1)$-DB-orientation of G in which the orientation C' of C is a circuit. Gray vertices in G' (resp. G'') induce a path satisfying the pair $(12, 17)$.

Proof. First, since G is $\mathcal{P}$-connected, there must exist an optimal solution G' for MIN-DB-GO with inputs G and $\mathcal{P}$. Let G'' be an orientation of G s.t. (i) C becomes a circuit C'' and (ii) the edges in $E(G) \backslash E(C)$ are oriented similarly as in G' (see Fig. 1 for an illustration). We now show that G'' is also an optimal solution for MIN-DB-GO with inputs G and $\mathcal{P}$. Let $(u, v) \in \mathcal{P}$. If $u, v \in V(C)$ then obviously the pair (u, v) is satisfied in G''. If $u \notin V(C)$ or $v \notin V(C)$, then let us consider a path $P' = a_1, a_2, \ldots a_m$ in G', from $u = a_1$ to $v = a_m$, that satisfies the pair (u, v). Let $x = min\ \{i : a_i \in V(C)\}$ and let $y = max\ \{i : a_i \in V(C)\}$. Then the pair (u, v) is satisfied in G'' by the path formed by (1) the path in G'' induced by the vertex set of the subpath of P' going from a_1 to a_x, (2) the subpath of C'' going from a_x to a_y and (3) the path of G'' induced by the vertex set of the subpath of P' going from a_y to a_m (see for example Fig. 1, in which $a_x = 3$ and $a_y = 1$). Let E_{DB} denote the set of doubly oriented edges in G'. The set of doubly oriented edges in G'' is $E_{DB} \backslash E(C)$. However, by minimality of $|E_{DB}|$, we know that $E_{DB} \cap E(C) = \emptyset$, and consequently G'' is also an optimal solution for MIN-DB-GO. □

In the following, we say that two instances $(G_1, \mathcal{P}_1)$ and $(G_2, \mathcal{P}_2)$ of MIN-DB-GO are *e*quivalent if and only if for every integer $k \geq 0$, there exists a $(\mathcal{P}_1, k)$-DB-orientation of G_1 if and only if there exists a $(\mathcal{P}_2, k)$-DB-orientation of G_2.

Let $G = (V, E, A)$ be a mixed graph and let $\mathcal{P} \subseteq V \times V$. Let $G_1 = (V_1, E_1, A_1)$ be the mixed graph obtained from G by orienting, iteratively, each cycle into a circuit. According to Property 2, $(G, \mathcal{P})$ and $(G_1, \mathcal{P})$ are equivalent. Let also $\mathcal{P}_1$ denote the set obtained from $\mathcal{P}$ by removing each pair $(u, v) \in \mathcal{P}$ s.t. there is a directed path in G_1 from u to v. In that case, the instance $(G_1, \mathcal{P}_1)$ of MIN-DB-GO obtained from $(G, \mathcal{P})$ will be called a *reduced instance*. Clearly, $(G_1, \mathcal{P}_1)$ and $(G_1, \mathcal{P})$ are equivalent, and thus the following property holds.

PROPERTY 3 (REDUCED INSTANCES). *Let $(G_1, \mathcal{P}_1)$ be a reduced instance of* MIN-DB-GO *obtained from instance $(G, \mathcal{P})$. Then $(G, \mathcal{P})$ and $(G_1, \mathcal{P}_1)$ are equivalent.*

PROPERTY 4 (CONTRACTION OF CIRCUITS). *Let $(G_1, \mathcal{P}_1)$ be a reduced instance of* MIN-DB-GO*, and let C' be a circuit in G_1. Let $(G_2, \mathcal{P}_2)$ be the instance of* MIN-DB-GO *defined as follows: (i) $\mathcal{P}_2 = \mathcal{P}_1$ and (ii) G_2 is the graph obtained from G_1 by contracting the vertices of C' in a single vertex. Then, $(G_1, \mathcal{P}_1)$ and $(G_2, \mathcal{P}_2)$ are equivalent.*

Proof. The graph $G_2 = (V_2, E_2, A_2)$ is defined as follows: $V_2 = (V_1 \backslash V(C')) \cup \{x_0\}$, $E_2 = (E_1 \backslash \{(u, v) : u \in V(C') \text{ or } v \in V(C')\}) \cup \{(u, x_0) : u \notin V(C') \text{ and } \exists v \in V(C') \text{ s.t. } (u, v) \in E_1\}$, $A_2 = (A_1 \backslash \{uv : u \in V(C') \text{ or } v \in V(C')\}) \cup \{ux_0 : u \notin V(C') \text{ and } \exists v \in V(C') \text{ s.t. } uv \in A_1\} \cup \{x_0 v : v \notin V(C') \text{ and } \exists u \in V(C') \text{ s.t. } uv \in A_1\}$. In other words, G_2 is obtained from G_1 by contracting the circuit C' in a single vertex x_0. Obviously, $|E_1| = |E_2|$.

