Revisiting the Minimum Breakpoint Linearization Problem☆

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Abstract

The gene order on a chromosome is a necessary data for most comparative genomics studies, but in many cases only partial orders can be obtained by current genetic mapping techniques. The Minimum Breakpoint Linearization Problem aims at constructing a total order from this partial knowledge, such that the breakpoint distance to a reference genome is minimized. In this paper, we first expose a flaw in two algorithms formerly known for this problem [6, 4]. We then present a new modeling for this problem, and use it to design three approximation algorithms, with ratios resp. $O(\log(k)\log\log(k))$, $O(\log^2(|X|))$ and m^2+4m-4, where k is the optimal breakpoint distance we look for, $|X|$ is upper bounded by the number of pair of genes for which the partial order is in contradiction with the reference genome, and m is the number of genetic maps used to create the input partial order.

Keywords: comparative genomics, breakpoint distance, partially ordered genome, approximation algorithms

1. Introduction

In a number of comparative genomics algorithms, a full knowledge of the order of the genes on the chromosomes for the species under study is required. However, we have access to a limited number of fully sequenced genomes, and for other species, we only have genetic maps, in which there remains uncertainties in the gene order. Hence, the problem of inferring a total order, compatible with the partial knowledge on these genetic maps and optimizing some objective function, is a first step to study nonetheless all genomes. In the past few years, growing attention has been given to this problem, in which the objective

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function is an evolutionary distance to a reference genome (*e.g.* number of rearrangements [10], reversal [9, 6], breakpoint [6, 2, 4], or common intervals [2] distance).

In this paper, we focus on the MBL problem, which aims at finding a linearization of a partial order while minimizing the breakpoint distance to a reference genome. In [6] and [4], the study of this problem uses the construction of a special graph, the adjacency-order graph, which leads to respectively a heuristic and an approximation algorithm (whose ratio depends on m, the number of genetic maps used to construct the studied genome). However, we have detected a flaw in this construction, which makes both above mentioned algorithms invalid on general data. Thus, in this paper, we define a new type of adjacency-order graphs, give its construction, and show that it is effective to solve the MBL problem. This renewed approach allows us to use general graph theory results [5] to obtain new approximation algorithms for MBL. Moreover, we also achieve an $O(m^2)$-approximation, in the same spirit as was done in [4].

To describe the MBL problem, let a genome be represented by a partial order Π over a given set $\Sigma = \{1, \ldots, n\}$ of markers. A *linearization* of Π is a total order (or a permutation) $\pi = \pi(1)\cdot\pi(2)\cdot\ldots\cdot\pi(n)$ on Σ, such that, for all markers i, j, if $i <_\Pi j$, then $i <_\pi j$ (alternatively, $\pi^{-1}(i) < \pi^{-1}(j)$, or i precedes j in the permutation π). In that case, π is said to be *compatible* with Π. An *interval* I of π is a list of successive values from π, that is $I = \pi(h)\cdot\pi(h+1)\cdot\ldots\cdot\pi(l)$, with $1 \leq h \leq l \leq n$. For any such interval, its length L is defined as $l - h + 1$. An *adjacency* in the total order π is an interval of length $L = 2$. The *breakpoint distance* $d_B(\pi_1, \pi_2)$ between two total orders π_1 and π_2 (over the same set Σ) is defined by the total number of adjacencies in π_1 which are not adjacencies in π_2. We call Id_n the identity permutation over $\Sigma = \{1, \ldots, n\}$.

The Minimum Breakpoint Linearization Problem, in its optimization formulation, can be defined as follows:

Problem : MBL
Input : A partial order Π.
Output : A linearization π of Π that minimizes $k = d_B(\pi, Id_n)$.

Fig. 1a shows an example of partial order Π, that yields four optimal linearizations (Fig. 1c) satisfying $d_B(\pi, Id_n) = 3$ for each linearization π.

It is worth noting that the input partial order is, in practice, obtained by combining a limited number m of *genetic maps* [8, 10]. A genetic map consists of an ordered list of blocks $B_1, B_2, \ldots, B_q$, each of which is an unordered list of markers, i.e. any two markers from the same block are incomparable. The blocks $B_1, B_2, \ldots, B_q$ induce a partial order Π as follows: for any $a \in B_i$ and $b \in B_j$, $a <_\Pi b$ iff $i < j$. Note that it is always assumed that combining two or more genetic maps never creates conflicts.

