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Structure of conflict graphs in constrained alignment problems and algorithms[*]

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We consider the constrained graph alignment problem which has applications in biological network analysis. Given two input graphs $G_1 = (V_1, E_1), G_2 = (V_2, E_2)$, two vertices u_1, v_1 of G_1 paired respectively to two vertices u_2, v_2 of G_2 induce an *edge conservation* if u_1, v_1 and u_2, v_2 are adjacent in their respective graphs. The goal is to provide a one-to-one mapping between some vertices of the input graphs in order to maximize edge conservation. However the allowed mappings are restricted since each vertex from V_1 (resp. V_2) is allowed to be mapped to at most m_1 (resp. m_2) specified vertices in V_2 (resp. V_1). Most of the results in this paper deal with the case $m_2 = 1$ which attracted most attention in the related literature. We formulate the problem as a maximum independent set problem in a related *conflict graph* and investigate structural properties of this graph in terms of forbidden subgraphs. We are interested, in particular, in excluding certain wheels, fans, cliques or claws (all terms are defined in the paper), which in turn corresponds to excluding certain cycles, paths, cliques or independent sets in the neighborhood of each vertex. Then, we investigate algorithmic consequences of some of these properties, which illustrates the potential of this approach and raises new horizons for further works. In particular this approach allows us to reinterpret a known polynomial case in terms of conflict graph and to improve known approximation and fixed-parameter tractability results through efficiently solving the maximum independent set problem in conflict graphs. Some of our new approximation results involve approximation ratios that are functions of the optimal value, in particular its square root; this kind of results cannot be achieved for maximum independent set in general graphs.

Keywords: Graph algorithms, graph alignment, constrained alignments, conflict graph, maximum independent set, protein-protein interaction networks, functional orthologs, H-free graphs

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1 Introduction

The *graph alignment* problem has important applications in biological network alignment, in particular in the alignments of protein-protein interaction (PPI) networks (Abaka et al. (2013); Aladag and Erten (2013); Sharan and Ideker (2006); Zaslavskiy et al. (2009); Alkan and Erten (2014)). Undirected graphs $G_1 = (V_1, E_1), G_2 = (V_2, E_2)$ (not necessarily connected) correspond to PPI networks for a pair of species, where the vertex sets V_1, V_2 represent the sets of proteins, and E_1, E_2 represent the sets of known protein interactions pertaining to the networks of species under consideration. The informal goal is to find similar patterns between two PPI networks by identifying a one-to-one mapping between some vertices of V_1 and V_2 that maximizes the "similarity" of the mapped proteins, usually scored with respect to the aminoacid sequence similarity and the conservation of interactions between mapped proteins. Functional orthology is an important application that serves as the main motivation to study the alignment problems as part of a comparative analysis of PPI networks. A successful protein interaction network alignment across multiple species could provide a basis for deciding the proteins with similar functions, which may further be used in predicting functions of proteins with unknown functions or in verifying those with known functions, in detecting common orthologous pathways between species, or in reconstructing the evolutionary dynamics (Faisal et al. (2015)).

A graph theory problem related to the biological network alignment problem is that of finding the *maximum common edge subgraph* (MCES) of a pair of graphs, a problem commonly employed in the matchings of 2D/3D chemical structures (Raymond and Willett (2002)). The MCES of two undirected graphs G_1, G_2 is a common subgraph (not necessarily induced) that contains the largest number of edges common to both G_1 and G_2. The NP-hardness of the MCES problem proposed in Garey and Johnson (1979) trivially implies that the biological network alignment problem is also NP-hard.

A specific version of the problem reduces its size by restricting the output alignment mappings to those chosen among certain subsets of protein mappings. The subsets of allowed mappings are assumed to be predetermined via some measure of similarity, usually that of sequence similarity (Abaka et al. (2013); Zaslavskiy et al. (2009)). The *constrained alignment* problem we consider herein can be considered as a graph theoretical generalization of this biological network alignment problem version. Formally, an instance $\prec G_1, G_2, S \succ$ is defined by a pair of undirected graphs $G_1 = (V_1, E_1), G_2 = (V_2, E_2)$ and a bipartite graph $S = (V_1 \cup V_2, E_S)$ with parts V_1 and V_2 representing possible matching between vertices of G_1 and vertices of G_2. For $i = 1, 2$, we denote by m_i, the maximum degree in S of vertices from part V_i. A *legal alignment* A is a matching of S, i.e., a set of independent edges (pairwise non adjacent). An edge $ab \in E_1$ is said to be *conserved*, if there is an edge $cd \in E_2$ such that bc and ad are in A, or ac and bd are in A. Then, the edge cd is equivalently called conserved and, by definition of a matching, the number of conserved edges of G_1 is equal to the number of conserved edges of G_2. The constrained alignment problem is that of finding a legal alignment that maximizes the number of conserved edges in G_1 (or equivalently in G_2).

Several related problems have been studied previously like, for instance, the *contact map overlap* problem introduced in Goldman et al. (1999). The goal is to maximize the number of conserved edges; however contrary to the constrained alignment problem, no constraint is given in terms of the bipartite graph S. Furthermore their problem definition assumes a linear order of the vertices of both G_1, G_2 which should be preserved by the output mapping. The problem of (μ_{G_1}, μ_{G_2})- *matching with orthologies*, was introduced in Fagnot et al. (2008). Similar to the constrained alignment problem, it is to find a mapping respecting a set of constraints represented by a bipartite graph S but all edges of G_1 are requested to be conserved. Assuming $m_i = \mu_{G_i}, i = 1, 2$ and denoting by $\Delta_i = \Delta(G_i), i = 1, 2$ for an instance of the problem, where $\Delta(G)$ denotes the maximum degree of graph G, the problem of (μ_{G_1}, μ_{G_2})-matching with orthologies is shown NP-complete even when $m_1 = 3, m_2 = 2$ and G_1 and G_2 are bipartite, $\Delta_1 \leq 1$ and $\Delta_2 \leq 2$, or if $m_1 = 3, m_2 = 1$ and $\Delta_1 \leq 3, \Delta_2 \leq 4$. It is linear-time solvable if $m_1 = 2$ and $m_2 \in O(1)$ (see also Fertin et al. (2009)). Finally, the problem *MAX*(μ_{G_1}, μ_{G_2}) considered in Fertin et al. (2009) is the optimization version of (μ_{G_1}, μ_{G_2})-matching with orthologies with the objective to maximize the number of conserved edges. It is almost the same as the constrained alignment problem with $m_i = \mu_{G_i}, i = 1, 2$ with the additional requirement that every vertex of G_1 is mapped to a vertex in G_2. We discuss more precisely the relations between these problems in Section 2. In Fertin et al. (2009), only the case $m_2 = \mu_{G_2} = 1$ is considered. It is shown APX-hard even if $m_1 = 2$ and $m_2 = 1$ (APX-complete if G_1 has bounded degree) and both graphs are bipartite. They also propose several approximability and fixed-parameter tractability results (see Ausiello et al. (1999) and Downey and Fellows (1999) for definitions about approximation and parameterized complexity, respectively). In particular, they show that the problem can be approximated within ratio $2\lceil 3\Delta_1/5 \rceil$ for even Δ_1 and ratio $2\lceil (3\Delta_1 + 2)/5 \rceil$ for odd Δ_1. They also show that the problem is fixed-parameter tractable on the size of the output assuming $m_2 = 1$, m_1 is constant and G_1 has a bounded degree.

In this paper, we consider the maximum constrained alignment problem as a maximum independent set problem in a related *conflict graph*, constructed from G_1, G_2, and S. Our aim is to investigate structural properties of this conflict graph in order to derive efficient algorithms for the alignment problem. Although a conflict graph is also proposed in Fertin et al. (2009) for $m_2 = 1$, with in particular a fixed-parameter tractability result based on a degree argument, no further structural property is provided. Here, we deepen this approach and strengthen algorithmic results. Our main results and comparison with known results are given in Tables 1, 2 and 3 at the end of this section.

Table 1 shows our main structural results: the basic metrics of the graph - size and maximum degree - in the most general case as well as forbidden subgraphs for the case $m_2 = 1$. Some of these results have direct algorithmic consequences but even those without algorithmic applications are interesting, in particular since they motivate some graph classes for further studies. This is in particular the case for classes of graphs excluding some wheels or fans (related definitions are given in Section 2).

Table 2 describes our approximation results that extend the results in Fertin et al. (2009) in several ways; it also illustrates the potential of our approach. For instance, an analysis of the degree of the conflict graph, generalizing the one in Fertin et al. (2009), immediately leads to an approximation ratio for the general case with a ratio $o(\Delta_1 + \Delta_2)$ when m_1, m_2 are constant; it is improved to $o(\Delta_1)$ if $m_2 = 1$ and m_1 is constant. For the case $m_2 = 1$ and m_1 constant, we propose as well a $O\left(\frac{|V_1|}{\log(|V_1|)}\right)$-approximation as well as a $O(\sqrt{\beta(I)})$-approximation, where $\beta(I)$ is the optimal value of instance I. To our knowledge such kinds of ratios are totally new for this problem. Finally, one of our structural results gives a $(min(\Delta_1, \Delta_2) + 1)$ approximation if $m_2 = 1$, improving also the previous known ratios.

Table 3 presents two fixed parameter tractability results with respect to the size of the output. Both extend the results of Fertin et al. (2009) to more general cases and both are direct consequences of structural results and known maximum independent set results.

Finally, a last illustration of the potential of the maximum independent set approach is the case where $m_2 = 1$ and G_1 is acyclic. This case was already shown polynomial in Abaka et al. (2013), using a specific dynamic programming method. A structural analysis of the conflict graphs allows to prove the same result and to interpret it as a maximum stable set polynomial case. Moreover it allows us to derive an explicit expression of the related complexity. Table 4 sums-up all known complexity results for the maximum constrained alignment problem. Despite being obtained for $\text{MAX}(\mu_{G_1}, \mu_{G_2})$ the hardness results also apply to the constrained alignment problem as noticed at the end of Section 2.

The paper is organized as follows. Section 2 gives the main definitions, introduces the conflict graph and investigates its first characteristics (size and degree), leading to first approximation and fixed parameter tractability results. Section 3 is dedicated to the case $m_2 = 1$ that raised the main attention in the literature. We first investigate in Subsection 3.1 some structural properties of the conflict graph in terms of forbidden subgraphs (wheels and fans and cliques and claws) with their algorithmic consequences. This part constitutes our main contribution. Then, in Subsection 3.2, we revisit the case where $m_2 = 1$ and G_1 is acyclic. Finally Section 4 discusses further research directions.

m_2	≥ 2	$m_2 = 1$		
m_1	≥ 3			$m_1 = 2$
G_1 and G_2		G_1 acyclic		
Structural property of $\mathcal{C}$	$\lvert V_{\mathcal{C}}\rvert \leq \min\limits_{i=1,2}(m_i^2 \lvert E_i\rvert)$ (Lem. 4)	Weakly triangulated (Th. 34)	W_t-free, $t \geq 7$ (Th. 15)	W_t-free, $t \geq 5$ (Th. 15)
	$\Delta(\mathcal{C}) \leq \sum\limits_{i=1,2} 2\Delta_i m_i(m_i - 1)$ (Lem. 6)		F_8-free (Th. 19)	F_6-free (Th. 19)
			$K_{1+{m_1}^2}$-free (Th. 27)	
	Bound of $\lvert E_{\mathcal{C}}\rvert$ using the first Zagreb Index (Lem. 7)		$(2\Delta_{min} + 2)$-free (Th. 29)	

Tab. 1: Main structural Properties of $\mathcal{C}$.

m_2	≥ 2	$m_2 = 1$	
m_1	≥ 3		$m_1 = 2$
Approximation ratio	$O\left(\frac{(\Delta_1+\Delta_2)\log\log(\Delta_1+\Delta_2)}{\log(\Delta_1+\Delta_2)}\right)$ (m_i const., $i = 1, 2$ - Prop. 9)	$\frac{6\Delta_1}{5} + \text{cst}$ (Fertin et al. (2009))	
		$O\left(\frac{\Delta_1 \log\log(\Delta_1)}{\log(\Delta_1)}\right)$ (m_1 constant - Prop. 11)	
		$\sqrt{3\beta(I)/2}$ (Prop. 21)	$\sqrt{\beta(I)}$ (Prop. 21)
		$\forall K > 0, \left\lceil \frac{\lvert V_1\rvert}{K \log(\lvert V_1\rvert)} \right\rceil$ (m_1 constant - Th. 25)	
		$\Delta_{min} + 1$ (Prop. 30)	

Tab. 2: Main approximation results ($\beta(I)$ denotes the optimal value of instance I).

m_2	Bounded ≥ 2	$m_2 = 1$	
m_1	Bounded ≥ 3		
G_1 and G_2	Bounded degree		Any degree
Parameterized tractability	FTP (Prop. 10)	FTP (Fertin et al. (2009))	FTP (Prop. 28)

Tab. 3: FTP results parameterized by the size of the output

m_2	≥ 1		
m_1	≥ 2		
G_1 and G_2	Even bipartite		G_1 acyclic
	Any degree	Bounded degree	
Complexity	APX-hard	APX-complete	Polynomial
	(Fertin et al. (2009))		(Abaka et al. (2013) and Subs. 3.2)

Tab. 4: Complexity of the constrained alignment problem

2 Definitions and first remarks

2.1 *Main definitions and the considered problem*

For all graph-theoretical definitions not given here, the reader is referred to Golumbic (2004). A *matching* in a graph is a set of independent edges, i.e., pairwise non adjacent. The extremities of the edges in the matching are called *saturated*. For any $t \geq 2$, P_t denotes a path with t vertices (*t-path*), C_t denotes a cycle with t vertices (*t-cycle*) and K_t denotes a clique with t vertices (*t-clique*). A P_t or a C_t will be denoted as list of successive vertices like $x_1 x_2 \cdots x_t$. In the case of a t-path x_1 and x_t are the extremities while, in the case of a t-cycle, x_1 is any vertex and the order correspond to one of the two possible orientations of the cycle. Sometimes, when a confusion is possible, the t-cycle will be denoted $x_1 x_2 \cdots x_t x_1$ to distinguish it from a t-path. Denote the complement of G with $\overline{G}$. An *induced subgraph* of $G = (V, E)$ is a subgraph of G induced by a subset of vertices, $X \subset V$. It will be denoted by $G[X]$. Given a graph H, G will be called *H-free* if it does not have any induced subgraph isomorphic to H. A partial graph of $G = (V, E)$ is a graph $G' = (V, E')$ with $E' \subset E$ and a partial induced subgraph is a partial graph of an induced subgraph. For a vertex $v \in V$ we will denote by $N(v)$ its (open) neighborhood and by $N[v] = N(v) \cup \{v\}$ its close neighborhood. For any vertex v we will denote by $G_v = G[N[v]]$ the subgraph induced by v and its neighborhood. For a vertex $v \in V$, $d_G(v)$ is its degree in G. When no ambiguity may occur, we simply denote Δ instead of $\Delta(G) = \max_{v \in V}(d_G(v))$.