Let $\mathcal{P}_2 = \mathcal{P}_1$. Now, let us show that the two instances $(G_1, \mathcal{P}_1)$ and $(G_2, \mathcal{P}_2)$ are equivalent. Let $G'_1 = (V_1, A'_1)$ be a $(\mathcal{P}_1, k)$-DB-orientation of G_1. We construct an orientation G'_2 of G_2 as follows. Let $(u, v) \in E_2$. If $u \neq x_0$ and $v \neq x_0$, then (u, v) is oriented in G'_2 similarly as in G'_1. If $u = x_0$, then there is a vertex $w \in V(C')$ s.t. $(w, v) \in E_1$. If $wv \in A'_1$ (resp. $vw \in A'_1$) we replace in G_2 the edge (x_0, v) by the arc $x_0 v$ (resp. vx_0). The case $v = x_0$ is similar. Let $(u, v) \in \mathcal{P}_1$ and let $P'_1 = a_1, a_2, \ldots, a_m$ be a directed path in G'_1 from $u = a_1$ to $v = a_m$ satisfying the pair (u, v). Let $x = min\ \{i : a_i \in V(C')\}$ and let $y = max\ \{i : a_i \in V(C')\}$. Then the pair (u, v) is satisfied in G'_2 by the path formed by (1) the path in G'_2 induced by the vertex set of the subpath of P'_1 going from a_1 to a_{x-1}, (2) the vertex x_0 (3) the path of G'_2 induced by the vertex set of the subpath of P'_1 going from a_{y+1} to a_m. Obviously, G'_2 is a $(\mathcal{P}_2, k)$-DB-orientation of G_2. Reciprocally, starting with a $(\mathcal{P}_2, k)$-DB-orientation of G_2, by the same way, one can construct a $(\mathcal{P}_1, k)$-DB-orientation of G_1. Hence, the property follows. □

Now, using the previous properties, we are able to show that in the MIN-DB-GO we may, without loss of generality, assume that the input mixed graph is a MAG.

PROPERTY 5 (REDUCTION TO MAG). *Let $(G, \mathcal{P})$ be an instance of the* MIN-DB-GO *problem. Then there exists an equivalent instance $(G_M, \mathcal{P}_M)$ of* MIN-DB-GO *s.t. G_M is a MAG.*

Proof. We construct the graph G_M and the set $\mathcal{P}_M$ by applying the following process:

1. Construct the reduced instance $(G_1, \mathcal{P}_1)$ obtained from $(G, \mathcal{P})$
2. Construct the graph G_2, obtained by contracting, in G_1, every circuit into a single vertex, and let $\mathcal{P}_2 = \mathcal{P}_1$
3. If G_2 is a MAG then set $G_M = G_2$ and $\mathcal{P}_M = \mathcal{P}_2$. Otherwise, set $G = G_2$ and $\mathcal{P} = \mathcal{P}_2$, and return to step 1.

Properties 3 and 4 ensure that $(G_M, \mathcal{P}_M)$ is equivalent to $(G, \mathcal{P})$, which proves the property. □

Therefore, we will always assume, in the remaining of the paper, that for any instance $(G, \mathcal{P})$ of MIN-DB-GO (resp. S-GO), $G = (V, E, A)$ is MAG and G is $\mathcal{P}$-connected. Note that we can also assume that G^* to be connected. Otherwise, we can consider separately each graph $G_1, G_2, \ldots, G_r$ induced, in G, by the vertices of the connected components of G^*.

Let $G = (V, E, A)$ be a MAG and $\mathcal{P} = \{(s_i, t_i) \in V \times V : 1 \leq i \leq m\}$ be a set of pairs of vertices. For each i, $1 \leq i \leq m$, we note by n_i the number of distinct paths in G from s_i to t_i. All along the paper, the integer B is the following value: $B = \max\{n_i : 1 \leq i \leq m\}$.

In the next sections, we study the complexity of S-GO (Section 4) and MIN-DB-GO (Section 5), by considering different constraints on the three following parameters: $\Delta(G^*)$, B and $|\mathcal{P}|$.

Remark that when $B = 1$ we can easily solve the S-GO and the MIN-DB-GO problems. Indeed, G is $\mathcal{P}$-connected and G^* is connected, thus if in addition we have $B = 1$, then for each pair $(s, t) \in \mathcal{P}$ there is a unique path P_i in G from s_i to t_i. Consequently, in order to satisfy the pair (s_i, t_i) we must orient P_i from s_i towards t_i. Then, we orient each remaining edge (u, v), in G, in a unique arbitrarily direction. Obviously, in this orientation we create a minimum number of doubly oriented edges, and thus MIN-DB-GO is optimally solved. If there is no doubly oriented edge at the end of the process, then we obtain a $\mathcal{P}$-orientation of G. Otherwise, G has no $\mathcal{P}$-orientation. The case $\Delta(G^*) = 1$ is obvious.