The Minimum Breakpoint Linearization Problem, based on the genome rearrangement problem defined by Zheng and Sankoff [10], was studied independently in [2] and [6] (we note that in the latter, the problem is denoted as PBD, and deals with two partial orders instead of one partial order and one total order). In [2], Blin et al. prove that MBL is **NP**-hard and give two

types of algorithms for solving MBL: (i) a heuristic and (ii) an exact, thus exponential-time, algorithm based on dynamic programming. Moreover, this last algorithm is efficient in the specific case where input genomes are created from a bounded number m of gene maps, in which the blocks have a bounded size. In [6], Fu and Jiang give an (independent) **NP**-hardness proof, and present the construction of the adjacency-order graph $\mathcal{G}_\Pi$ of a partial order Π (Π being represented as a DAG, called DAG(Π)). Their central theorem, claiming that "*All the possible common adjacencies in an acyclic adjacency-order graph $\mathcal{G}_\Pi$ could always co-exist in some linearization of DAG(Π)*", is used in a heuristic they provide for the problem, and is also used by Chen and Cui [4] to obtain an $\frac{m^2+m}{2}$-approximation algorithm. However, as shown in Theorem 2, the above mentioned theorem from [6] is false, and consequently both those algorithms are invalid for the general MBL Problem.

The paper is organized as follows. In Section 2, we point out the **APX**-hardness of MBL and give our counter-example to the central theorem in [6]. Section 3 is devoted to the definition of a new adjacency-order graph, which is used in Section 4 to show that solving MBL may be reduced to solving a variant of the well-known Feedback Vertex Set problem. Section 5 presents three approximation algorithms, two of which are based on state-of-the-art algorithms for the variant of Feedback Vertex Set we are interested in, whereas the third is specific to partial orders created from genomic maps, and has a ratio depending on the number m of those genomic maps. Section 6 is the conclusion.

2. Revisiting Previous Works

In this section, we focus on previous works: we first show that adapting the **NP**-hardness proof for MBL from [2] leads to an **APX**-hardness proof. We then give a counterexample to Theorem 1 from [6], which implies, among others, that the approximation algorithm from [4] is invalid.

Theorem 1. *The* MBL *problem is* **APX**-*hard.*

Proof. In [2], Blin et al. show the **NP**-hardness of MBL by reducing it from the Maximum Independent Set problem. The polynomial reduction they use, which they called PO-construction, leads them to the following theorem.

Theorem [2] A connected graph $G = (V, E)$ admits an independent set $V' \subseteq V$ such that $|V'| \geq k$ iff there exists a linearization π' of Π such that $d_B(\pi', \pi) \leq (3n + 2) - k$, where π and Π result from a PO-construction of G.

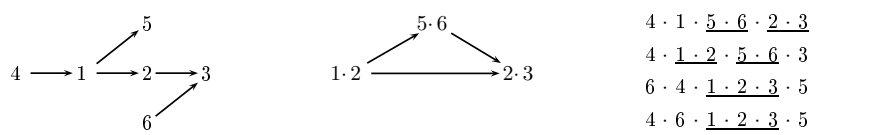
The PO-construction given in [2] is in fact an L-reduction [7], if we consider the restriction of Maximum Independent Set on cubic graphs, i.e. graphs for which every vertex has degree 3. We write $\alpha(G)$ the maximum value of an independent set of G, and $\mathrm{OPT}_{MBL}(\Pi, \pi)$ the optimal value for MBL, with input π and Π. It is known that, for all cubic graphs G with n vertices, $\alpha(G) \geq \frac{n}{4}$. So $\mathrm{OPT}_{MBL}(\Pi, \pi)$, where π and Π result from the PO-construction of a cubic graph G, is at most $3n + 2 - \alpha(G) \leq 11\alpha(G) + 2$: this gives the

first inequality of the L-reduction. Concerning the second inequality, we again assume that π and Π are obtained from a PO-construction of a cubic graph G. If we have a linearization π' of Π such that $d_B(\pi', \pi) = k'$, then we can find an independent set of G of size k with $k \geq 3n + 2 - k'$. Then $|k - \alpha(G)| \leq -(3n + 2 - k') + \alpha(G) = |k' - \mathrm{OPT}_{MBL}(\Pi, \pi)|$. Finally, since the restriction of Maximum Independent Set on cubic graphs is an **APX**-hard problem [1], we conclude that MBL is **APX**-hard as well.