A graph is called *weakly triangulated* if it is C_t-free and $\overline{C_t}$-free, for $t \geq 5$.

For $t \geq 3$, a *wheel* W_t is a graph consisting of a t-cycle C_t with an additional vertex, called *center*, adjacent to all the vertices of the cycle C_t. A fan graph F_t consists of a path P_t with t vertices and a new vertex v that is adjacent to all the vertices of the path. As a consequence, a graph $G = (V, E)$ is W_t-free (resp. F_t-free) if and only if, for every vertex $v \in V$, G_v is C_t-free (resp. P_t-free).

An *independent set* is a set of pairwise non adjacent vertices, i.e., they induced a graph without any edge. Given a graph G, $\alpha(G)$ denotes its independent number, i.e., the maximum size of an independent set in G. Consider a graph class $\mathcal{G}$ and a polynomial algorithm determining, for every graph $G \in \mathcal{G}$ of a graph class, an independent set of size $\lambda(G)$, is said to guarantee the approximation ratio of $\rho(G)$, for a function $\rho \geq 1$, on $\mathcal{G}$ if:

$$\forall G \in \mathcal{G},\ \frac{\alpha(G)}{\lambda(G)} \leq \rho(G)$$

Polynomial approximation algorithms are defined similarly for other graph maximization problems. If an algorithm guarantees a ratio that belongs to the class of functions $O(f)$ (resp. $o(f)$), then we will simply say that the algorithm guarantees a ratio of $O(f)$ (resp. $o(f)$) or constitutes a $O(f)$- (resp. $o(f)$-)approximation. The reader is referred to Ausiello et al. (1999) for all concepts in approximation not defined here. Throughout the paper we only use natural logarithms, so $\log$ stands for $\log_e$.

Finally, in Subsection 2.3, we will use the *first Zagreb index* of a graph G; it is denoted $M_1(G)$. $M_1(G)$ is defined as the sum of squares of degrees of the vertices. It has been extensively studied, in particular for its interest in computational chemistry (see, e.g. Nikolić et al. (2003) for an introduction to this index).

The constrained alignment problem is formally defined as follows:

Input: $I = \prec G_1, G_2, S \succ$, where $G_1 = (V_1, E_1), G_2 = (V_2, E_2)$ are undirected graphs and $S = (V_1 \cup V_2, E_S)$ is a bipartite graph with parts V_1, V_2; I will be called an *instance*.

Output: A matching A of S, called legal alignment;

Objective: Maximize the number of conserved edges in G_1, or equivalently in G_2, i.e., the number of pairs $(ab, cd) \in E_1 \times E_2$, where $ad, bc \in A$ or $ac, bd \in A$.

For the ease of description, the edges of the bipartite graph S will be called *similarity edges*. A legal alignment is called *minimal* if the removal of any similarity edge in the alignment creates an alignment that conserves less edges. Any legal alignment includes at least one minimal alignment and consequently, an optimal minimal alignment is an optimal alignment. Therefore, we can restrict ourselves to minimal alignments.

We conclude this subsection with few remarks comparing the constrained alignment problem and relaqted problems introduced in Section 1. Note that the conserved edges of G_1 and G_2 as well as their extremities respectively induce isomorphic partial subgraphs of G_1 and G_2. So, if S is a complete bipartite graph, then the problem corresponds to finding two isomorphic partial subgraphs of G_1 and G_2 with a maximum number of edges, which is exactly the maximum common edge subgraph. However, in our case, the bipartite graph S constraints the possible isomorphisms since a vertex of V_1 (resp. V_2) can only be mapped to one of its neighbors in S. In an applied context, such constraints represent a priori knowledge about the system that makes only some matchings meaningful.

The only difference with the problem *MAX*(μ_{G_1}, μ_{G_2}), with $m_i = \mu_{G_i}, i = 1, 2$ (Fertin et al. (2009)), is that in this latter problem, the matching A is required to saturate all vertices in G_1, thus defining an injective (one-to-one) mapping from V_1 to V_2. Contrary to the problems considered in Fagnot et al. (2008); Fertin et al. (2009), our problem is symmetric in G_1, G_2. All our results can be equivalently formulated by swapping indexes 1 and 2. When we will assume that one of G_1, G_2 has a specific structure, in particular acyclic like in Subsection 3.2, we can assume without loss of generality that the condition holds for G_1. Roughly speaking, the problems considered in Fagnot et al. (2008); Fertin et al. (2009) correspond to detecting, in G_2 a specific structure as close as possible to the pattern represented by G_1. Our version however, aims to detect similar patterns in the two graphs. We believe that both versions make sense for the suggested applications.

With the constraint for the solution to define an injective mapping from V_1 to V_2, some instances of MAX(μ_{G_1}, μ_{G_2}) may have no feasible solution while every instance of the constrained alignment problem has at least one feasible solution. For this reason, Fertin et al. (2009) restrict their problem to the so called *trim instances* for which S has a matching saturating V_1, every vertex in V_2 has a degree at least 1 in S and there is no *bad edge* in G_1, i.e., an edge that cannot be conserved for any matching of S. The constrained alignment problem does not require the first assumption. Removing bad edges as well as isolated vertices in S can be performed in polynomial time and leads to an equivalent instance. So, we can assume that there is neither bad edge nor isolated vertex in S.

Note finally that any (m_1, m_2)-instance of the constrained alignment problem (with $m_2 > 0$) can be transformed into an instance of MAX($m_1 + 1, m_2$) with the same optimal value by adding to V_2 a set V_I of $|V_1|$ independent vertices and linking, in S, every vertex in V_1 to its copy in V_I. This transformation does not modify m_2. In addition, note that, with the restriction that S has no isolated vertex, the alignment problem with $m_2 = 1$ is equivalent to MAX($\mu_{G_1}, 1$) problem and if there is no bad edge, then all instances are trim instances for the latter problem. Indeed, if all vertices of V_1 have a degree at least 1 in S and if vertices in V_2 have the degree 1 S, then all maximal matchings of the graph S saturate V_1. As a consequence, all known results for MAX($\mu_{G_1}, 1$) also hold for the alignment problem with $m_2 = 1$.

2.2 Conflict graph

2.2.1 The notion of c_4s and their conflicting configurations

For the following, we will call c_4 some specific 4-cycles $abcd$, where $ab \in E_1$, $cd \in E_2$ and $ad, bc \in E_S$. These are partial induced C_4's of the graph $(V_1 \cup V_2, E_1 \cup E_2 \cup E_S)$, obtained as the union of G_1, G_2 and S, for the instance $\prec G_1, G_2, S \succ$. Throughout the paper, we adopt the following notations to avoid any confusion between the different graphs we will refer to. When referring to c_4s, we will use simple letters from a to w (without indexes) to denote vertices of $V_1 \cup V_2$. A c_4 is then denoted as a list of four vertices, where the two first ones are in V_1 and the two last are in V_2. Letters x, y, z (sometimes with indexes) will denote vertices of the conflict graph defined below.

We say that two c_4s *conflict*, if at least two of their similarity edges are adjacent but distinct (then, they cannot coexist in any matching of S). Let $efgh$ be a c_4 conflicting with the c_4 $abcd$, where $ef \in E_1$, $gh \in E_2$, and $eh, fg \in E_S$. In the case $m_2 = 1$, we can identify five generic configurations corresponding to the relative position of $efgh$ with respect to $abcd$. These possible configurations are shown in Figure 1; note that if $e, f \in \{a, b\}$ or $g, h \in \{cd\}$, then only the label in $\{a, b, c, d\}$ is represented. In $Conf_{1a}$, we have $a = f$, and the rest of the vertices are all distinct; in this case, we say that it is a $Conf_{1a}$ conflict. Analogously, in $Conf_{1b}$, we have $b = e$, and the rest of the vertices are all distinct. In $Conf_2$, we have $a = e, b = f$, and the rest of the vertices are all distinct. In $Conf_{3a}$, we have $a = e, b = f, c = g$, and the rest of the vertices d, h are distinct. Analogously, in $Conf_{3b}$, we have $a = e, b = f, d = h$, and the rest of the vertices c, g are distinct. So, the number in the name of the conflicting configuration represents the number of vertices the two c_4s have in common. Similar to $Conf_{1a}$ conflict, we will refer to $Conf_{1b}$, $Conf_2$, $Conf_{3a}$ or $Conf_{1b}$ conflicts.

For larger m_2, one can also observe all symmetric conflicting configurations obtained by exchanging V_1 and V_2 with similarity edges adjacent on V_2 vertices plus one configuration with two similarity edges adjacent on a V_1 vertex and two adjacent on a V_2 vertex.

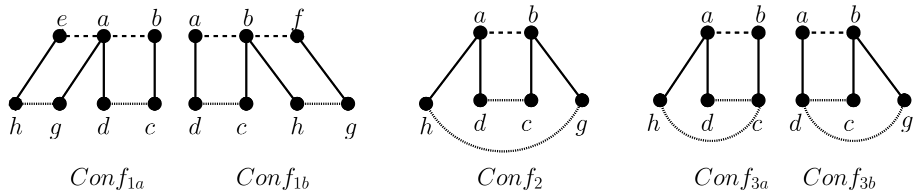


Fig. 1: Given two conflicting c_4s, $abcd$ and $efgh$, all possible conflicting configurations with respect to $abcd$, when $m_2 = 1$. For each configuration, the vertices at the top are V_1 vertices and the vertices at the bottom are V_2 vertices.

2.2.2 The conflict graph and its independent sets

With a given instance $\prec G_1, G_2, S \succ$, we associate a *conflict graph*, $\mathcal{C} = (V_\mathcal{C}, E_\mathcal{C})$, as follows. For each c_4, create a vertex in $V_\mathcal{C}$ and for each pair of conflicting c_4s, create an edge between their respective vertices in $E_\mathcal{C}$.

We will denote by γ the one-to-one correspondence mapping vertices of the conflict graph $\mathcal{C}$ to c_4s in $(V_1 \cup V_2, E_1 \cup E_2 \cup E_S)$. Thus, for any vertex $x \in V_\mathcal{C}$ of the conflict graph, $\gamma(x)$ is the corresponding c_4; for instance, if the related c_4 is $abcd$ with $a, b \in V_1, ab \in E_1$ and $c, d \in V_2, cd \in E_2$, we will write $\gamma(x) = abcd$. We call $\gamma(x)$ "the c_4 associated with x". In Theorem 19, we will need the notation $\gamma(x) \cap \{a, b\}$ to denote the set of vertices in $\{a, b\}$ and visited by the c_4 $\gamma(x)$.

With this construction of the conflict graph, the constrained alignment problem reduces to the maximum independent set problem as stated in the following proposition. This will be illustrated in the example detailed in Paragraph 2.2.4.

Proposition 1
(i) *There is a one-to-one correspondence (bijective mapping) between independent sets in the conflict graph and minimal alignments in the instance $\prec G_1, G_2, S \succ$. An independent set of p vertices maps to an alignment that conserves p edges.*
(ii) *A maximum independent set of $\mathcal{C}$ maps to to an optimal alignment for $\prec G_1, G_2, S \succ$.*
(iii) *The maximum possible number of conserved edges is $\alpha(\mathcal{C})$.*

Proof: **(i)** Let $\{x_1, \ldots, x_p\}$ be an independent set in the conflict graph $\mathcal{C}$; by definition of the conflict graph, the c_4s $\gamma(x_i), i = 1, \ldots, p$ are pairwise not conflicting in the graph $(V_1 \cup V_2, E_1 \cup E_2 \cup E_S)$ and consequently their similarity edges constitute a legal alignment A. An edge $ab \in E_1$ is conserved for this alignment if and only if there are two edges ad, bc in A and $cd \in E_2$; in this case $abcd = \gamma(x_i)$ for some $i \in \{1, \ldots, p\}$. Since two distinct non conflicting c_4s cannot share an edge of G_1 (neither of G_2), exactly p edges of G_1 are conserved by this alignment. This also implies that the alignment A is minimal.

Conversely, for any minimal legal alignment that conserves p edges of G_1, the conserved edges are in one-to-one correspondence with non-conflicting c_4s in the graph $(V_1 \cup V_2, E_1 \cup E_2 \cup E_S)$. Through γ^{-1}, these c_4s correspond to an independent set $\{x_1, \ldots, x_p\}$ in $\mathcal{C}$.

(ii) Since the one-to-one correspondence transforms an independent of cardinality p set into an alignment conserving p edges, a maximum independent set maps to an alignment maximising the number of conserved edges.

(iii) It follows immediately that the maximum possible number of conserved edges is $\alpha(\mathcal{C})$.

□

Corollary 2 *Any polynomial approximation algorithm for the maximum independent set in a graph G guaranteeing the ratio $\rho(\mathcal{G})$ can be turned into a polynomial approximation algorithm for the constrained alignment problem guaranteeing the ratio $\rho(\mathcal{C})$, where $\mathcal{C}$ is the conflict graph associated with the instance $\prec G_1, G_2, S \succ$.*

Proof: The conflict graph as well as the mapping γ can be computed in polynomial time with respect to the size $|V_1| + |V_2|$ of the instance $\prec G_1, G_2, S \succ$ since it only requires identifying all c_4s and testing the compatibility of every two c_4s. The conflict graph is of polynomial size (details about its size are given in Subsection 2.3) and it follows immediately from the proof of Proposition 1-(i) that, given an independent set of size p in $\mathcal{C}$, computing the corresponding minimal alignment that conserves p edges can be done in polynomial. We conclude by using the fact that the maximum possible number of conserved edges is $\alpha(\mathcal{C})$. □

Approximation ratios for the maximum independent set problem are usually expressed as functions of the number of vertices and/or maximum degree of the graph instance. To derive an approximation ratio for the constrained alignment expressed as a function of the instance $\prec G_1, G_2, S \succ$ will require evaluating the main parameters of the conflict graph. This is the purpose of the Subsection 2.3.