	$\Delta(G^*) = 2$	$\Delta(G^*) = 3$		
		$B = 2$	$B = 3$	B is unbounded
S-GO	P [Cor. 1]	P [Th. 1]	NPC [Thm. 3]	NPC [Th. 3]
MIN-DB-GO	Open	APX-h [Th. 9]	NPC [Th. 6], Non-approx. [Th. 7], APX-h [Th. 9]	NPC [Th. 6], Non-approx. [Th. 7], APX-h and W[1]-h [Th. 8]

Table 1. Complexity of S-GO and MIN-DB-GO when G is a MAG and G^* is a bounded degree graph. Recall that $B = \max\{n_i, 1 \leq i \leq |\mathcal{P}|\}$, where n_i is the number of distinct paths in G from s_i to t_i. Note also that the result provided in Theorem 1 remains valid even when $\Delta(G^*)$ is unbounded.

	$\lvert\mathcal{P}\rvert \leq 2$	$\lvert\mathcal{P}\rvert \geq 3$ (and $\lvert\mathcal{P}\rvert = \mathcal{O}(1)$)	
		$B = \mathcal{O}(1)$	B is unbounded
S-GO	P [Arkin et al. [1]]	P [Th. 2]	Open
MIN-DB-GO	P [Th. 4]	P [Th. 5]	Open

Table 2. Complexity of S-GO and MIN-DB-GO when G is a MAG and $|\mathcal{P}|$ is a constant.

The complexity results, when $B \geq 2$ and $\Delta(G^*) \geq 2$, are summarized in Table 1 and Table 2. Interestingly, Table 1 shows that parameter B defines the border between easy ($B = 2$) and difficult ($B = 3$) instances of S-GO, even when G^* is of small degree ($\Delta(G^*) = 3$). Unlike S-GO, the problem MIN-DB-GO is difficult even when $B = 2$. In Table 2, we show the complexity of both problems when $|\mathcal{P}|$ is a constant. Due to space constraints, some proofs are omitted in this paper.

4 Complexity of the S-GO problem

It has been shown that the S-GO problem is polynomial-time solvable on undirected graphs [7] and NP-complete on general MAGs [1]. In this section, we investigate the complexity of the S-GO problem for MAGs with bounded $\Delta(G^*)$ and/or bounded B (see Table 1), and for bounded $|\mathcal{P}|$ (see Table 2).

4.1 Easy cases

THEOREM 1. *The* S-GO *problem is polynomial-time solvable when G is a MAG and $B = 2$.*

Proof. For each pair $(s_i, t_i) \in \mathcal{P}$ there are in G at most two paths from s_i to t_i and such paths can be computed in polynomial-time. If for a pair $(s_i, t_i) \in P$, there is only one path from s_i to t_i, then we orient it from s_i towards t_i and we remove the pair (s_i, t_i) from the set $\mathcal{P}$. We continue this process until (1) G is no longer P-connected or (2) $\mathcal{P} = \emptyset$ or (3) for each pair $(s_i, t_i) \in P$ there are exactly two paths from s_i to t_i. The first case implies that G has no $\mathcal{P}$-orientation. In the second case we arbitrarily orient each edge, in the resulting graph, in a unique direction to obtain a $\mathcal{P}$-orientation. Finally, in the last case we reduce to an instance of the S-GO problem in which there are, in G, exactly two paths from s_i to t_i for all $(s_i, t_i) \in \mathcal{P}$.

We note by X_{i1} and X_{i2} the two paths, in G, from s_i to t_i. Given $i, j \in \{1, 2, \ldots |\mathcal{P}|\}$, $i \neq j$, and $a, b \in \{1, 2\}$, we say that the two paths X_{ia} and X_{jb} are in *conflict* if orienting X_{ia} from s_i towards t_i and X_{jb} from s_j towards t_j, creates a doubly oriented edge. Now, we construct an instance $(\mathcal{X}, \mathcal{C})$ of the problem 2-SAT as follows. Let $\mathcal{X} = \{x_{i1}, x_{i2} \ : \ 1 \leq i \leq |\mathcal{P}|\}$ be the variable set. For all $i \in \{1, 2, \ldots, |\mathcal{P}|\}$, we add the clause $c_i = (x_{i1} \vee x_{i2})$. For all $i, j \in \{1, 2, \ldots, |\mathcal{P}|\}$, $i \neq j$, and $a, b \in \{1, 2\}$, we add the clause

$(\overline{x_{ia}} \vee \overline{x_{jb}})$, if paths X_{ia} and X_{jb} are in conflict. Let us show that there is an assignment of the variables in $\mathcal{X}$ that satisfies all clauses in $\mathcal{C}$ if and only if G has a $\mathcal{P}$-orientation. Indeed, consider a truth assignment of clauses in $\mathcal{C}$ and let x_{ih_i}, $1 \leq h_i \leq 2$, be a true literal of clause c_i, $1 \leq i \leq |\mathcal{P}|$. We orient in G the path X_{ih_i}, from s_i towards t_i, for all i, $1 \leq i \leq |\mathcal{P}|$. This orientation cannot create any doubly oriented edges. Otherwise, there are $i, j \in \{1, 2, \dots |\mathcal{P}|\}$, $i \neq j$ such that the paths X_{ih_i} and X_{jh_j} are in conflict, implying that the clause $(\overline{x_{ih_i}} \vee \overline{x_{jh_j}})$ is unsatisfied. To finish the orientation of G, we orient arbitrarily the remaining edges in G without creating any doubly oriented edge.