□

The following theorem refers to the definition of *adjacency-order graph* (written $\mathcal{G}_\Pi$) given in [6]. The construction of this graph for any Π is not reported here, instead it is described for the directed acyclic graph given in Fig. 1a.

Theorem 2. *All the adjacencies appearing in the adjacency-order graph $\mathcal{G}_\Pi$ (as defined in [6]) of a DAG Π may not always coexist in a linearization of Π, even if $\mathcal{G}_\Pi$ is acyclic.*



(a) DAG(Π) represents the partial order Π

(b) $\mathcal{G}_\Pi$, as defined in [6]

(c) Optimal linearizations of Π

Figure 1: Counterexample of the main theorem from [6]

Proof. Consider the directed acyclic graph $DAG(\Pi)$ obtained from the following partial order (see Fig. 1a):

$$\Pi: \quad 4 < 1 < 2 < 3; \quad 1 < 5; \quad 6 < 3$$

Here, there are only three possible common adjacencies between Π and Id_n: $1 \cdot 2$, $2 \cdot 3$ and $5 \cdot 6$. Following the definitions proposed in [6], there are three arcs in the adjacency-order graph $\mathcal{G}_\Pi$ (Fig. 1b): one from $1 \cdot 2$ to $2 \cdot 3$ (because of the common marker), one from $1 \cdot 2$ to $5 \cdot 6$ (because $1 < 5$ in Π), and one from $5 \cdot 6$ to $2 \cdot 3$ (because $6 < 3$ in Π). In that case, $\mathcal{G}_\Pi$ is acyclic; however, its three adjacencies cannot coexist in any linearization of Π (see Fig. 1c: there can be at most two adjacencies in the same linearization). Thus Theorem 2, which contradicts Theorem 1 in [6], is proved.

□

3. Defining a New Adjacency-Order Graph G_Π

The direct consequence of Theorem 2 is that the adjacency-order graph defined in [6] cannot be exploited. Hence, we introduce here the construction of

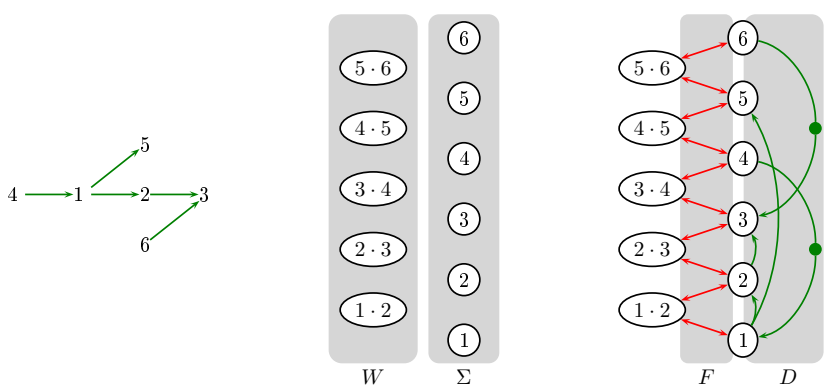
a new type of adjacency-order graph, whose main structural property will lead us to three different approximation algorithms.

This new adjacency-order graph G_Π contains both the features of the partial order Π and of the identity permutation Id_n. Some of the cycles in this graph will express the incompatibilities between the order Π and the permutation Id_n. In order to count or to bound the breakpoint distance between a linearization π of Π and Id_n, one has to identify the vertices in the adjacency-order graph needed to break all these conflict-cycles, and to count or bound their number. The MBL problem thus becomes a graph theory problem, which allows us either to use existing algorithms or to build-up new algorithms based on graphs.