Remark 3 *Several minimal alignments (thus, several independent sets of the conflict graph) may correspond to the same set of conserved edges.*

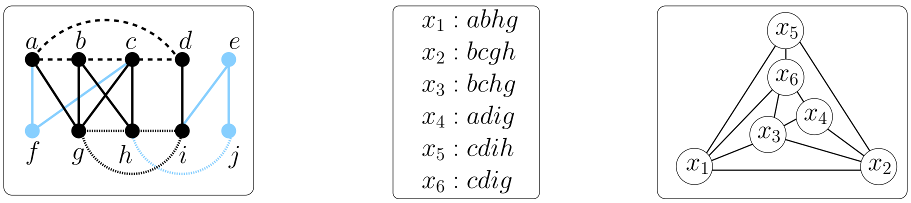
Consider for instance as the graph G_1 a path abc of length 2 and as the graph G_2 a path def. If similarity edges are ad, be, cf, af and cd, then, the two minimal alignments $\{ad, be, cf\}$ and $\{af, be, cd\}$ conserve the same edges ab and bc of G_1. We give in paragraph 2.2.4 another possible situation, where two different alignments correspond to the same conserved edges in G_1 but not in G_2.

2.2.3 The underlying graph

A direct consequence of Proposition 1 is that removing from the instance $\prec G_1, G_2, S \succ$ all G_1-edges, G_2-edges or similarity edges that do not belong to any c_4 does not change the problem in the sense that minimal alignments remain the same. For this reason, we consider the graph $\mathcal{C}_U = (V_U, E_U)$ obtained from the union of G_1, G_2, and S by excluding all the vertices and edges that are not part of any c_4s. In particular, this includes removing all bad edges (Fertin et al. (2009)) of G_1 and G_2. We call $\mathcal{C}_U$ the *underlying graph* associated with the instance $\prec G_1, G_2, S \succ$. It can be seen as a simplified equivalent instance and consequently, we can always assume that we work on $\mathcal{C}_U$ instead of $(V_1 \cup V_2, E_1 \cup E_2 \cup E_S)$ or, equivalently, that each edge in $E_1 \cup E_2 \cup E_S$ belongs to at least one c_4. In particular, in all our results, m_i can be seen as the maximum number of similarity edges in E_U incident to vertices of $V_i \cap V_U$.

2.2.4 An example

Figure 2 gives an example that illustrates the notions of conflict graph, of underlying graph, the function γ and the correspondence between minimal alignments in the original instance and independent sets in the conflict graph. The left chart represents the instance $I = \prec G_1, G_2, S \succ$ and the related underlying graph $\mathcal{C}_U$. G_1 is represented on the top, with vertices $V_1 = \{a, b, c, d, e\}$ and dashed edges and G_2 on the bottom with vertices $V_2 = \{f, g, h, i, j\}$ and dotted edges. Blue edges/vertices correspond to edges/vertices in $(V_1 \cup V_2, E_1 \cup E_2 \cup E_S)$ that are not part of the underlying graph. So, the underlying graph $\mathcal{C}_U$ appears



$< G_1, G_2, S >$ *and* $\mathcal{C}_U$ *List of* c_4s *Conflict graph* $\mathcal{C}$

Fig. 2: An instance $\prec G_1, G_2, S \succ$ with the underlying graph $\mathcal{C}_U$ and the conflict graph $\mathcal{C}$. $V_1 = \{a, b, c, d, e\}$ and $V_2 = \{f, g, h, i, j\}$. In the left graph, dashed lines correspond to edges in E_1 while dotted lines correspond to edges in E_2. Blue edges and vertices (left graph) are edges and vertices in $(V_1 \cup V_2, E_1 \cup E_2 \cup E_S)$ that are not part of the underlying graph and can be ignored. The list of c_4s also defines the function γ.

in black color. In the original instance $m_1 = 3$ but, in the equivalent simplified instance defined by $\mathcal{C}_U$, it becomes 2.

The list of c_4s and the related function γ are represented in the middle part of the figure. Note that $adcb$ or $bhcg$ are 4-cycles in $\mathcal{C}_U$ but not c_4s.

Finally, the related conflict graph is represented on the right hand side. This instance has four different optimal solutions corresponding to the minimal alignments $\{ag, bh, di\}$, $\{bh, cg, di\}$, $\{bg, ch, di\}$ and $\{ag, di, ch\}$. They correspond respectively to the independent sets $\{x_1, x_4\}$, $\{x_2, x_6\}$, $\{x_3, x_5\}$ and $\{x_4, x_5\}$ in the conflict graph. Each optimal solution corresponds to two conserved edges in E_1: $\{ab, ad\}$, $\{bc, cd\}$, $\{bc, cd\}$ and $\{ad, cd\}$, respectively. In this example, these conserved edges correspond to an induced P_3 in the graph G_1 but, in the graph G_2, the related conserved edges which are respectively $\{gh, gi\}$, $\{gh, hi\}$, $\{gh, gi\}$ and $\{gi, hi\}$, are not induced subgraphs of G_2 but only partial induced subgraphs. Note finally that the two alignments $\{bh, cg, di\}$ and $\{bg, ch, di\}$ correspond to the same conserved edges in G_1 but not in G_2. This is another illustration of Remark 3.

In what follows we provide several graph-theoretic properties of conflict graphs arising from possible constrained alignment instances under various restrictions. Such properties are then employed in applying relevant independent set results.

Throughout the paper we will assume $|V_1| \geq 2$ and $|V_2| \geq 2$ since, in the opposite case, the conflict graph is empty and the maximum alignment problem would be trivial (the only minimal alignment is empty). For a vertex $x \in V_i$ of G_i, $i = 1, 2$, we will denote by $d_i(x)$ its degree in G_i.

2.3 General properties of the conflict graph and applications

In this subsection we first investigate the first basic properties of the conflict graph and deduce first approximation results using some standard results on the maximum independent set problem. For an instance $\prec G_1, G_2, S \succ$, we denote by $\mathcal{C} = (V_\mathcal{C}, E_\mathcal{C})$ the related conflict graph.

Lemma 4 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, the number $|V_\mathcal{C}|$ of vertices of $\mathcal{C}$ satisfies:*

$$|V_\mathcal{C}| \leq \min\left({m_1}^2|E_1|, {m_2}^2|E_2|, \tfrac{1}{2}m_1m_2|V_1|\Delta_2, \tfrac{1}{2}m_1m_2|V_2|\Delta_1\right).$$

Proof: Consider a similarity edge $xy \in E_S$, $x \in V_1, y \in V_2$. The edge xy can belong to at most $\min(m_1 d_1(x), m_2 d_2(y))$ different c_4s. Consequently the number of possible c_4s satisfies:

$$|V_{\mathcal{C}}| \leq \frac{1}{2} \sum_{xy \in E_S} \min(m_1 d_1(x), m_2 d_2(y)).$$

Since x has at most m_1 incident edges in S and $d_2(y) \leq \Delta_2$ we deduce:

$$|V_{\mathcal{C}}| \leq \frac{m_1}{2} \sum_{x \in V_1} \min(m_1 d_1(x), m_2 \Delta_2) \leq \min({m_1}^2 |E_1|, \frac{1}{2} m_2 m_1 |V_1| \Delta_2).$$

Similarly we have:

$$|V_{\mathcal{C}}| \leq \min(m_2 |E_2|, \frac{1}{2} m_2 m_1 |V_2| \Delta_1),$$

which concludes the proof. □

Given an independent set in $\mathcal{C}$, Proposition 1 states that all similarity edges involved in the related c_4s constitute a matching. Consequently,

the optimal value $\alpha(\mathcal{C})$ can be bounded using Lemma 4 with $m_1 = 1$ and $m_2 = 1$. This leads immediately to the following bound:

Corollary 5 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, the independence number of $\mathcal{C}$ satisfies:*

$$\alpha(\mathcal{C}) \leq \min\left(|E_1|, |E_2|, \tfrac{1}{2}|V_1|\Delta_2, \tfrac{1}{2}|V_2|\Delta_1\right).$$

The following lemma generalises the bound for degrees provided in Fertin et al. (2009) for the case where $m_2 = 1$.

Lemma 6 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, let $\gamma(x) = abcd$ be a c_4 corresponding to a vertex x in $\mathcal{C}$, then the degrees in $\mathcal{C}$ satisfy:*

(i) $d_{\mathcal{C}}(x) \leq m_1(m_1-1)(d_1(a)+d_1(b)) - (m_1-1)^2 + m_2(m_2-1)(d_2(c)+d_2(d)) - (m_2-1)^2$;

(ii) $\Delta(\mathcal{C}) \leq 2\Delta_1 {m_1}^2 + 2\Delta_2 {m_2}^2 - 2\Delta_1 m_1 - 2\Delta_2 m_2 - {m_1}^2 - {m_2}^2 + 2m_1 + 2m_2 - 2$.

Proof: **(i)** Denote the set of c_4s in $\mathcal{C}$ conflicting with $\gamma(x)$ with $S_1 \cup S_2$, where S_1 is the set of c_4s in conflict with $\gamma(x)$ that include ad or bc, and S_2 consists of all other c_4s conflicting with $\gamma(x)$. It is clear that, if a c_4 from S_1 shares the edge ad (bc) with $\gamma(x)$, it must also include either b (a) or c (d) in order to create a conflict with $\gamma(x)$. In any case, since the total number of valid similarity edges (edges that can create the conflict with $\gamma(x)$) incident to b and c (a and d) is bounded by $m_1 + m_2 - 2$, this implies that $|S_1|$ is upper-bounded by $2m_1 + 2m_2 - 4$. For the second set S_2, we first note that a pair of similarity edges can create only one c_4. This implies that any edge in G_1 different from ab can be part of at most ${m_1}^2 - m_1$ different c_4s in S_2 and any edge in G_2 different from cd can be part of at most ${m_2}^2 - m_2$ different c_4s in S_2. Since the number of G_1 edges incident to a or b, and different from ab is $d_1(a) + d_1(b) - 2$, and respectively the number of G_2 edges incident to c or d, and different from cd is at most $d_2(c) + d_2(d) - 2$, the number of c_4s in S_2 that do not include ab or cd is bounded by $(d_1(a)+d_1(b)-2)({m_1}^2 - m_1) + (d_2(c)+d_2(d)-2)({m_2}^2 - m_2)$. The edges ab and cd themselves can be part of at most $(m_1-1)^2$ and $(m_2-1)^2$ different c_4s in S_2 respectively, which concludes the proof of **(i)**. **(ii)** is immediately deduced since $d_1(a), d_1(b) \leq \Delta_1$ and $d_2(c), d_2(d) \leq \Delta_2$. □

When evaluating the number of edges of the conflict graph, the first Zagreb index of the graphs G_1 and G_2 appear naturally, as stated in the following lemma. Note that if $m_1 = 1$ (resp., $m_2 = 1$), then the bound only depends on G_2 (resp., G_1).

Lemma 7 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, the number $|E_{\mathcal{C}}|$ of edges of $\mathcal{C}$ is bounded by:*

$$|E_{\mathcal{C}}| \le \frac{1}{2}\left({m_1}^2(m_1-1)\left(m_1 M_1(G_1) - (m_1-1)|E_1|\right) + {m_2}^2(m_2-1)\left(m_2 M_1(G_2) - (m_2-1)|E_2|\right)\right).$$

Proof: We have $|E_{\mathcal{C}}| = \frac{1}{2}\sum_{x \in V_{\mathcal{C}}} d_{\mathcal{C}}(x)$. Using Lemma 6 and the fact that ab (resp., cd) participates to at most ${m_1}^2$ (resp., ${m_2}^2$) c_4s we get:

$$\begin{aligned} 2|E_{\mathcal{C}}| &\le {m_1}^2(m_1-1)\sum_{ab \in E_1}[m_1(d_1(a)+d_1(b)) - (m_1-1)] \\ &\quad + {m_2}^2(m_2-1)\sum_{cd \in E_2}[m_2(d_2(c)+d_2(b)) - (m_2-1)] \\ &\le m_1^3(m_1-1)\sum_{ab \in E_1}(d_1(a)+d_1(b)) - {m_1}^2(m_1-1)^2|E_1| \\ &\quad + m_2^3(m_2-1)\sum_{cd \in E_2}(d_2(c)+d_2(d)) - {m_2}^2(m_2-1)^2|E_2| \end{aligned} \tag{1}$$

We conclude by noting that $\sum_{ab \in E_1}(d_1(a)+d_1(b)) = M_1(G_1)$ and similarly for cd in the graph G_2. $\square$

If we want a bound for $|E_{\mathcal{C}}|$ only dependent on the degree, number of vertices and edges of G_1, G_2, then several upper bounds exist for the first Zagreb index. We mention here two of these bounds.

Theorem 8 *Given a connected graph $G = (V, E)$ with maximum degree Δ and minimum degree δ,*
(i) *(Liu and Liu (2009)) $M_1(G) \le \frac{|E|^2(\Delta+\delta)^2}{n\Delta\delta}$;*
(ii) *(Fath-Tabar (2011)) $M_1(G) \le 4\frac{|E|^2}{|V|} + \frac{|V|}{4}(\Delta-\delta)^2$.*

Note that the bound $M_1(G) \le 2\Delta|E|$ is trivial for all graph $G = (V, E)$ and with maximum degree Δ. This bound meets the two bounds in Theorem 8 for regular graphs. In Subsection 3.2, we will consider the class of acyclic graphs. For this class ($\delta = 1$ and $|E| \le |V|$), the bound **(i)** immediately gives $M_1(G) \le |E|\frac{(\Delta+1)^2}{\Delta} \le |E|(\Delta+3)$, thus twice better than the trivial bound. Note also that in the case where one of these graphs has much less edges, $|E_1| \in o(|E_2|)$ or $|E_2| \in o(|E_1|)$, then a direct application of Lemma 4, using $|E_{\mathcal{C}}| \le |V_{\mathcal{C}}|^2$, can give better bounds.

Lemma 7 and Theorem 8 will be used in Subsection 3.2. Below we provide direct consequences of Lemmas 4 and 6 leading to the design of polynomial-time approximation algorithms for the constrained alignment problem.