Now, let us show the reverse implication. We consider the set $\{Y_{1h_1}, Y_{2h_2}, \dots, Y_{|\mathcal{P}|h_{|\mathcal{P}|}}\}$ s.t. Y_{ih_i} is a directed path from s_i to t_i, in a $\mathcal{P}$-orientation of G. Each path Y_{ih_i} is the orientation (from the source towards the target vertex) of a mixed path $X_{ih_i} = G[V(Y_{ih_i})]$, $h_i \in \{1, 2\}$, for all $1 \leq i \leq |\mathcal{P}|$. We set to $true$ the variable set $\{x_{ih_i} \ : \ 1 \leq i \leq |\mathcal{P}|\}$ and we set to $false$ the remaining variables. Obviously, this assignment satisfies the clause set $\{c_i \ : \ 1 \leq i \leq |\mathcal{P}|\}$. By contradiction, assume now that some clause $(\overline{x_{ia}} \vee \overline{x_{jb}})$ is not satisfied. Then $x_{ia} = true$ and $x_{jb} = true$. Consequently, in the resulting $\mathcal{P}$-orientation of G, the path X_{ia} (resp. X_{jb}) is oriented from s_i towards t_i (resp. from s_j towards t_j). A contradiction, because a $\mathcal{P}$-orientation cannot use, simultaneously, two paths that are in conflict. As the problem 2-SAT is polynomial-time solvable [2], we deduce that one can solve in polynomial-time the S-GO problem when graph G is a MAG s.t. there are in G at most two paths from s_i to t_i, for all $(s_i, t_i) \in \mathcal{P}$. □

COROLLARY 1. *The* S-GO *problem is polynomial-time solvable when G is a MAG and* $\Delta(G^*) = 2$.

Proof. The graph G^* is connected. Thus when $\Delta(G^*) = 2$, the graph G^* must be a path or a cycle, and consequently $B \leq 2$. If $B = 1$ the S-GO problem is trivial. If $B = 2$, we deduce from the previous result (Theorem 1) that the S-GO problem is polynomial-time solvable. □

Now, we show that the S-GO problem is polynomial-time solvable when both parameters B and $|\mathcal{P}|$ are bounded.

THEOREM 2. *The* S-GO *problem is polynomial-time solvable when G is a MAG,* $|\mathcal{P}| = \mathcal{O}(1)$ *and* $B = \mathcal{O}(1)$.

4.2 Difficult cases

We showed in Theorem 1 that the S-GO problem is easy when $B \leq 2$. However, in the following theorem, we show that when $B = 3$ the problem S-GO becomes difficult.

THEOREM 3. *The* S-GO *problem is* NP*-complete even when the graph G is a MAG,* $\Delta(G^*) = 3$ *and* $B = 3$.

Proof. Arkin et al. [1] provided an NP-completeness proof of the S-GO problem on general MAGs. Their proof is based on a reduction for the Satisfiability problem (SAT). Here, we modify the mixed graph G constructed from their reduction to ensure that $\Delta(G^*) = 3$. For this, we reduce to our problem, the problem 3-SAT in which each variable appears at most in four clauses [15]. Let $(\mathcal{C}_m, \mathcal{V}_n)$ be an instance of 3-SAT s.t. $\mathcal{C}_m = \{c_1, \dots c_m\}$ is a set of clauses and $\mathcal{V}_n = \{x_1, \dots, x_n\}$ is a variable set, and for all j, $1 \leq j \leq n$, the variable x_j satisfies the following condition: (1) x_j and $\overline{x_j}$ appear at most in four clauses. In addition, one can require second condition: (2) for each variable x_j, there is at least one clause that contains x_j and at least one clause that contains $\overline{x_j}$. Otherwise, w.l.o.g the variable x_j can be fixed to *true* or *false*. Now, let us construct an instance $(G, \mathcal{P})$ of the S-GO problem. For each clause c_i, we create two vertices s_i and t_i, $1 \leq i \leq m$. For each variable x_j, we create these 15 vertices: $\{u_j, v_j\} \cup \{a_{jk}, b_{jk}, a'_{jk}, b'_{jk}\}_{1 \leq k \leq 3}$. Then, we add an edge (u_j, v_j) and the four following directed paths: $a_{j1}a_{j2}a_{j3}u_j$, $v_jb_{j3}b_{j2}b_{j1}$, $a'_{j1}a'_{j2}a'_{j3}v_j$ and finally $u_jb'_{j3}b'_{j2}b'_{j1}$, for all $1 \leq j \leq n$. For each variable x_j, there are k_j clauses containing x_j and k'_j clauses containing $\overline{x_j}$ s.t. $1 \leq k_j \leq 3$, $1 \leq k'_j \leq 3$ and $k_j + k'_j \leq 4$. Let $\{c_{i_1}, c_{i_2}, \dots, c_{i_{k_j}}\}$ (resp. $\{c_{i'_1}, c_{i'_2}, \dots, c_{i'_{k'_j}}\}$) be the set of clauses that contain x_j (resp. $\overline{x_j}$). We add an arc $s_{i_\alpha}a_{j\alpha}$ and an arc $b_{j\alpha}t_{i_\alpha}$, for all $\alpha \in \{1, 2, \dots k_j\}$. Also, we add an arc $s_{i'_\beta}a'_{j\beta}$ and an arc $b'_{j\beta}t_{i'_\beta}$, for all $\beta \in \{1, 2, \dots k'_j\}$. To finish our construction, we set $\mathcal{P} = \{(s_i, t_i), 1 \leq i \leq m\}$. An example of construction is illustrated in Fig. 2. According to conditions (1) and (2), one can easily show that $\Delta(G^*) = 3$. In addition, for each pair (s_i, t_i) there are exactly three paths in G fro s_i to t_i, because each clause in $\mathcal{C}_m$ contains exactly three literals. Thus $B = 3$.