Adjacency-order graph. Let $\Pi = (\Sigma, D)$ be a directed acyclic graph (DAG) representing a partial order over $\Sigma = \{1, \ldots, n\}$ (see Fig. 2a), *i.e.* we write $i <_\Pi j$ iff there is a directed path from i to j in Π. We create a set W of vertices representing the adjacencies of the identity permutation Id_n by $W = \{i \cdot (i+1) \mid 1 \leq i < n\}$. Finally, let $V = \Sigma \cup W$ (Fig. 2b). Note that, in the following, we will not distinguish the vertices of Σ and their corresponding integers (this will always be clear from the context). Moreover, the natural order $<$ over the integers is also used as an order over Σ. We now construct a set of arcs F (denoted by an arrow $\rightarrow$) in the following way:

$$\begin{aligned} F = \quad & \{i \cdot (i+1) \rightarrow i \mid 1 \leq i < n\} \ \cup \ \{i \cdot (i+1) \rightarrow i+1 \mid 1 \leq i < n\} \\ \cup \quad & \{i \rightarrow i \cdot (i+1) \mid 1 \leq i < n\} \ \cup \ \{i+1 \rightarrow i \cdot (i+1) \mid 1 \leq i < n\} \end{aligned}$$

Each arc in F has one end in W and one end in Σ. We write $E = D \cup F$ (Fig. 2c) and we define the *adjacency-order* graph G_Π of Π by $G_\Pi = (V, E)$.



(a) Original DAG Π (b) Vertices of G_Π (c) Arcs of G_Π

Figure 2: Construction of an adjacency-order graph. The symmetric arcs in F are represented as double arrows. The arcs in X are marked with a large dot.

In G_Π, the arcs of D that go top-down (see Fig. 2c) intuitively show incompatibilities between the order in Π and the order in Id_n. We call such

an arc *conflict-arc*, that is, an arc $i \to j \in D$ such that $i > j$, and we note $X[G_\Pi]$ (or only X, if there is no ambiguity) the set containing all conflict-arcs: $X[G_\Pi] = \{i \to j \in D \mid i > j\}$. Now, every cycle containing a conflict-arc is called a *conflict-cycle*. In Theorem 5, we prove that the adjacencies involved in conflict-cycles are incompatible, so that we need to remove at least one adjacency from each of those cycles to obtain a linearization of Π. We also define a weight map $w[G_\Pi]$ on the vertices of G_Π, which associates 1 to each $u \in W$, and ∞ to $u \in \Sigma$.

Notations. An arc between u and v is written $u \to v$, or $u \to_{E'} v$ if it belongs to some subset E'. A *path* P is a (possibly empty) sequence of arcs written $u \xrightarrow{P}{}^* v$, or $u \xrightarrow{P}{}^*_{E'} v$ if P uses only arcs from E'. A non-empty path Q is written with a + sign: $u \xrightarrow{Q}{}^+ v$. A *cycle* is a non-empty path $u \xrightarrow{\mathcal{C}}{}^+ v$ with $v = u$.

Given in G_Π a path $P = v_0 \to v_1 \to \ldots \to v_\ell$, we use the following notations: $\ell(P) = \ell$ is the length of P, $V(P) = \{v_h \mid 0 \leq h \leq \ell\}$, $W(P) = V(P) \cap W$, $\Sigma(P) = V(P) \cap \Sigma$, $E(P) = \{v_h \to v_{h+1} \mid 0 \leq h < \ell\}$, $F(P) = E(P) \cap F$, $D(P) = E(P) \cap D$, $X(P) = E(P) \cap X$. A cycle $\mathcal{C}$ is said to be *simple* if all vertices v_h are distinct (except $v_0 = v_\ell$), which implies $\ell(\mathcal{C}) = |V(\mathcal{C})| = |E(\mathcal{C})|$.

First Properties. The following lemma gives a way to exhibit conflict-arcs in some cycles of G_Π. It is used in Property 4 to give an insight on how conflict-cycles can appear in the adjacency-order graph.

Lemma 3. *Let $\mathcal{C}$ be a (not necessarily simple) cycle of G_Π. Let $c \in \Sigma$, such that there exists $a, b \in \Sigma(\mathcal{C})$ with $a \leq c < b$. Then at least one of the following propositions is true:*

(i) $\mathcal{C}$ contains an arc $u \to_X v$ with $v \leq c < u$

(ii) $\mathcal{C}$ contains both arcs $c+1 \to_F c\cdot(c+1)$ and $c\cdot(c+1) \to_F c$