The best known approximation ratios guaranteed by polynomial algorithms for the maximum independent set problem are $O(\Delta \log\log\Delta / \log\Delta)$ (Halldórsson (2000)) and $O(n/\log^2 n)$ (Boppana and Halldórsson (1992)), where Δ and n denote respectively the maximum degree and the number of vertices of the input graph. Combining it with Lemmas 4 and 6 leads to the following approximation for the general setting.

Proposition 9
(i) *For any positive constant m_1, m_2, the constrained alignment problem can be approximated in polynomial time with an approximation ratio of $O((\Delta_1+\Delta_2)\log\log(\Delta_1+\Delta_2)/\log(\Delta_1+\Delta_2))$;*

(ii) *If only m_2 (resp. m_1) is constant, then the constrained alignment problem can be approximated in polynomial time with an approximation ratio of $O(|E_1|/\log^2|E_1|)$ (resp. $O(|E_2|/\log^2|E_2|)$).*

It is known that using bounded search techniques (Downey and Fellows (1999)), one can find an independent set of size k in a graph G in $O(n(\Delta(G)+1)^k)$ time, or return that no such subset exists. In Fertin et al. (2009), this result is used to show that the constrained alignment problem is fixed-parameter tractable for bounded degree graphs with $m_2 = 1$. Lemma 6 immediately provides a generalisation for the general setting.

Proposition 10 *Provided that G_1 and G_2 are bounded degree graphs, for any positive constants m_1, m_2, the constrained alignment problem is fixed-parameter tractable for parameter k and solvable in $O(min(|E_1|,|E_2|)(D+1)^k)$ time, where k is the number of final conserved edges and $D = O(\Delta_1+\Delta_2)$.*

In what follows we consider the case $m_2 = 1$ - which, to our knowledge, is the most studied case - and investigate specific properties of the conflict graph. This case, by itself already very hard, simplifies the possible conflicts and then perfectly illustrates the use of the conflict graph. As explained in the conclusion, the following results motivate the further study of conflict graphs and their independent sets for a more general set-up.

3 The case $m_2 = 1$

The case with $m_2 = 1$ is the main case considered in Fertin et al. (2009). We remind that, in this case, the possible conflicting configurations are listed in Figure 1. Some improved results deal with the particular case $m_1 = 2$. It is known that the problem is APX-hard even for the case where $m_1 = 2$ and both G_1, G_2 are bipartite (Fertin et al. (2009)).

3.1 Structure of $\mathcal{C}$ and approximation

In this subsection we present graph theoretic properties of conflict graphs in terms of forbidden subgraphs when $m_1 = 2$. In addition to providing valuable information regarding structural properties of conflict graphs, it has also algorithmic applications, mainly approximation results.

Note first that, if $m_2 = 1$, Lemma 6 states that the maximum degree of the conflict graph is at most $2({m_1}^2 - m_1)\Delta_1 + m_1(2 - m_1) - 1$ and consequently Proposition 9 can be immediately replaced by:

Proposition 11 *For $m_2 = 1$ and any positive constant m_1, the constrained alignment problem can be approximated in polynomial time with an approximation ratio of $O(\Delta_1 \log\log(\Delta_1)/\log(\Delta_1))$.*

This approximation ratio in $o(\Delta_1)$ improves the result of Fertin et al. (2009) - $2\lceil 3\Delta_1/5\rceil$ for even Δ_1 and $2\lceil(3\Delta_1 + 2)/5\rceil$ for odd Δ_1 - also obtained for $m_2 = 1$. We will give later another improvement in the case where Δ_2 is less than this ratio.

We first establish some properties of conflict graphs when $m_2 = 1$ - Facts 1 and 2, Lemmas 12 and 14 and Corollary 13 - that will be useful for the main structural and algorithmic results. Then, in paragraphs 3.1.1 and 3.1.2, we derive structural results and their algorithmic consequences.

Fact 1 *Any pair of conflicting c_4s in $\mathcal{C}_U$ must share at least one vertex from G_1.*

Fact 2 *Any pair of distinct c_4s in $\mathcal{C}_U$ sharing two vertices from G_1 has a conflict.*

Lemma 12 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, suppose $m_2 = 1$ and consider an induced subgraph H of $\mathcal{C}$ such that $\overline{H}$ is connected and H has an induced P_3. Then the c_4s in H cannot all share a vertex from G_1.*

Proof: Let $x_1x_2x_3$ be an induced P_3 in H and let $\gamma(x_1) = abcd$. Assume for the sake of contradiction that $a \in G_1$ is a vertex common to all the c_4s associated with vertices of H. For every two vertices y, z in H not linked by an edge, $\gamma(y)$ and $\gamma(z)$ must share the similarity edge including a to avoid any conflict. As a consequence and since $\overline{H}$ is connected, all the c_4s associated with vertices of H must share the edge ad. This implies that any conflict between any pair of these c_4s can only be either a $Conf_{3a}$ or a $Conf_{3b}$ conflict, which further implies that all the c_4s $\gamma(x_i), i = 1, 2, 3$ include b. By Fact 2 and since $x_1 \neq x_3$, this implies a conflict between $\gamma(x_1)$ and $\gamma(x_3)$, a contradiction. □

For instance, a P_4 or $P_3 + K_1$ - the independent union of a P_3 and an isolated vertex - clearly both satisfy the conditions on H: they both have an induced P_3 and moreover, $\overline{P_4}$ is a P_4 as well while $\overline{P_3 + K_1}$ is a triangle with a pendent vertex, both connected. So, we immediately deduce:

Corollary 13 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, if $m_2 = 1$, the four c_4s of an induced P_4 or an induced $P_3 + K_1$ of $\mathcal{C}$ cannot all share a vertex from G_1.*

The following lemma will be useful for studying the structure of $\mathcal{C}$.

Lemma 14 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, suppose $m_2 = 1$ and that we have in $\mathcal{C}$ an induced P_5 $x_1x_2x_3x_4x_5$ as well as two vertices y_1, y_2 not linked to $x_i, i = 2, 3, 4$ and an additional vertex x linked to the seven vertices y_1, y_2, x_1, x_2, x_3, x_4, x_5. Denote $\gamma(x) = abcd$. Then if $\gamma(y_1)$ does not include b, neither does $\gamma(y_2)$.*

Proof: Since $y_1, y_2, x_1, x_2, x_3, x_4, x_5$ are all linked to x, Fact 1 ensures the related c_4s include a or b. Assume for the sake of contradiction that $\gamma(y_1)$ does not include b while $\gamma(y_2)$ does. Since $\gamma(y_1)$ conflicts with $\gamma(x)$, we have $\gamma(y_1) = aklm$ with $k \in V_1 \setminus \{a, b\}$ and $m \neq d$. Let $\gamma(y_2) = bpqr$, $r \neq c$. Since $m_2 = 1$, m, d, c, r are all paire wise distinct.

As mentioned above $\gamma(x_j), j = 1, \ldots 5$ must include a or b. Since $\gamma(x_j), j = 2, 3, 4$ do not conflict with $\gamma(y_1)$ nor with $\gamma(y_2)$, if it includes a it must include the edge am and if it includes b it must include the edge br. Moreover, none of them can include both a and b. Indeed, in this case $\gamma(x_j) = abrm$ for some $j = 2, 3, 4$ and since any $\gamma(x_{j'})$, $j' \in \{2, 3, 4\} \setminus \{j\}$, can neither include an edge am', $m' \neq m$ nor br', $r' \neq r$, it cannot conflict with $\gamma(x_j)$, a contradiction.

On the other hand, since $\gamma(x_3)$ has a conflict with both $\gamma(x_2)$ and $\gamma(x_4)$ and since $\gamma(x_2)$ and $\gamma(x_4)$ are not conflicting, there must be two similarity edges uv, uv', $u \in V_1 \setminus \{a, b\}$, $v, v' \in V_2, v \neq v'$, where uv is an edge of $\gamma(x_3)$ and uv' is an edge of both $\gamma(x_2)$ and $\gamma(x_4)$. Since $\gamma(x_2) \neq \gamma(x_4)$, one of them includes the edge am and the other includes the edge br.

We consider below the possible cases that all lead to a contradiction.

Case-1: Suppose $\gamma(x_2) = auv'm$ and $\gamma(x_4) = buv'r$, thus $\gamma(x_3)$ is either $auvm$ or $buvr$.

Case-1.1: If $\gamma(x_3) = auvm$, then since $\gamma(x_1)$ conflicts with $\gamma(x_2)$ but not with $\gamma(x_3)$ it must include the edge uv but in this case it would conflict with $\gamma(x_4)$.

Case-1.2: Similarly if $\gamma(x_3) = buvr$, then since $\gamma(x_5)$ conflicts with $\gamma(x_4)$ but not with $\gamma(x_3)$ it must include the edge uv but in this case it would conflict with $\gamma(x_2)$.

Case-2: Suppose now $\gamma(x_2) = buv'r$ and $\gamma(x_4) = auv'm$, thus $\gamma(x_3)$ is either $auvm$ or $buvr$. In both cases we get the same contradiction as in Case-1 exchanging the roles of am and br. This concludes the proof. □

3.1.1 Wheels and Fans

Theorem 15 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$,*
(i) *If $m_2 = 1$, $\mathcal{C}$ is W_t-free, for $t \geq 7$;*
(ii) *If furthermore $m_1 = 2$, $\mathcal{C}$ is also W_5 and W_6-free.*

Proof: Assume for the sake of contradiction an induced W_t exists with $t \geq 5$ and let x be the center vertex with $\gamma(x) = abcd$. Let $x_1x_2 \ldots x_tx_1$ be the induced C_t of the wheel W_t in the conflict graph. By Fact 1 every $\gamma(x_i), 1 \leq i \leq t$ must include at least one of a or b. By Corollary 13 (the cycle C_t has an induced P_4), it is not possible for all of these c_4s to share a, nor can they all share b. This implies that there must exist a pair of conflicting c_4s, $\gamma(x_i), i = 1, \ldots, t$, such that their corresponding vertices in $\mathcal{C}$ are neighbors in C_t, one including a and the other including b and one of them does not contain both a and b. Without loss of generality, let the former be $\gamma(x_t) = aklm$ with $k \in V_1 \setminus \{a, b\}$ and the latter be $\gamma(x_{t-1}) = bpqr$.

(i) Assume first $t \geq 7$. Then apply Lemma 14 with $y_1 = x_t$ and $y_2 = x_{t-1}$ gives a contradiction.

(ii) Now we show directly that there is also a contradiction if $m_1 = 2$ and $t = 5, 6$.

We consider two cases $\gamma(x_{t-1}) = abrd$, and $\gamma(x_{t-1}) = bkl'r$, $l' \neq l$ ensuring the conflict between $\gamma(x_{t-1})$ and $\gamma(x_t)$. In both cases $r \neq c$ ensures the conflict between $\gamma(x_{t-1})$ and $\gamma(x)$.

Case-1: $\gamma(x_{t-1}) = abrd$. Since $\gamma(x_2), \gamma(x_1)$ have no conflict with $\gamma(x_{t-1})$ but with $\gamma(x)$, they both include br and not am. Moreover, since $\gamma(x_2)$ does not conflict $\gamma(x_t)$, it cannot include a and thus $\gamma(x_2) = buvr, u \neq a$. Since $\gamma(x_1)$ conflicts with both $\gamma(x_t)$ and $\gamma(x_2)$ we have $u = k$, $v = l$ and $\gamma(x_1) = bkl'r, l' \neq l, \gamma(x_2) = bklr$. Then, since $\gamma(x_3)$ conflicts with $\gamma(x_2)$ but not with $\gamma(x_1)$, it must include the edge kl'. To conflict with $\gamma(x)$ it should include am or br, a contradiction since $x_3 \neq x_t, x_3 \neq x_1$.

Case-2: $\gamma(x_{t-1}) = bkl'r, l' \neq l$.

Since $\gamma(x_1)$ conflicts with $\gamma(x_t)$ and with $\gamma(x)$ and since $x_1 \neq x_{t-1}$, $\gamma(x_1)$ cannot include br and thus includes am and $\gamma(x_1) = akl'm$.

$\gamma(x_{t-2})$ conflicts with $\gamma(x_{t-1})$ but not with $\gamma(x_t)$ and includes am or br. Since $x_{t-2} \neq x_t$ the only possibility is $\gamma(x_{t-2}) = bklr$. Then, $\gamma(x_2)$ conflicts with $\gamma(x_1)$ but not with $\gamma(x_t)$ and includes am or br; the two only candidates are $aklm$ and $bklm$, both impossible since $x_2 \neq x_t, x_2 \neq x_{t-2}$ (note that $t - 2 \geq 3$). It concludes the proof. □

Note that for $m_1 > 2$, it is still possible to have a W_5 and W_6 in a conflict graph as illustrated in Figure 3. Note also that W_4 and $w_3 = K_4$ can still exist in $\mathcal{C}$ even if $m_1 = 2$. Figure 4 gives a sample construction with a W_4 while Figure 6 gives an example with a K_4. It means that, in terms of induced wheels, Theorem 15 leaves no gap.

The following lemma gives an example how considering the different kind of conflicts, for $m_2 = 1$ and $m_1 = 2$, (see Figure 1) helps understanding the structure of the conflict graph.

Lemma 16 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, suppose $m_2 = 1$ and $m_1 = 2$ and consider a vertex x in $\mathcal{C}$ and the set S^1_x of c_4s that conflict $\gamma(x)$ with a $Conf_{1a}$ or $Conf_{1b}$ configuration. Then, $\mathcal{C}[S^1_x]$ is an independent collection of C_4s, P_3s, P_2s and isolated vertices.*

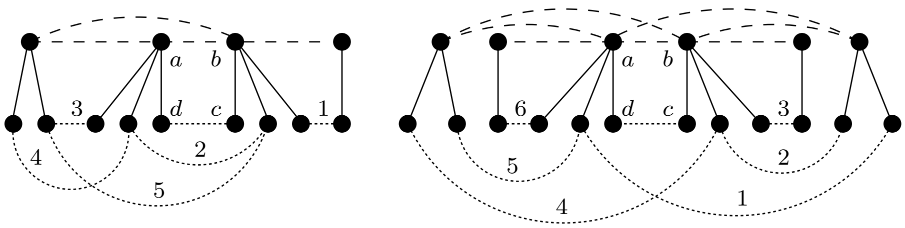


Fig. 3: Sample configurations for $\mathcal{C}_U$s inducing W_5 (left) and W_6 (right) in their respective conflict graphs for the case where $m_1 = 3$. The central vertices of the wheels in each case correspond to the c_4s indicated with $abcd$.