We claim that there is an assignment satisfying all the clauses in $\mathcal{C}_m$ if and only if there exists a $\mathcal{P}$-orientation of G. Indeed, consider an assignment satisfying all the clauses in $\mathcal{C}_m$, similarly to the proof presented in [1], if $x_j = true$ (resp. $x_j = false$) then we orient the edge (u_j, v_j) from u_j to v_j (resp. from v_j to u_j). Let l_i be a true literal of clause c_i. Then, there is a variable x_j s.t. $l_i = x_j$ or $l_i = \overline{x_j}$. If $l_i = x_j$ (resp. $l_i = \overline{x_j}$) then there is an integer k_i, $1 \leq k_i \leq 3$, such that $s_i a_{jk_i}, b_{jk_i} t_i \in A(G)$ (resp. $s_i a'_{jk_i}, b'_{jk_i} t_i \in A(G)$). Thus, the pair (s_i, t_i) is satisfied by the path $s_i a_{jk_i} a_{j(k_i+1)} \dots u_j v_j b_{j3} \dots b_{jk_i} t_i$ (resp. $s_i a'_{jk_i} a'_{j(k_i+1)} \dots v_j u_j b'_{j3} \dots b_{jk_i} t_i$).

Now, let us prove the reverse implication. Given a $\mathcal{P}$-orientation G' of G, we set the variable x_j to $true$ (resp. to $false$) if the edge $u_j v_j \in A(G')$ (resp. $v_j u_j \in A(G')$). Let c_i be a clause in $\mathcal{C}_m$. Then the pair (s_i, t_i) is satisfied in by a directed path P in G', from s_i to t_i, going through an arc $u_j v_j$ or an arc $v_j u_j$. If P contains the arc $u_j v_j$ then the clause c_i must contain the literal x_j and thus c_i is satisfied. If P contains the arc $v_j u_j$ (consequently $x_j = false$) thus the clause c_i must contain the literal $\overline{x_j}$ and thus c_i is also satisfied. □

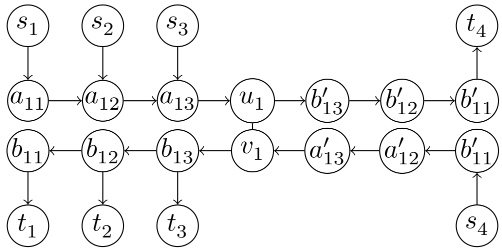

Figure 2. Construction of an instance $(G, \mathcal{P})$ of the S-GO problem, from an instance of 3-SAT in which each variable appears at most in four clauses. Here, the variable set is $\mathcal{V} = \{x_j, 1 \leq j \leq 6\}$ and the clause set is $\mathcal{C} = \{c_i, 1 \leq i \leq 4\}$ s.t. $c_1 = (x_1 \vee \overline{x_2} \vee x_3)$, $c_2 = (x_1 \vee x_4 \vee x_5)$, $c_3 = (x_1 \vee \overline{x_4} \vee \overline{x_6})$ and $c_4 = (\overline{x_1} \vee \overline{x_5} \vee x_6)$. The set of pairs of vertices is $\mathcal{P} = \{(s_i, t_i), 1 \leq i \leq 4\}$. In this figure, we show only the subgraph corresponding to variable x_1.