Proof. Define $c^+ = \{d \mid d > c\} \cup \{d\cdot(d+1) \mid d > c\}$ and $c^- = \{d \mid d \leq c\} \cup \{d\cdot(d+1) \mid d < c\}$. Then $c^+ \cup \{c\cdot(c+1)\} \cup c^-$ is a partition of V. We show that when proposition (i) is false, proposition (ii) is necessarily true. Assume that proposition (i) is false. Since $\mathcal{C}$ contains vertices in both $c^+ \cup \{c\cdot(c+1)\}$ and c^- (resp. b and a), it thus contains an arc $u \to v$ with $u \in c^+ \cup \{c\cdot(c+1)\}$ and $v \in c^-$. We must have $u \to v \in F$, otherwise $u \to v \in D$ implies $u \to v \in X$ (since $u > v$), and proposition (i) would be true, a contradiction. Necessarily $u = c\cdot(c+1)$ and $v = c$ (there is no arc in F going out of c^+ into c^-). So $\mathcal{C}$ contains the arc $c\cdot(c+1) \to c$. Using the same argument, we can show that there is an arc $u' \to v'$ in $\mathcal{C}$ with $u' \in c^+$ and $v' \in \{c\cdot(c+1)\} \cup c^-$. Since $u' \to v'$ cannot be in X (since proposition (i) is false) nor in $D - X$ (these arcs go from c^- to c^+), then it is in F, and we can only have $u' = c+1$ and $v' = c\cdot(c+1)$. So $\mathcal{C}$ also uses the arc $c\cdot(c+1) \to_F c$, and thus proposition (ii) is true.

□

Property 4. *Let $\mathcal{C}$ be a simple cycle with $|D(\mathcal{C})| \geq 2$. Then $\mathcal{C}$ is a conflict-cycle.*

Proof. Let $a = \min(\Sigma(\mathcal{C}))$, $b = \max(\Sigma(\mathcal{C}))$, and $u \rightarrow_D v$ and $u' \rightarrow_D v'$ two arcs of D appearing in $\mathcal{C}$. By contradiction, we suppose $\mathcal{C}$ is not a conflict-cycle (i.e., $\mathcal{C}$ contains no arc of X). For each $c \in \Sigma$ with $a \leq c < b$, we can use Lemma 3: only proposition (ii) can be true for each c, and there is an arc of F going out of $c+1$ and another going into c appearing in cycle $\mathcal{C}$. Since this cycle is simple, we have $u \neq c+1$ and $v \neq c$ for all $a \leq c < b$ (and similarly, $u' \neq c+1$ and $v' \neq c$). By definition of a and b, u, u', v, v' cannot be out of the interval $\{a, \ldots, b\}$, so $u = u' = a$ and $v = v' = b$. It implies that the simple cycle $\mathcal{C}$ uses twice the same arc $a \rightarrow_D b$, a contradiction.

□

4. Cutting all Conflict-Cycles in G_Π Is Enough

Now that we have defined how to construct G_Π starting from the input partial order Π, we turn to proving the main structural result of our paper: conflict-cycles contain all the conflicts between the partial order Π and the identity permutation Id_n (see Theorem 5). More precisely, when appropriate adjacencies in Id_n (identified as vertices in W) are removed, the remaining adjacency-order graph has no conflict-cycle and this condition is necessary and sufficient to obtain a linearization of Π that preserves all the remaining adjacencies in Id_n.

Theorem 5. *Let Π be a partial order, $G_\Pi = (V, E)$ its adjacency-order graph (with $V = \Sigma \cup W$ and $E = D \cup F$), and $W' \subseteq W$. Then there exists a total order π over Σ, compatible with Π, and containing every adjacency from W' iff $G_\Pi[W' \cup \Sigma]$ has no conflict-cycle.*

Proof. ($\Rightarrow$) Let π be a linearization of Π containing every adjacency of W'. The following lemma will allow us to conclude by contradiction.

Lemma 6. *In this Lemma, we use the preconditions of Theorem 5 and the fact that π is a linearization of Π containing every adjacency of W'. Let $P = v_1 \rightarrow v_2 \rightarrow \ldots \rightarrow v_\ell$ be a path with vertices in $W' \cup \Sigma$ such that (H1) the vertices v_i, $1 \leq i \leq \ell$ are pairwise distinct, (H2) $\ell \geq 2$, (H3) $v_1, v_\ell \in \Sigma$, and (H4) for any $1 \leq i < \ell$, $v_i \rightarrow v_{i+1} \in F$.*
Let $a = \min(v_1, v_\ell)$ and $b = \max(v_1, v_\ell)$. Then the sequence $a \cdot (a+1) \cdot (a+2) \cdot \ldots \cdot b$ is an interval of π. Moreover, $\Sigma(P) = \{a, \ldots, b\}$ and $W(P) = \{c \cdot (c+1) \mid a \leq c < b\}$.