Proof: Since $m_1 = 2$, in $c_4 \in S_x^1$, at most two c_4s can conflict a fixed c_4 and consequently the graph $\mathcal{C}[S_x^1]$ has degree at most 2, which means it is an independent collection of cycles and paths. For any $t \geq 1$, consider a connected component of $\mathcal{C}[S_x^1]$ of size t.

Assume we have u_1, u_2, u_3 in $\mathcal{C}[S_x^1]$ with edges u_1u_2 and u_2u_3. Since $m_1 = 2$ $\gamma(u_1), \gamma(u_2)$ and $\gamma(u_3)$ cannot all include a and neither can they all include b. Suppose without loss of generality that two of them include a and one b and in this case, the structure of conflicts $Conf_{1a}$ and $Conf_{1b}$ imposes that $\gamma(u_2)$ includes a, say $\gamma(u_2) = aklm$ with $k, l, m \notin \{b, c, d\}$. Suppose then without loss of generality that $\gamma(u_1)$ includes a and $\gamma(u_3)$ includes b: $\gamma(u_1) = akl'm, l' \neq l$ and necessarily $\gamma(u_3) = brl'k$ to create a conflict with $\gamma(u_2)$. Moreover, since $m_2 = 1$, $r \notin \{c, d, m, l, l'\}$.

Note then that we cannot have any conflict between $\gamma(u_3)$ and $\gamma(u_1)$, which means that $\mathcal{C}[S_x^1]$ is triangle-free. Moreover suppose a fourth c_4, $\gamma(u_4)$ conflicting $\gamma(u_3)$ in $\mathcal{C}[S_x^1]$. It necessarily includes kl and thus conflicts $\gamma(u_1)$, which means that $\mathcal{C}[S_x^1]$ is P_4-free, which completes the proof. Figure 4 (Right) describes the structure of $\mathcal{C}[S_x^1]$, where N_t, $t = 1, 2, 3, 4$, is the union of components of $\mathcal{C}[S_x^1]$ of size t. $\square$

Corollary 17 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$, if $m_1 = 2$ and $m_2 = 1$, then for every $x \in V_{\mathcal{C}}$, removing at most two vertices to $\mathcal{C}_x$ makes it an independent collection of C_4s, P_3s, P_2s and isolated vertices.*

Proof: If $m_1 = 2$, at most one c_4 conflicts $\gamma(x)$ with a $Conf_{3a}$ configuration, and at most one with $Conf_{3b}$ configuration. Let us remove these vertices. There can be at most one c_4 conflicting $\gamma(x)$ with a $Conf_2$ configuration and moreover such a c_4 necessarily corresponds to an isolated vertex in $\mathcal{C}[S_x^1]$. Since all the other neighbors of x correspond to $Conf_{1a}$ or $Conf_{1b}$ configurations, Lemma 16 immediately concludes the proof. $\square$

Corollary 18 *If $m_1 = 2$ and $m_2 = 1$ we are ensured to find in polynomial time a legal alignment with at least $(\Delta(\mathcal{C}) - 2)/2$ conserved edges.*

Proof: It is an immediate consequence of Corollary 17 applied to a vertex x of maximum degree in $\mathcal{C}$.

An exhaustive search or just the detection of $Conf_{3a}$ and $Conf_{3b}$ configurations involving $\gamma(x)$ allows to identify the vertices to be removed to make $\mathcal{C}_x$ an independent collection of C_4s, P_3s, P_2s and isolated vertices. Picking in this collection an independent set of two vertices in each C_4s and P_3, one vertex in

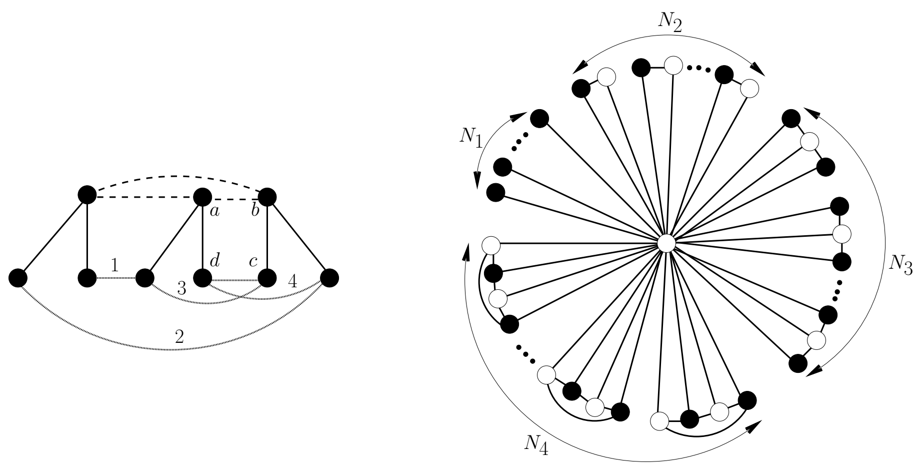


Fig. 4: **Left:** Sample construction for a W_4 in $\mathcal{C}$. The central vertex of the wheel corresponds to the c_4 $abcd$. The upper partition corresponds to vertices of G_1 and the lower partition to those of G_2. Similarity edges are drawn between the partitions. **Right:** Depiction of the construction defined in Lemma 16. The vertex x is shown in the center and vertices in S_x^1 are shown at the peripheral. N_t corresponds to all vertices in components of $\mathcal{C}[S_x^1]$ of size t. The black vertices constitute a maximum independent set of $\mathcal{C}[S_x^1]$.

each P_2 and all the isolated vertices gives a independent set of size at least $(\Delta(\mathcal{C}) - 2)/2$ in $\mathcal{C}$. Using Proposition 1 and the fact that the function γ can be computed in polynomial time (see Corollary 2) allows to conclude. $\square$

The following result concerns the existence of induced fans F_t in the conflict graph. Note that for $2 \le t \le t'$, F_t is an induced subgraph of $F_{t'}$ and consequently an F_t-free graph is also $F_{t'}$-free.

Theorem 19 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$ such that $m_2 = 1$, then:*
(i) *For $m_1 \ge 3$, $\mathcal{C}$ is F_8-free;*
(ii) *For $m_1 = 2$, $\mathcal{C}$ is F_6-free.*

Proof: Consider an induced F_t and let $\gamma(x) = abcd$ be the center vertex.

(i) Assume for the sake of contradiction that $t = 8$ and denote by $z_1 z_2 \cdots z_8$ be the induced P_8 in the neighborhood of x. By Fact 1 every c_4 $\gamma(z_i), i = 1, \dots, 8$ must include at least one of a or b in $\mathcal{C}_U$.

Suppose first $\gamma(z_1) \cap \{a, b\} = \gamma(z_8) \cap \{a, b\}$. Without loss of generality we assume they both include b and either both include a as well or none of them. Consider then the subgraph induced by z_1, z_2, z_3, z_8, inducing a $P_3 + K_1$. By Corollary 13, the c_4s $\gamma(z_1), \gamma(z_2), \gamma(z_3)$ and $\gamma(z_8)$ cannot all include b and let $i \in \{2, 3\}$ such that $\gamma(z_i)$ does not include b. Then, Lemma 14 with $y_1 = z_1$ and $y_2 = z_i$ and $z_4, \dots z_8$ corresponding to $x_1, \dots x_5$ leads to a contradiction.

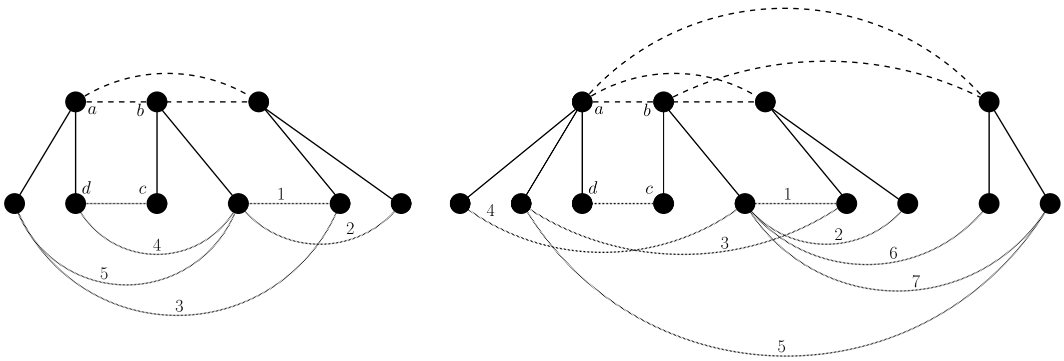


Fig. 5: **Left:** Sample configuration for $\mathcal{C}_U$ inducing F_5 for the case where $m_1 = 2$. **Right:** Sample configuration for $\mathcal{C}_U$ inducing F_7 for the case where $m_1 = 3$. In each case the central vertex corresponds to the c_4 indicated with $abcd$. Each G_2 edge is marked with the related c_4 in $P_5 = 12345$ (left) or $P_7 = 1234567$ (right).

Suppose now $\gamma(z_1) \cap \{a, b\} \neq \gamma(z_8) \cap \{a, b\}$, then one only includes b and we get a contradiction as well by applying Lemma 14 with $y_1 = z_1$ and $y_2 = z_8$ and $z_2, \ldots z_6$ corresponding to $x_1, \ldots x_5$, which concludes the proof of **(i)**.

(ii) Assume now $m_1 = 2$. Corollary 17 immediately shows that it is possible to remove at most two neighbors of x so that x cannot be the center of a F_4. It excludes the possibility of a F_6 in this case. □

Figure 5-Left shows an example of F_5 in a conflict graph with $m_1 = 2$ and $m_2 = 1$ and Figure 5-Right shows an F_7 in a conflict graph with $m_1 = 3$ and $m_2 = 1$.

Theorems 15 and 19 as well as Corollary 17 give us information about the structure of the subgraphs $\mathcal{C}_x$, $x \in V_{\mathcal{C}}$, induced by $N[x]$: as already mentioned a graph G is W_t-free (resp. F_t-free) if for all vertex x, G_x is C_t-free (resp. P_t-free), two classes of graphs that raised a lot of interest from researchers (see, eg., de Ridder et al. (2010); Brandstädt et al. (1999)).

We give now an example how to use the structure of neighborhoods to approximate the maximum independent set problem. It will give us algorithmic applications of Corollaries 17 and 13.

A very classical approximation algorithm for maximum independent set in a graph $G = (V, E)$ is the algorithm `2-opt` determining an independent set $\tilde{S}$ such that $\forall u \in \tilde{S}, \forall v, w \in V \setminus \tilde{S}, (\tilde{S} \setminus \{u\}) \cup \{v, w\}$ is not and independent set (there is no 2-improvement). Let us revisit the very usual analysis of `2-opt` (see, e.g., Demange and Paschos (2005)) which consists in considering the bipartite graph B induced by $\tilde{S} \cup S^*$, where S^* is an optimum independent set. Denote by $\lambda(G) = |\tilde{S}|$ the value of the solution provided by the algorithm on G and $\alpha(G) = |S^*|$ the independent number of G. Then the number of edges of B is at least $2\alpha(G) - \lambda(G)$ since 2-optimality ensures that, for every two edges $\tilde{v}u, \tilde{v}w$ in B incident to the same vertex $\tilde{v} \in \tilde{S}$, there is an additional edge incident to u or v. On the other hand this number is at most $\Delta_\alpha \lambda(G)$, where Δ_α is the minimum among all optimal independent sets S of the maximum number of vertices in S a vertex can be adjacent to:

$$\Delta_\alpha = \min_{\substack{|S| = \alpha(G) \\ S \text{ independent}}} \max_{v \in V} |N(v) \cap S|.$$

This implies:

$$\frac{\alpha(G)}{\lambda(G)} \leq \frac{(\Delta_\alpha + 1)}{2}. \tag{2}$$

This remark emphasises that the usual maximum degree can actually be replaced by Δ_α. We propose below a strategy that can be used where large independent sets can be found in polynomial time in the neighborhood of each vertex. It leads to a new kind of approximation ratios depending on the independence number.

Theorem 20 *Consider a class of graphs $\mathcal{G}$ for which there is a polynomial time algorithm A approximating the maximum independent set problem within the ratio ρ for every graph G_x, where $G = (V, E) \in \mathcal{G}$ and $x \in V$.*
Then the maximum independent set problem can be approximated within $\sqrt{3\rho(G)\alpha(G)/4}$.

Proof: The strategy, for an input graph $G = (V, E)$ in $\mathcal{G}$ is as follows:

> Apply A in all subgraphs $G_x, x \in V$;
> Compute also a `2-opt`-solution;
> Take the best solution among the $|V| + 1$ different solutions obtained.

Note first that, if $\alpha(G) \leq 2$, then `2-opt` finds an optimal solution, so we assume $\alpha(G) \geq 3$.

Suppose first that $\Delta_\alpha > \sqrt{4\rho(G)\alpha(G)/3}$. Then, when applied to a graph G_x such that $\alpha(G_x) = \Delta_\alpha$, the algorithm A computes a solution of value at least $\sqrt{4\alpha(G)/(3\rho(G))}$ leading to the approximation ratio $\sqrt{3\rho(G)\alpha(G)/4}$.

Suppose now $\Delta_\alpha \leq \sqrt{4\rho(G)\alpha(G)/3}$, then Relation (2) gives the ratio:

$$\frac{\sqrt{\frac{4}{3}\rho(G)\alpha(G)} + 1}{2} \leq \sqrt{\rho(G)\alpha(G)}\frac{\frac{2}{\sqrt{3}} + \frac{1}{\sqrt{3}}}{2} = \sqrt{\rho(G)\alpha(G)}\frac{\sqrt{3}}{2}$$

where the inequality uses $\rho(G)\alpha(G) \geq \alpha(G) \geq 3$. In all cases, the ratio is at most $\sqrt{3\rho(G)\alpha(G)/4}$, which concludes the proof. $\square$

Given an instance $I = \prec G_1, G_2, S \succ$, we denote by $\beta(I)$ the optimal value of the constrained alignment problem on I.

Proposition 21 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$ and $m_2 = 1$,*
***(i)** The constrained alignment problem can be approximated within $\sqrt{3\beta(I)/2}$;*
***(ii)** If furthermore $m_1 = 2$, this is improved to $\sqrt{\beta(I)}$.*

Proof:

This is a direct application of Theorem 20.