5 Complexity of MIN-DB-GO

Let DB-GRAPHORIENTATION denote the decision version of the minimization problem MIN-DB-GO. The S-GO problem, investigated in the previous section (Section 4), is a particular case of the problem DB-GRAPHORIENTATION when no doubly oriented edge is allowed. Hence, each $\mathcal{P}$-orientation of G is a solution of MIN-DB-GO. However, if there is no $\mathcal{P}$-orientation of G, then we conclude just that at least one edge must be doubly oriented in a solution of MIN-DB-GO, but in general that gives no information about the number of edges to be doubly oriented to solve the MIN-DB-GO problem.

In this section, we study the complexity of MIN-DB-GO when the input graph is a MAG (see Table 1 and Table 2). As in the previous section, we suppose that G is a $\mathcal{P}$-connected MAG.

5.1 Easy cases

We first show that, similarly to the S-GO problem, the MIN-DB-GO problem is also polynomial-time solvable for general MAGs when $|\mathcal{P}| \leq 2$.

THEOREM 4. *The* MIN-DB-GO *problem is polynomial-time solvable when G is a MAG and* $|\mathcal{P}| \leq 2$.

Proof. The case $|\mathcal{P}| = 1$ is obvious. Let $G = (V, E, A)$ be a MAG and $\mathcal{P} = \{(s_1, t_1), (s_2, t_2) \in V \times V\}$.

A $\mathcal{P}$-*essential* edge is an edge $e = (u, v) \in E$, s.t. if we orient e from u to v or from v to u, the graph G is no longer $\mathcal{P}$-connected. One can compute the $\mathcal{P}$-essential edges in polynomial-time [1].

Let E_{ess} (resp. E_{min}) be the set of $\mathcal{P}$-essential edges (resp. the set of doubly oriented edges in a solution of the MIN-DB-GO problem).

We show that $E_{min} = E_{ess}$. Let $e = (u, v) \in E_{ess}$. If we orient e in a unique direction (from u to v or from v to u) then, by definition of $\mathcal{P}$-essential edges, there is an integer i, $1 \leq i \leq 2$, s.t. there is no path in G from s_i to t_i. Thus, whatever the orientation of edges in $E - \{e\}$, if e is not doubly oriented, then the pair (s_i, t_i) would not be satisfied. Hence, we must doubly orient each edge $e \in E_{ess}$, which implies that $E_{ess} \subseteq E_{min}$.

Conversely, let $G' = (V, E', A')$ denote the mixed graph obtained from G after replacing each $\mathcal{P}$-essential edge (u, v) by the arcs uv and vu, i.e., $V(G') = V(G)$, $E(G') = E(G) \backslash E_{ess}$ and $A' = A \cup \{uv, vu : (u, v) \in E_{ess}\}$. The graph G' does not contain any $\mathcal{P}$-essential edge, then G' has a $\mathcal{P}$-orientation G'' [1]. Thus, G'' is an orientation of G that satisfies all the pairs in $\mathcal{P}$ and creates $|E_{ess}|$ doubly oriented edges, which implies that $|E_{ess}| \geq |E_{min}|$. Since we have already shown that $E_{ess} \subseteq E_{min}$, we conclude that $E_{min} = E_{ess}$.

Now, to solve the MIN-DB-GO problem when $|\mathcal{P}| = 2$, we apply the following process.

1. Compute the $\mathcal{P}$-essential edges of G using the polynomial-time algorithm presented in [1];
2. Construct a mixed graph G' by replacing each $\mathcal{P}$-essential edge (u, v) by two arcs uv and vu;
3. Apply the polynomial-time algorithm presented in [1] to compute a $\mathcal{P}$-orientation of G'.

□

As in the S-GO problem, the MIN-DB-GO problem is polynomial-time solvable when both parameters $|\mathcal{P}|$ and $|B|$ are bounded.

THEOREM 5. *The* MIN-DB-GO *problem is polynomial-time solvable when G is a MAG, $|\mathcal{P}| = \mathcal{O}(1)$ and $B = \mathcal{O}(1)$.*

5.2 Difficult cases

Let DB-GO denote the decision version of the MIN-DB-GO problem. We show in the next result that the DB-GO problem is NP-complete even when $\Delta(G^*) = 3$.

THEOREM 6. *The problem* DB-GO *is* NP*-complete when G is a MAG and $|\mathcal{P}|$ is unbounded even when $\Delta(G^*) = 3$ and $B = 3$.*

In the remaining of this section, we study the approximability and the parameterized complexity of the MIN-DB-GO problem.

THEOREM 7. *Unless* P = NP*, the* MIN-DB-GO *problem is non-approximable when the graph G is a MAG and $|\mathcal{P}|$ is unbounded even when $\Delta(G^*) = 3$ and $B = 3$.*

The MIN-DB-GO problem is also APX-hard and W[1]-hard when $|\mathcal{P}|$ and B are unbounded even when $\Delta(G^*) = 3$.

THEOREM 8. *The* MIN-DB-GO *problem is* APX*-hard and* W[1]*-hard (parametrized by the number of doubly oriented edges) when G is a MAG and $|\mathcal{P}|$ and B are unbounded, even when $\Delta(G^*) = 3$.*

Proof. We propose an L-reduction from the APX-hard problem MINIMUM SET COVER [12,13]: given a ground set $\mathcal{X} = \{X_1, \ldots, X_n\}$, and a collection of sets $\mathcal{C} = \{S_1, \ldots, S_m\}$ s.t. $S_i \in 2^{\mathcal{X}}$, for all $1 \leq i \leq m$, the goal is to find a minimum set cover $\mathcal{C}'$, i.e., a set $\mathcal{C}' \subseteq \mathcal{C}$ s.t. $\mathcal{C} = \bigcup_{S_i \in \mathcal{C}'} S_i$ and $|\mathcal{C}'|$ is minimum.

We note by α_j, $1 \leq j \leq n$, the number of the sets containing X_j. Let us construct an instance $(G, \mathcal{P})$ of the MIN-DB-GO problem. For each $X_j \in \mathcal{X}$, we create the vertex set $\{x_j\} \cup \{x_j^k, 1 \leq k \leq \alpha_j\}$, then we create the directed path $x_j^1 x_j^2 \ldots x_j^{\alpha_j} x_j$. For each S_i, we add the vertex set $\{s_i, s_i'\} \cup \{s_i^j, 1 \leq j \leq |S_i|\}$, and we add an edge (s_i', s_i) and a directed path $s_i s_i^1 s_i^2 \ldots s_i^{|S_i|}$.

Let $X_l \in \mathcal{X}$ be the $j-$th element in a set S_i, for each j, $1 \leq j \leq |S_i|$, we add an arc from s_i^j towards *only one* vertex from the set $\{x_l^k, 1 \leq k \leq \alpha_l\}$. Such a vertex is chosen in such a way that the indegree of each vertex x_l^k is at most two, for all $1 \leq k \leq \alpha_l$. To finish the construction of G, we add a vertex r_1 connected, by two edges, to the vertices s_1' and s_2'. Then, we add a new vertex r_2 connected, by two edges, to the vertices r_1 and v_3'. We continue the creation of vertices r_i connected, by edges, to r_{i-1} and s_{i+1}', for all $3 \leq i \leq m - 1$. The set of pairs to satisfy is $\mathcal{P} = \{(r_{m-1}, x_j), 1 \leq j \leq n\} \cup \{(s_i, s_i'), 1 \leq i \leq m\}$ with $m = |\mathcal{C}|$. An example of construction is illustrated in Fig. 3. The degree of each vertex r_i in G is at most three and also each vertex s_i^j is connected to exactly one vertex $x_{i'}^{j'}$. Thus, one can easily check that $\Delta(G^*) = 3$.

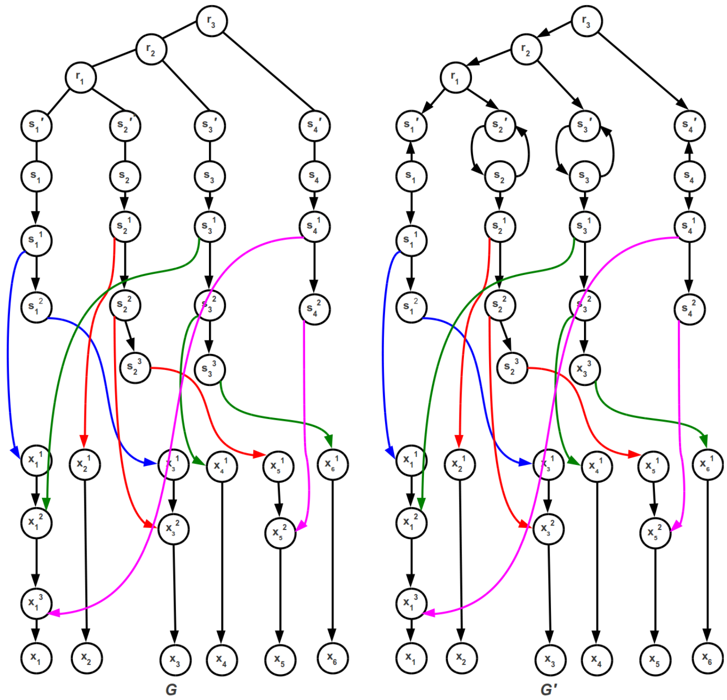

Figure 3. (a) Construction of an instance $(G, \mathcal{P})$ of the S-GO problem from an instance of MINIMUM SET COVER problem. Here, $\mathcal{X} = \{X_1, X_2, X_3, X_4, X_5, X_6\}$ and $\mathcal{C} = \{S_1, S_2, S_3, S_4\}$ s.t. $S_1 = \{X_1, X_3\}$, $S_2 = \{X_2, X_3, X_5\}$, $S_3 = \{X_1, X_4, X_6\}$ and $S_4 = \{X_1, X_5\}$. The set of pairs is $\mathcal{P} = \{(s_1, s'_1), (s_2, s'_2), (s_3, s'_3), (s_4, s'_4), (r_3, x_1), (r_3, x_2), (r_3, x_3), (r_3, x_4), (r_3, x_5), (r_3, x_6)\}$. (b) The graph G' is an orientation of G obtained from the set cover $\mathcal{C}' = \{S_2, S_3\}$ and satisfying all the pairs in $\mathcal{P}$.