(i) Consider a vertex x in the conflict graph $\mathcal{C}$ and the graph $\mathcal{C}_x$. We denote $\gamma(x) = abcd$. Using Fact 1, the c_4s in the neighborhood of x in $\mathcal{C}$ can be partitioned into $N_{x,a}$ and $N_{x,b}$, where all c_4s in $N_{x,a}$ include a while the others include b but not a. This partition can be determined in polynomial time. Corollary 13 ensures that $\mathcal{C}[N_{x,a}]$ and $\mathcal{C}[N_{x,b}]$ are P_4-free. It is well known that the maximum independent set problem can be solved in linear time in P_4-free graphs (also called *cographs*) (see, e.g., Golumbic (2004)). Determining a maximum independent set in $\mathcal{C}[N_{x,a}]$ and $\mathcal{C}[N_{x,b}]$ and choosing the best one

clearly solves the maximum independent set problem in $\mathcal{C}_x$ within an approximation ratio of 2. We apply Theorem 20 with constant $\rho(G) = 2$.
(ii) If $m_1 = 2$, then Corollary 17 ensures that a maximum independent set can be found in polynomial time in graph $\mathcal{C}[N_x]$ and we apply Theorem 20 with constant $\rho(G) = 1$. □

Note that we obtain a ratio depending on the optimal value, which is not usual. Roughly speaking this result means that the logarithmic version of the problem - where the objective is to maximise the logarithm of the number of similarities in a legal alignment - is $\frac{3}{2}$-approximable. For instance, such a ratio for the maximum independent set in conflict graphs cannot be achieved in general graphs: the usual $n^{1-\varepsilon}$-hardness result (Håstad (1999)) states that, under some complexity hypothesis, the logarithm of the independence number cannot be approximated within a constant ratio.

Combining Proposition 21 with Corollary 5 leads to the following ratio:

Proposition 22 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$ and $m_2 = 1$,*
(i) *The constrained alignment problem can be approximated within the ratio:*
$$\min\left(\sqrt{3/2}\sqrt{|E_1|}, \sqrt{3/2}\sqrt{|E_2|}, (1/2)\sqrt{3|V_1|\Delta_2}, (1/2)\sqrt{3|V_2|\Delta_1}\right);$$
(ii) *If furthermore $m_1 = 2$, this ratio becomes:*
$$\min\left(\sqrt{|E_1|}, \sqrt{|E_2|}, \tfrac{\sqrt{2}}{2}\sqrt{|V_1|\Delta_2}, \tfrac{\sqrt{2}}{2}\sqrt{|V_2|\Delta_1}\right);$$

Proof: Using the definition of the approximation ratio guaranteed by an algorithm for a maximization problem, any upper bound of a guaranteed approximation ratio is still a guaranteed approximation ratio. Using Proposition 1-(iii), the optimal value $\beta(I)$ of the instance $I = \prec G_1, G_2, S \succ$ of the constrained alignment problem equals the independence number $\alpha(\mathcal{C})$ of the related conflict graph. By Corollary 5, we deduce
$$\beta(I) \leq \min\left(|E_1|, |E_2|, \frac{1}{2}|V_1|\Delta_2, \frac{1}{2}|V_2|\Delta_1\right).$$
Since the function $\sqrt{\cdot}$ is increasing, we conclude the proof using Proposition 21. □

Proposition 11 states the ratio $O(\Delta_1 \log\log(\Delta_1)/\log(\Delta_1))$ in the case $m_2 = 1$ and m_1 is constant. When $|E_1| \in o(|\Delta_1|^2)$ or $|E_2| \in o(|\Delta_1|^2)$, the ratio obtained in Proposition 22-(i) can be better than the ratios we achieved as functions of the maximum degree. In addition, Proposition 22-(i) does not require any assumption about m_1.

Given the known results for the maximum independent set, a natural question is whether the constrained alignment problem is $O(|V_1|/\log^2(|V_1|))$-approximable or even whether any approximation in $o(|V_1|\log\log(|V_1|)/\log(|V_1|)$ can be guaranteed. We give a first answer to this question in Theorem 25 below. The ratio $O(\sqrt{|E_1|})$ gives also a first answer for some classes of graphs satisfying $|E_1| \in o(|V_1|^2)$ (but Δ_1 still large). In particular, if G_1 is acyclic, we have $|E_1| \leq |V_1|$ and consequently:

Corollary 23 *Instances of the constrained alignment problem satisfying $m_2 = 1$ and G_1 acyclic can be approximated within the ratio $O(\sqrt{|V_1|})$.*

Let now $I = \prec G_1, G_2, S \succ$ be an instance of the constrained alignment problem with conflict graph $\mathcal{C}$ and $m_2 = 1$; suppose we are given a subset $F \subset V_1$ and a maximal matching M of $S[F \cup V_2]$, the subgraph of S corresponding to similarity edges incident to F. We denote by $V_{\mathcal{C},F,M}$ the set of c_4s in $V_{\mathcal{C}}$ including at least one vertex of F and no similarity edge uv with $u \in F, v \in V_2, uv \notin M$; in other words, these c_4s include vertices in F but only with similarity edges in M. Then, considering the subgraph $\mathcal{C}[V_{\mathcal{C},F,M}]$ of $\mathcal{C}$ induced by these c_4s, we have:

Lemma 24 *For any induced P_3, $x_1x_2x_3$, in $\mathcal{C}[V_{\mathcal{C},F,M}]$, x_1 and x_3 have the same neighborhood in $\mathcal{C}[V_{\mathcal{C},F,M}]$. In particular $\mathcal{C}[V_{\mathcal{C},F,M}]$ is P_4-free.*

Proof: Since $m_2 = 1$ and by definition of $V_{\mathcal{C},F,M}$, for every two conflicting c_4s in $V_{\mathcal{C},F,M}$, there must be a vertex $u \in V_1 \setminus F$ and two disjoint vertices $v, v' \in V_2$ such that uv is an edge of the former and uv' an edge of the latter; moreover the other similarity edges of these c_4s are in M. Suppose we are given an induce P_3, $x_1x_2x_3$, in $\mathcal{C}[V_{\mathcal{C},F,M}]$. There are such vertices u, v, v', where $\gamma(x_1)$ and $\gamma(x_3)$ both include the edge uv while $\gamma(x_2)$ includes uv'. Moreover, every c_4 in $V_{\mathcal{C},F,M}$ that conflicts with $\gamma(x_3)$ (resp. $\gamma(x_1)$) must include a similarity edge $uw, w \neq v$ and thus it conflicts with $\gamma(x_1)$ (resp. $\gamma(x_3)$), which concludes the proof. □

We deduce the following theorem that gives a first step towards non trivial $o(|V_1|)$ approximation ratios. It corresponds to a sequence of approximation algorithms parametrized by K, called *approximation chain* in Demange and Paschos (1997).

Theorem 25 *Consider instances of the constrained alignment problem satisfying $m_2 = 1$ and m_1 constant and let K be a positive constant. One can find in polynomial time a legal alignment guaranteeing the approximation ratio of $\left\lceil \frac{|V_1|}{K \log(|V_1|)} \right\rceil$.*

Proof: Consider an instance $I = \prec G_1, G_2, S \succ$ verifying the assumptions and denote by $\mathcal{C}$ the related conflict graph. We recall that $|V_1| \geq 2$. Denote by $\beta(I) = \alpha(\mathcal{C})$ the optimal value for the instance I. Let S^* be a maximum independent set of $\mathcal{C}$, $|S^*| = \alpha(\mathcal{C})$. Our strategy is to subdivide the vertex set of the conflict graph, $V_{\mathcal{C}}$, into $O\left(\frac{|V_1|}{\log(|V_1|)}\right)$ subsets such that the maximum independent set can be solved in polynomial time on the subgraph induced by each part. This subdivision is not necessarily a partition.

Fix a constant K and partition vertices of V_1 into $B_K = \left\lceil \frac{|V_1|}{K \log(|V_1|)} \right\rceil$ sets of vertices $F_j, j = 1, \dots B_K$ with $|F_j| \leq K \log(|V_1|)$. For each of them we denote by U_j the set of all c_4s in $V_{\mathcal{C}}$ including at least one vertex of F_j and by W_j the graph $W_j = \mathcal{C}[U_j]$. Note that:

$$\bigcup_{j=1,\dots,B_K} U_j = V_{\mathcal{C}} \tag{3}$$

We claim that there is a polynomial-time algorithm that computes, for every $j = 1, \dots, B_K$, a maximum independent set of W_j. Note first that the similarity edges involved in c_4s contributing to any independent set of W_j form a matching of the graph $S[F_j \cup V_2]$ and consequently, is part of a maximal matching of this graph. Denoting by $\mathcal{M}_j$ the set of maximal matchings of $S[F_j \cup V_2]$, we deduce:

$$\alpha(W_j) = \max_{M \in \mathcal{M}_j} \alpha(\mathcal{C}[V_{\mathcal{C},F_j,M}]) \tag{4}$$

Lemma 24 ensures that, for any fixed maximal matching $M \in \mathcal{M}_j$, $\mathcal{C}[V_{\mathcal{C},F_j,M}]$ is P_4-free. In this case a maximum independent set can be computed in polynomial (linear) time (Golumbic (2004)). The related complexity is $O(|V_{\mathcal{C},F_j,M}|) \leq O(m_1|F_j||V_1|)$ since c_4s in $V_{\mathcal{C},F_j,M}$ include at least one edge of

M and $|M| \leq |F_j|$. But m_1 is a fixed constant and $|F_j| \leq K\log(|V_1|)$. Thus, we can exhaustively list all maximal matchings of $S[F_j \cup V_2]$ in $O\left(m_1^{K\log(|V_1|)}\right) = O\left(|V_1|^{K\log(m_1)}\right)$, a polynomial function.

Our algorithm runs as follows:

> *For all $j = 1, \ldots, B_K$ and all maximal matching M of $S[F_j \cup V_2]$, compute $\mathcal{C}[V_{\mathcal{C},F_j,M}]$ and a maximum independent set - keep the best such solution.*

Computing each $\mathcal{C}[V_{\mathcal{C},F_j,M}]$ and a maximum independent set takes, for bounded m_1, $O\left(|V_1|\log(|V_1|)\right)$; the whole complexity is then $O\left(\log(|V_1|)|V_1|^{1+K\log(m_1)}\right)$, a polynomial function.

To complete the proof we need to justify it guarantees the required ratio. Equation (3) ensures that the value $\lambda(I)$ of the computed solution satisfies:

$$\lambda(I) = \max_{j=1,\ldots,B_K} \alpha(W_j) \geq \max_{j=1,\ldots,B_K} |S^* \cap U_j| \geq \frac{\beta(I)}{B_K}$$

which shows that the related approximation ratio is $B_k = \left\lceil \frac{|V_1|}{K\log(|V_1|)} \right\rceil$. □

3.1.2 Cliques and Claws

Next we present results regarding the existence of cliques as subgraphs of conflict graphs for any m_1. Assume that there is a clique K_t, $t \geq 1$, in $\mathcal{C}$ and let a corresponding c_4 associated with a vertex x from this K_t be $\gamma(x) = abcd$. We partition all the corresponding c_4s in K_t into three disjoint reference sets with respect to $\gamma(x)$. Let S_1, S_2 consist of all the c_4s respectively conflicting $\gamma(x)$ with a $Conf_{1a}$ and $Conf_{1b}$ configuration. Let S_3 be the set of all c_4s with other kinds of conflicts ($Conf_2$, $Conf_{3a}$ or $Conf_{3b}$) with $\gamma(x)$ and $\gamma(x)$ itself.

Lemma 26 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$ and the reference sets defined as above, then any pair of c_4s from different reference sets do not share a similarity edge.*

Proof: Note that since the pair of c_4s correspond, in $\mathcal{C}$, to different vertices of the same clique K_t, they should conflict by sharing at least one vertex from G_1. We consider two cases. For the first case assume one of the c_4s is in S_1 or S_2, and the other is in S_3. Without loss of generality assume the former c_4 is in S_1 including vertices s and a from G_1, where $s \neq b$. Since the latter c_4 from S_3 includes both a, b from G_1, the pair of c_4s can only share the vertex a from G_1 giving rise to a $Conf_{1a}$ or a $Conf_{1b}$ conflict between them. For the second case assume one of the c_4s is in S_1 and the other is in S_2. In this case the former must have a $Conf_{1a}$ conflict whereas the latter must have a $Conf_{1b}$ conflict with the reference $\gamma(x) = abcd$. Since $a \neq b$ the c_4s from S_1 and S_2 can only share one vertex from G_1, thus giving rise to a $Conf_{1a}$ or a $Conf_{1b}$ conflict between the pair. In both cases we show that both c_4s are in $Conf_{1a}$ or $Conf_{1b}$ conflict with each other. The fact that any pair of c_4s with a $Conf_{1a}$ or a $Conf_{1b}$ conflict do not share a similarity edge completes the proof. □

Theorem 27 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$ and $m_2 = 1$, the maximum size of any clique in $\mathcal{C}$ is ${m_1}^2$, or equivalently $\mathcal{C}$ is $K_{1+{m_1}^2}$-free.*

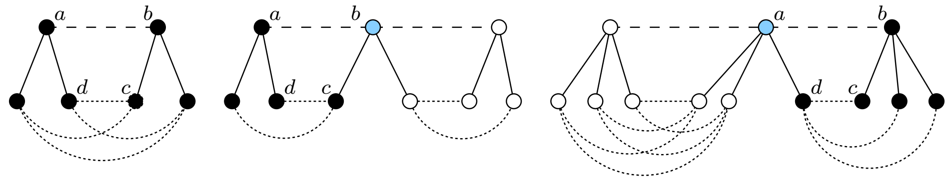


Fig. 6: Sample $\mathcal{C}_U$s giving rise to $K_{m_1{}^2}$s in their respective conflict graphs. The reference c_4 is $\gamma(x) = abcd$. The first two show sample constructions for $m_1 = 2$ and the last for $m_1 = 3$. The employed reference sets as described in the proof of Theorem 27 are as follows: *(Left)* All c_4s are in S_3, *(Middle)* c_4s in S_3 are those induced by black vertices and b, c_4s in S_2 are those induced by white vertices and b, *(Right)* c_4s in S_3 are those induced by black vertices and a, c_4s in S_1 are those induced by white vertices and a.

Proof: We consider two cases.