We claim that, for every integer $k \geq 0$, there is a set cover of $\mathcal{C}$ of cardinality k if and only if there is a $(\mathcal{P}, k)$-DB-orientation of G.

$\Rightarrow$: Given a set cover $\{S_{i_1}, S_{i_2}, \ldots, S_{i_k}\}$, we doubly orient the edge (s_{i_j}, s'_{i_j}), for all $1 \leq j \leq k$. Then, we replace each edge (v_i, v'_i) by the arc $s_i s'_i$, for all $i \in \{1, 2, \ldots, m\} \backslash \{i_1, i_2, \ldots, i_k\}$. Finally, we orient the tree induced by the vertex set $\{r_i, 1 \leq i < m\} \cup \{s'_i, 1 \leq i \leq m\}$, to create a directed tree of root r_{m-1}.

$\Leftarrow$: Let E_{DB} be the set of doubly oriented edges in a $(\mathcal{P}, k)$-DB-orientation. Let $\mathcal{C}' = \{S_i : (s_i, s'_i) \in E_{DB}\}$. We will show that the set $\mathcal{C}'$ is a set cover of $\mathcal{C}$. Suppose that there is $X_j \in \mathcal{X}$ s.t. $X_j \notin S_i$ for all $S_i \in \mathcal{C}'$. Let $\mathcal{C}_j$ denote the collection of the sets containing X_j, i.e., $\mathcal{C}_j = \{S \in \mathcal{C} : X_j \in S\}$. The graph G is constructed in such a way that, to satisfy any pair (r_{m-1}, x_j), we must replace an edge (s'_i, s_i) by the arc $s'_i s_i$ s.t. $S_i \in \mathcal{C}_j$. On the other hand, we have to orient each edge (s'_i, s_i), from s_i towards s'_i, to satisfy the pair $(s_i, s'_i) \in \mathcal{P}$. Then the edge (s'_i, s_i) must be doubly oriented, which implies that $S_i \in \mathcal{C}'$. This is a contradiction, because $\mathcal{C}' \cap \mathcal{C}_j = \emptyset$.

The above reduction is an L-reduction that preserves the parameter k (the cardinality of the set cover and the number of doubly oriented edges). Since the problem MINIMUM SET COVER is APX-hard and W[1]-hard when parametrized by k [12,13], then the MIN-DB-GO problem is also APX-hard and W[1]-hard when parametrized by the number of doubly oriented edges. □

Now let us show that, unlike the S-GO problem, the MIN-DB-GO problem remains difficult even when $B = 2$.

THEOREM 9. *The problem* MIN-DB-GO *is* APX-*hard when G is a MAG and $|\mathcal{P}|$ is unbounded, even when $B \in \{2, 3\}$ and $\Delta(G^*) = 3$.*

Proof. Again, we use the above reduction (proof of Theorem 8), but we consider the variant MINIMUM SET COVER-K of the MINIMUM SET COVER problem in which each $X_j \in \mathcal{X}$ appears in exactly K sets in $\mathcal{C}$ s.t. K is a constant ≥ 2. For each pair of vertices $(s_i, s'_i) \in \mathcal{P}$ there is a unique path in G, from s_i to s'_i (that is the edge (s_i, s'_i)), for all $1 \leq i \leq m$. In addition, the fact that each $X_j \in \mathcal{X}$ appears in exactly K sets in $\mathcal{C}$, implies that for each pair (r_{m-1}, x_i) there are, in G, K paths from r_{m-1} to s_i, for all $1 \leq i \leq n$. Thus $B = K$ and also the graph G is constructed so that we have $\Delta(G^*) = 3$.

As the problem MINIMUM SET COVER-K is APX-hard [11], then we conclude that MIN-DB-GO is APX-hard when G is a MAG s.t. $\Delta(G^*) = 3$ and $|\mathcal{P}|$ is unbounded, even when, B is a constant ≥ 2 (and thus when $B \in \{2, 3\}$) . □

6 Conclusion

In this work, we considered two problems that are concerned with the orientation of mixed graphs, both motivated, among others, by biological applications. We studied the complexity of both problems, and in particular we provided polynomial-time algorithms for some restricted instances, and several hardness and inapproximability results. However, some interesting problems remain open so far, such as the following ones:

– Explore the possibility of obtaining fixed-parameterized tractable (FPT) algorithms for MIN-DB-GO.
– Study the approximability of MIN-DB-GO on specific graph classes.
– Study the complexity of S-GO and MIN-DB-GO when $|\mathcal{P}| \geq 3$ is a constant.

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