Case-1: We first handle the case where at least one of S_1, S_2 is empty. Assume without loss of generality S_1 is empty. Let p be the number of similarity edges incident to b in the c_4s of S_3. Since each pair of similarity edges, one incident to a and one incident to b, gives rise to at most one c_4, the number of c_4s in S_3 is at most $m_1 p$. By Lemma 26, c_4s in S_3 cannot share an edge from S with the c_4s in S_2. This implies that the number of similarity edges incident to b in the c_4s of S_2 is at most $m_1 - p$. Let bc' be such an edge and let $S_{bc'}$ denote the set of c_4s in S_2 sharing bc'. Since any pair of c_4s from $S_{bc'}$ share a similarity edge, they must be in a $Conf_{3a}$ or $Conf_{3b}$ conflict with each other and thus must share one more vertex from G_1 in addition to the vertex b. This implies that $|S_{bc'}| \leq m_1$ which further implies a total of at most $(m_1 - p)m_1$ c_4s in S_2. The clique consisting of c_4s from S_2, S_3 has at most $m_1{}^2$ vertices.

Case-2: Now we handle the case where S_1 and S_2 are both not empty. It must be the case that all c_4s in $S_1 \cup S_2$ must share a vertex e from G_1 such that $e \neq a$, $e \neq b$. This is due to the fact that any pair of c_4s, one from S_1 the other from S_2, can only have a $Conf_{1a}$ or $Conf_{1b}$ conflict and the shared node in this conflict cannot be neither a nor b. Let p, q be the number of edges from S incident respectively to a and b in the c_4s of S_3.

The number of c_4s in S_3 is at most pq. By Lemma 26, the number of similarity edges edges incident to a in the c_4s of S_1 are at most $m_1 - p$ and the number of similarity edges incident to b in the c_4s of S_2 are at most $m_1 - q$. Let r be the number of similarity edges incident to e in the c_4s of S_1. Again by Lemma 26, the number of similarity incident to e in the c_4s of S_2 are at most $m_1 - r$. This implies that the maximum number of c_4s in S_1 and S_2 are respectively $(m_1 - p)r$ and $(m_1 - q)(m_1 - r)$. The size of the clique consisting of c_4s from all three reference sets is at most $pq + (m_1 - p)r + (m_1 - q)(m_1 - r)$, where $1 \leq p, q, r \leq m_1$. Without loss of generality let $p \leq q$. Then we have $pq + (m_1 - p)r + (m_1 - q)(m_1 - r) \leq pq + (m_1 - p)m_1 \leq m_1{}^2$. $\square$

We note that $K_{m_1{}^2}$ is possible in a conflict graph $\mathcal{C}$ for any positive integer m_1. Indeed *Case-1* of the above proof provides an actual construction method; see Figure 6.

Note that under the setting of $m_2 = 1$, the size of $V_{\mathcal{C}}$ is bounded by $|E_2|$ (Lemma 4). It is known that the maximum independent set problem is fixed-parameter tractable, parameterized by the size of the output, in the class of K_r-free graphs for constant integer r (Raman and Saurabh (2006); Dabrowski et al. (2012)). Combining this result with Theorem 27, leads to the following result:

Proposition 28 *The constrained alignment problem is fixed-parameter tractable when m_1 is any fixed positive integer constant and $m_2 = 1$.*

Note that the analogous result in Fertin et al. (2009) is more restrictive since it applies only to the bounded degree graphs.

We conclude this part by considering induced claws in conflict graphs. A *d-claw* is an induced subgraph of an undirected graph, that consists of an independent set of d vertices, called $talons$, and the $center$ vertex that is adjacent to all vertices in this set. Let $\Delta_{min} = min(\Delta_1, \Delta_2)$.

Theorem 29 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$ and $m_2 = 1$, then $\mathcal{C}$ is $(2\Delta_{min} + 2)$-claw-free.*

Proof: Let $abcd$ be the corresponding c_4 associated with the center vertex of a claw. Let $abkl$ be the c_4 corresponding to a talon that has a $Conf_2$, $Conf_{3a}$ or $Conf_{3b}$ conflict with $abcd$. Since any other c_4 corresponding to a talon with a $Conf_2$, $Conf_{3a}$ or $Conf_{3b}$ conflict with $abcd$ would also have to share the vertices a, b, by Fact 2, it would conflict with $abkl$, which is not possible. Thus, the total number of talons the c_4s of which create a $Conf_2$, $Conf_{3a}$ or $Conf_{3b}$ conflict with $abcd$ is at most 1. With regards to the number of talons corresponding, in $\mathcal{C}_U$, to a $Conf_{1a}$ or $Conf_{1b}$ conflict with $abcd$, we first count the maximum number of possible $Conf_{1a}$ conflicts. Let $apqr$ be the c_4 of a talon with a $Conf_{1a}$ conflict with $abcd$. Any talon the c_4 of which conflicts with $abcd$ through a $Conf_{1a}$ conflicting configuration must share the edge ar, since otherwise it would conflict with $apqr$. Any G_1 edge incident to vertex a can belong only to a single c_4 since otherwise by Fact 2 there would be a conflict between a pair of c_4s corresponding to talons. In addition, since $m_2 = 1$, every G_2 edge can belong only to a single c_4. Thus the number of talons inducing in $\mathcal{C}$ $Conf_{1a}$ conflicts is bounded by Δ_{min}. The same holds for $Conf_{1b}$ conflicts giving rise to at most $(2\Delta_{min} + 1)$ talons that are independent. □

The above theorem in conjunction with the result of Berman (2000) which states that a $d/2$ approximation for maximum independent sets can be found in polynomial-time for d-claw free graphs gives rise to a polynomial-time approximation for the constrained alignment problem.

Proposition 30 *If $m_2 = 1$, the constrained alignment problem can be $(\Delta_{min} + 1)$-approximated in polynomial time.*

This results improves (by at least a factor $5/6$) the approximation ratio of $2\lceil 3\Delta_1/5\rceil$ for even Δ_1 and $2\lceil (3\Delta_1 + 2)/5\rceil$ for odd Δ_1 proposed in (Fertin et al. (2009)). As already mentioned, the $o(\Delta_1)$-approximation stated in Proposition 11 already improved it. If $\Delta_2 \in O(\Delta_1)$, then the ratio in Proposition 11 is better but if $\Delta_2 \in o(\Delta_1)$, then the ratio established in Proposition 30 can be better than the one in Proposition 11.

We conclude Subsection 3.1 by emphasizing that some of our structural results lead to a new hardness result for the maximum independent set problem. Indeed, the combination of Lemma 6, Theorem 15, Theorem 19 and Theorem 19 states that, for any instance of the constrained alignment problem with $m_1 = 2, m_2 = 1$ and G_1, G_2 are of bounded degree, the related conflict graph is $(W_t\ (t \geq 5), F_6, K_5)$-free and of bounded degree.

On the other hand, the constrained alignment problem is shown to be APX-complete even for the case where $m_2 = 1, m_1 = 2$, both G_1, G_2 are bipartite and of bounded degree (Fertin et al. (2009)). As a consequence, we derive the following new hardness result for the maximum independent set problem:

Proposition 31 *The maximum independent set problem is APX-complete in the class of bounded degree, $(W_t\ (t \geq 5), F_6, K_5)$-free graphs.*

3.2 Acyclic G_1 and $m_2 = 1$

We conclude by investigating the case where G_1 is acyclic and $m_2 = 1$ for which the constrained alignment problem is shown to be polynomial-time solvable in Abaka et al. (2013) without a precise complexity analysis. We refine this previous analysis by showing that in this case the conflict graph has a very particular structure. More precisely it is *weakly triangulated* (C_t-free and $\overline{C_t}$-free, for $t \geq 5$). Weakly triangulated graphs are known to be perfect (Hayward (1985)) and moreover the maximum independent set problem can be solved in $O(|V||E|)$ in a graph $G = (V, E)$ (Hayward et al. (2007)). It allows us to deduce a new polynomial-time algorithm for this case with its complexity analysis. This illustrates again how the structure of the conflict graph can be used to achieve algorithmic results.

We need two technical lemmas; remind that, given an instance $\prec G_1, G_2, S \succ$ the graph $\mathcal{C}_U$ is defined in Subsection 2.2.

Lemma 32 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$ where G_1 is acyclic. Suppose a P_k, denoted by p, is an induced subgraph of the conflict graph $\mathcal{C}$. For $k \geq 4$, the c_4s of $\mathcal{C}_U$ corresponding to the end vertices of p neither share a vertex nor an edge in $\mathcal{C}_U$.*

Proof: Suppose first that p_k is an induced P_k, $k \geq 4$ in the conflict graph and consider the two c_4s in $\mathcal{C}_U$ associated with the extremities of p_k. They can neither share an edge from G_2 nor a vertex from G_2 without sharing a similarity edge incident to it ($m_2 = 1$). They also cannot share an edge from G_1 nor a vertex from G_1 without sharing a similarity edge incident to it since otherwise they would conflict. Thus we simply need to show that they do not share a similarity edge.

The proof is by strong induction on k. For the base case $k = 4$, suppose there is a P_4 $x_1x_2x_3x_4$ in the conflict graph and that the c_4s $\gamma(x_1)$ and $\gamma(x_4)$ share a similarity edge. Let $\gamma(x_1) = abcd$ and let $\gamma(x_4) = befc$ with the edge $bc \in S$ in common. There are two cases for $\gamma(x_2)$. Since it does not conflict with $\gamma(x_4)$, it must either be of the form $gahi$, where $h, i \notin \{d, c, f\}$ ($Conf_{1a}$ conflict with $\gamma(x_1)$) or of the form $abch$ where $h \notin \{d, c, f\}$ ($Conf_{3a}$ conflict with $\gamma(x_1)$). Now considering $\gamma(x_3)$, to create a conflict with $\gamma(x_4)$, one edge of $\gamma(x_3)$ must be ej where $j \notin \{d, c, f, h, i\}$. Placing the other edge of $\gamma(x_3)$ from E_S such that it creates a conflict with $\gamma(x_2)$ is now impossible, since it either gives rise to a cycle in G_1 (cycle abe or $abeg$, $g \notin \{a, b, e\}$) or creates a conflict with $\gamma(x_1)$.

For the inductive part, assume that the lemma holds for all k' where $4 \leq k' < k$. Consider the c_4s of $\mathcal{C}_U$ corresponding to the vertices of a P_k, $x_1 \cdot x_{k-1}x_k$ in the conflict graph. Let $\gamma(x_1) = abcd$ and $\gamma(x_{k-1}) = efgh$. By the inductive hypothesis, these two c_4s are disjoint. Consider in $\mathcal{C}_U$ the subset H of edges from E_1 that belong to the c_4s associated with vertices in the P_{k-1}, $x_1 \cdots x_{k-1}$. H contains in particular ab and ef. Edges in H form a connected subgraph of G_1 and without loss of generality we assume that the shortest path between b and e contains neither a nor f. This path has at least one edge; let its last edge be $e'e \in G_1$ which is part of $\gamma(x_j)$ for some j, $1 \leq j \leq (k-2)$. Let $\gamma(x_j) = e'exy$ and $\gamma(x_k) = pqrs$. If at least one of p, q is on the path, say p, and $p \neq e'$, $p \neq e$, then q must be one of e or f, since $pqrs$ must conflict with $efgh$, which implies a cycle in G_1. If $p = e'$ then $q = e$ to create a conflict with $efgh$ without creating a cycle in G_1. This implies a conflict between $pqrs$ and $e'exy$, which is impossible since $x_1 \cdots x_k$ is an induced path. Finally, if $p = e$, $q \neq e'$, $abcd$ and $pqrs$ do not share a similarity edge, which concludes the proof. □

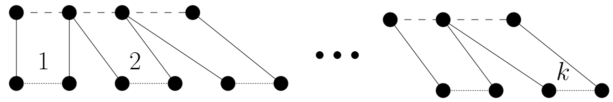


Fig. 7: Chain configuration of a k-path in $\mathcal{C}_U$.

The subgraph of $\mathcal{C}_U$ that corresponds to an induced P_k, $x_1 \cdots x_{k-1}x_k$ in the conflict graph $\mathcal{C}$ is said to be in *chain configuration* if each c_4, $\gamma(x_i)$, $i = 1, \ldots k$, shares only a distinct G_1-vertex with the next c_4, $\gamma(x_{i+1})$, if $i < k$ and one with the previous one, $\gamma(x_{i-1})$, if $i > 1$ and does not share any G_1- or G_2-vertices with any other of these c_4s; see Figure 7 for a sample chain configuration. Note that a chain configuration imposes a certain order of the involved c_4s in $\mathcal{C}$.

Lemma 33 *Let $\prec G_1, G_2, S \succ$ be an instance of the constrained alignment problem with conflict graph $\mathcal{C}$ and acyclic G_1. Let x_1, x_2, x_3 be three vertices of $\mathcal{C}$ such that $\gamma(x_1)$ and $\gamma(x_3)$ do not share a vertex nor an edge in $\mathcal{C}_U$ and $\gamma(x_2)$ conflicts with both $\gamma(x_1)$ and $\gamma(x_3)$. Then $\gamma(x_1), \gamma(x_2)$ and $\gamma(x_3)$ must be in chain configuration where $\gamma(x_2)$ is in the middle in any left to right order.*

Proof: If the conflict configuration of $\gamma(x_1)$ and $\gamma(x_2)$ were of $Conf_2, Conf_{3a}$ or $Conf_{3b}$, then $\gamma(x_3)$ could conflict with $\gamma(x_2)$ only if it shared a vertex in $\mathcal{C}_U$ (more specifically a vertex from G_1, since $m_2 = 1$) with $\gamma(x_1)$, which is not possible. It follows that the only possible conflict configuration for $\gamma(x_1)$ and $\gamma(x_2)$ is $Conf_{1a}$ or $Conf_{1b}$. Applying the same reasoning to the conflict between $\gamma(x_2)$ and $\gamma(x_3)$, it follows that all three must be in chain configuration, where $\gamma(x_2)$ is in the middle of the chain in any left to right order. $\square$

We are now ready to prove the main result of this subsection.

Theorem 34 *Given an instance $\prec G_1, G_2, S \succ$ with conflict graph $\mathcal{C}$ such that G_1 is acyclic and $m_2 = 1$ then $\mathcal{C}$ is weakly triangulated.*

Proof: Assume first for the sake of contradiction that C_k is an induced subgraph of a conflict graph for $k \geq 5$. The cycle $C_k = x_1 \cdots x_{k-1}x_kx_1$ can be divided into $(k-2)$ P_3s: $x_1x_2x_3$, $x_2x_3x_4$, …, $x_{k-2}x_{k-1}x_k$. We show that for each P_3s, $x_ix_{i+1}x_{i+2}$, $1 \leq i \leq k-2$, $\gamma(x_i), \gamma(x_{i+1}$ and $\gamma(x_{i+2})$ must be in chain configuration in $\mathcal{C}_U$. There exists indeed a $(k-1)$-path starting at vertex x_i and ending at vertex (x_{i+2}) as an induced subgraph of C_k, thus of $\mathcal{C}$ as well. Since $k \geq 5$, by Lemma 32, the c_4s $\gamma(x_i)$ and $\gamma(x_{i+2})$, neither share a vertex nor an edge in $\mathcal{C}_U$. By definition of C_k, they do not conflict. Since $\gamma(x_{i+1})$ conflicts with both $\gamma(x_i)$ and $\gamma(x_{i+2})$, by Lemma 33, all three must be in chain configuration, where $\gamma(x_{i+1})$ is in the middle of the configuration in any left to right order. Since each of the $k-2$ triples (x_1, x_2, x_3), (x_2, x_3, x_4), …, (x_{k-2}, x_{k-1}, x_k) is in chain configuration similarly, the c_4s corresponding to the whole path $x_1x_2 \cdots x_{k-1}x_k$, $\gamma(x_1), \gamma(x_2) \ldots \gamma(x_{k-1}\gamma(x_k)$ are in chain configuration in this order. This implies there cannot be a conflict between $\gamma(x_1)$ and $\gamma(x_k)$, since in the opposite case it would correspond to a cycle in graph G_1. This contradicts the fact vertices x_1 and x_k are adjacent in $\mathcal{C}$.

To prove that $\overline{C_k}$ is not an induced subgraph in any conflict graph, we first note that since $\overline{C_5}$ is isomorphic to C_5, $\overline{C_5}$ cannot be an induced subgraph of any conflict graph. For $k > 5$, we prove it by contradiction as well. Suppose $\overline{C_k}$, with $k > 5$ is an induced subgraph of $\mathcal{C}$. Consider the path $x_{k-1}x_1x_{k-2}x_k$. This is an induced 4-path in $\overline{C_k}$, thus also in $\mathcal{C}$. By Lemma 32, $\gamma(x_k)$ and $\gamma(x_{k-1})$ do not share any vertex and neither an edge in $\mathcal{C}_U$. By definition of $\overline{C_k}$ they do not conflict. Since $\gamma(x_2)$ conflicts with both $\gamma(x_{k-1})$ and $\gamma(x_k)$ (vertex x_2 is adjacent to x_{k-1} and x_k in $\overline{C_k}$), by Lemma 33, $\gamma(x_{k-1}), \gamma(x_2)$, and $\gamma(x_k)$ must be in chain configuration in that order. By the same reasoning $\gamma(x_{k-1}), \gamma(x_3)$, and $\gamma(x_k)$ must be in chain configuration again in the same order. However this is only possible if $\gamma(x_2)$ and $\gamma(x_3)$ are identical, which constitutes a contradiction. $\square$

In Abaka et al. (2013), the constrained alignment problem is shown to be polynomial-time solvable if G_1 is acyclic and $m_2 = 1$, using a dynamic programming approach. Theorem 34 gives an alternative proof using the $O(|V||E|)$ algorithm for maximum independent set in weakly triangulated graphs (Hayward et al. (2007)). In this case, Lemma 7 and Theorem 8. **(i)** give $|E_{\mathcal{C}}| \leq \frac{1}{2}m_1^3(m_1-1)|V_1|(\Delta_1+3)$ while Lemma 4 gives $|V_{\mathcal{C}}| \leq {m_1}^2|V_1|$. The related complexity is $O(\Delta_1|V_1|^2)$ if m_1 is a fixed constant.

4 Concluding remarks

We consider the constrained alignment of a pair of input graphs. We heavily investigate the combinatorial properties of a conflict graph which was introduced in Fertin et al. (2009) but not studied in detail as far as graph theoretical properties are concerned. The constrained alignment problem appears as being closely related to the maximum independent set problem in conflict graphs. Known results on the maximum independent set problem associated with several structural properties of conflict graphs lead to algorithmic results for the constrained alignment problem: a polynomial-time case, polynomial-time approximations, and fixed-parameter tractability results.

Our contribution is twofold. First, we improve known approximation results for the constrained alignment problem in several ways. In terms of the maximum degrees of G_1 and G_2, we propose the first $o(\Delta_1+\Delta_2)$-approximation using basic properties of conflict graphs. This ratio is similar to the known approximation ratios, function of the maximum degree, for the maximum independent set problem in G_1 and G_2. This is due to the fact that the maximum degree of the conflict graph is of the same order as $\Delta_1+\Delta_2$. On the contrary, the number of vertices of the conflict graph does not allow to derive interesting results from known maximum independent set approximation ratios expressed as functions of the number of vertices. We design the first non trivial approximation result with a ratio function of $|V_1|$ for the constrained alignment problem. The related ratio, $O(\frac{|V_1|}{\log(|V_1|)})$, is better than $O\left(\frac{|V_1|\log\log(|V_1|)}{\log(|V_1|)}\right)$ directly obtained from ratios function of the degree but it is still large compared to the $O(\frac{|V_1|}{\log^2(|V_1|)})$-approximation of the maximum independent set in G_1.

> A first open question raised by these results is to strengthen hardness approximation results for the constrained alignment problem and in particular to investigate whether a ratio of $O(|V_1|^{1-\varepsilon})$ or even a constant approximation can be achieved in polynomial time. It is indeed well-known that such ratios cannot be achieved for the maximum independent set problem.

We also derive a ratio of $O(\sqrt{\beta(I)})$ for the constrained alignment problem with $m_2 = 1$, while a similar result is not possible for the maximum independent set in general graphs unless P=NP. This kind of unusual result (Theorem 20 and Proposition 21) seems interesting to investigate.

> Studying more in detail in which extend similar $\rho(\alpha(G))$-approximation results, parametrised by the size of the optimal solution, can be obtained for the maximum independent set problem or other problems is an interesting line of research raised by this work.

Our second contribution is about structural results on the conflict graph. After general considerations (Subsection 2.3) valid for any m_1, m_2, we focus on the case $m_2 = 1$ (any m_1) that has been considered in Fagnot et al. (2008); Fertin et al. (2009). For this case, we investigate graph classes that all can be characterised by forbidden subgraphs H in the neighborhood of any vertex: the case where H is a large clique or a large independent set is pretty usual, it just corresponds, in the whole graph, to exclude large cliques and/or large claws. The case where H is an induced path or cycle - thus excluding wheels or fans - is less current even thought the classes of H-free graphs themselves have raised great interest in the recent years: for instance many researches deal with maximum independent set problem in graphs excluding C_t or P_t for some t. In particular, it is known that the maximum independent set problem is polynomial for P_5-free graphs (Lokshantov et al. (2014)) and the case of larger t is still unknown. For instance, if the maximum independent set problem was polynomial in P_8-free graphs, then combining Theorems 19 and 20 would lead to a $\sqrt{\beta(I)}$-approximation for the constrained alignment problem. Note also that P_4-free subgraphs of $\mathcal{C}$ play a crucial role for several results in this work; it would be interesting to study whether this approach can be applied in a more general setting using P_5-free subgraphs instead of P_4-free ones.

> So far, this work motivates the study of maximum independent set in graphs excluding fans and/or wheels and more generally in classes of graphs with forbidden subgraphs in the neighborhood of any vertex.

Theorem 20 gives a first step in this direction with a strategy to efficiently solve the maximum independent set in a graph $G = (V, E)$ when a good solution can be found in all subgraphs $G_v, v \in V$.

As a first attempt to investigate properties of the conflict graph to derive efficient algorithms, the case $m_2 = 1$ revealed to be very rich and promising as it allows to derive interesting properties of the conflict graph, even for large values of m_1. Even if, as outlined in Fagnot et al. (2008), the underlying biological application motivates the case where both m_1 and m_2 are small, it is worth to note that reduction of the constrained alignment problem to a maximum independent set problem in the conflict graph is valid for any values of m_1, m_2. As mentioned in Subsection 2.1, the largest possible values for m_1, m_2 ($m_1 = |V_2|, m_2 = |V_1|$) leads to another well studied problem, the maximum common edge subgraph problem that includes many well-known problems like the maximum clique problem. If m_1, m_2 are large, the size of the conflict graph increases very fast and it becomes dense. As a consequence, this approach is likely to lead to good computational results if at least one of m_1, m_2 is small.

> The last research direction we want to outline is to investigate properties of conflict graphs for larger values of m_2 for, at least, some classes of graphs G_1 and G_2.

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References

G. Abaka, T. Bıyıkoğlu, and C. Erten. Campways: constrained alignment framework for the comparative analysis of a pair of metabolic pathways. *Bioinformatics*, 29(13):145–153, 2013.

A. E. Aladag and C. Erten. Spinal: scalable protein interaction network alignment. *Bioinformatics*, 29(7): 917–924, 2013.

F. Alkan and C. Erten. Beams: backbone extraction and merge strategy for the global many-to-many alignment of multiple ppi networks. *Bioinformatics*, 30(4):531–539, 2014.

G. Ausiello, M. Protasi, A. Marchetti-Spaccamela, G. Gambosi, P. Crescenzi, and V. Kann. *Complexity and Approximation: Combinatorial Optimization Problems and Their Approximability Properties*. Springer-Verlag New York, Inc., Secaucus, NJ, USA, 1st edition, 1999.

P. Berman. A $d/2$ approximation for maximum weight independent set in d-claw free graphs. In *Proceedings of the 7th Scandinavian Workshop on Algorithm Theory*, SWAT '00, pages 214–219, 2000.

R. Boppana and M. M. Halldórsson. Approximating maximum independent sets by excluding subgraphs. *BIT Numerical Mathematics*, 32(2):180–196, 1992.

A. Brandstädt, V. B. Le, and J. P. Spinrad. *Graph Classes: A Survey*. Society for Industrial and Applied Mathematics, Philadelphia, PA, USA, 1999.

K. Dabrowski, V. V. Lozin, H. Müller, and D. Rautenbach. Parameterized complexity of the weighted independent set problem beyond graphs of bounded clique number. *Journal of Discrete Algorithms*, 14:207–213, 2012.

H. N. de Ridder et al. Information System on Graph Classes and their Inclusions (ISGCI). `http://www.graphclasses.org`, 2010.

M. Demange and V. T. Paschos. Improved approximations for maximum independent set via approximation chains. *Applied Mathematics Letters*, 10(3):105–110, 1997.

M. Demange and V. T. Paschos. Polynomial approximation algorithms with performance guarantees: An introduction-by-example. *European Journal of Operational Research*, 165(3):555–568, 2005.

R. G. Downey and M. R. Fellows. *Parameterized Complexity*. Springer-Verlag, 1999.

I. Fagnot, G. Lelandais, and S. Vialette. Bounded list injective homomorphism for comparative analysis of protein-protein interaction graphs. *Journal of Discrete Algorithms*, 6(2):178–191, 2008.

F. E. Faisal, L. Meng, J. Crawford, and T. Milenković. The post-genomic era of biological network alignment. *EURASIP J Bioinform Syst Biol*, 2015:3, Dec 2015.

G. Fath-Tabar. Old and new zagreb indices of graphs. *MATCH Communications in Mathematical and in Computer Chemistry*, 65:79–84, 2011.

G. Fertin, R. Rizzi, and S. Vialette. Finding occurrences of protein complexes in protein–protein interaction graphs. *Journal of Discrete Algorithms*, 7(1):90 – 101, 2009.

M. R. Garey and D. S. Johnson. *Computers and Intractability: A Guide to the Theory of NP-Completeness*. W. H. Freeman & Co., New York, NY, USA, 1979.

D. Goldman, S. Istrail, and C. H. Papadimitriou. Algorithmic aspects of protein structure similarity. In *Proceedings of the 40th Annual Symposium on Foundations of Computer Science*, FOCS '99, pages 512–521, Washington, DC, USA, 1999. IEEE Computer Society.

M. C. Golumbic. *Algorithmic Graph Theory and Perfect Graphs (Annals of Discrete Mathematics, Vol 57)*. North-Holland Publishing Co., Amsterdam, The Netherlands, 2004.

M. M. Halldórsson. Approximations of weighted independent set and hereditary subset problems. *Journal of Graph Algorithms and Applications*, 4(1):1–16, 2000.

J. Håstad. Clique is hard to approximate within $n^{1-\varepsilon}$. *Acta Mathematica*, 182(1):105–142, 1999.

R. B. Hayward. Weakly triangulated graphs. *Journal of Combinatorial Theory, Series B*, 39(3):200–208, 1985.

R. B. Hayward, J. P. Spinrad, and R. Sritharan. Improved algorithms for weakly chordal graphs. *ACM Transactions on Algorithms*, 3(2), 2007.

M. Liu and B. Liu. New sharp upper bounds for the first zagreb index. *MATCH Communications in Mathematical and in Computer Chemistry*, 62:689–698, 2009.

D. Lokshantov, M. Vatshelle, and Y. Villanger. Independent set in p5-free graphs in polynomial time. In *Proceedings of the Twenty-fifth Annual ACM-SIAM Symposium on Discrete Algorithms*, SODA '14, pages 570–581, Philadelphia, PA, USA, 2014. Society for Industrial and Applied Mathematics.

S. Nikolić, G. Kovacević, A. Milicević, and N. Trinajstić. The zagreb indices 30 years after. *Croatica Chemica Acta*, 76(2):113–124, 2003.

V. Raman and S. Saurabh. Triangles, 4-cycles and parameterized (in-)tractability. In *Proceedings of the 10th Scandinavian Conference on Algorithm Theory*, SWAT'06, pages 304–315, 2006.

J. W. Raymond and P. Willett. Maximum common subgraph isomorphism algorithms for the matching of chemical structures. *Journal of Computer-Aided Molecular Design*, 16(7):521–533, 2002.

R. Sharan and T. Ideker. Modeling cellular machinery through biological network comparison. *Nature Biotechnology*, 24(4):427–433, 2006.

M. Zaslavskiy, F. R. Bach, and J.-P. Vert. Global alignment of protein-protein interaction networks by graph matching methods. *Bioinformatics*, 25(12):259–267, 2009.