Proof. Using H4, we can consider only the bipartite graph $(W' \cup \Sigma, F)$. With H3 we obtain that ℓ is odd, and $v_{2i-1} \in \Sigma$ (for any $1 \leq i \leq \frac{\ell+1}{2}$) whereas $v_{2i} \in W'$ (for any $1 \leq i \leq \frac{\ell-1}{2}$). Moreover, H2 implies that $\ell \geq 3$. The proof is by induction on ℓ:

For $\ell = 3$. Since $v_1 \to_F v_2$ and $v_1 \in \Sigma$, there are two possible cases: (i) $v_2 = v_1 \cdot (v_1 + 1)$ and (ii) $v_2 = (v_1 - 1) \cdot v_1$.

(i) $v_2 = v_1 \cdot (v_1 + 1)$. Then $v_3 = v_1 + 1$ (since $v_2 \to_F v_3$ and $v_3 \neq v_1$, due to H1). In this case, $a = v_1$, $b = a + 1$ and $a \cdot b$ is an interval of π (indeed, it corresponds to the adjacency v_2 which belongs to W').

(ii) $v_2 = (v_1 - 1) \cdot v_1$. Likewise, $v_3 = v_1 - 1$, $a = v_3$, $b = a + 1$, and $a \cdot b$ is an interval of π.

Finally, in both cases we have $\Sigma(P) = \{v_1, v_3\} = \{a, b\}$ and $W(P) = \{v_2\} = \{a \cdot (a + 1)\}$: the lemma is true for $\ell = 3$.

For $\ell = \ell' + 2$, $\ell' \geq 3$. By induction, the lemma is true for the path $P' = v_1 \to \ldots \to v_{\ell'}$. Again, we need to consider two different cases (see Fig. 3a and 3b): (i) $v_1 < v_{\ell'}$ and (ii) $v_1 > v_{\ell'}$.

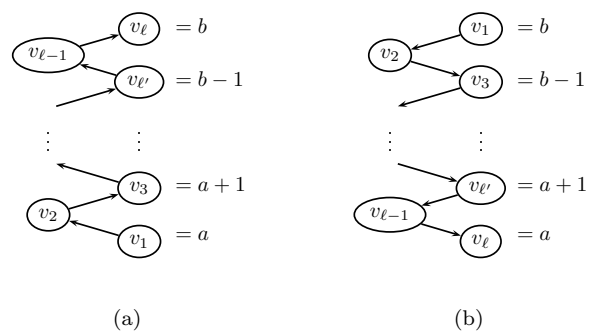


Figure 3: Two types of paths are possible in $(W' \cup \Sigma, F)$.

(i) In this case, $v_{\ell'-1} = (v_{\ell'} - 1) \cdot v_{\ell'}$, and by H1, $v_{\ell-1} = v_{\ell'+1} = v_{\ell'} \cdot (v_{\ell'} + 1)$, and $v_\ell = v_{\ell'+2} = v_{\ell'} + 1$. If we write $a' = v_1$ and $b' = v_{\ell'}$, then by induction the sequence $a' \cdot a' + 1 \ldots b'$ is an interval of π. And the sequence $b' \cdot b' + 1$ is also an interval of π, since it corresponds to vertex $v_{\ell'+1} \in W'$. So the full sequence $a' \cdot a' + 1 \ldots b' \cdot b' + 1$ is an interval of π. This proves the first part of the lemma, since $a = v_1 = a'$ and $b = v_\ell = b' + 1$. The second part is also true with $\Sigma(P) = \Sigma(P') \cup \{b\}$ and $W(P) = W(P') \cup \{(b - 1) \cdot b\}$.

(ii) This case is symmetric to the previous one, with $a = a' - 1 = v_{\ell'} - 1$, $b = b' = v_1$ and $v_\ell = a$. We link together the sequences $(a' - 1) \cdot a'$ and $a' \cdot (a' + 1) \ldots b'$ to prove that $a' \cdot (a' + 1) \ldots b'$ is an interval of π. Moreover, $\Sigma(P) = \Sigma(P') \cup \{a\}$ and $W(P) = W(P') \cup \{a \cdot (a + 1)\}$.

□

Proof of Theorem 5 (continued): We suppose, by contradiction, that there exists in $G_\Pi[W' \cup \Sigma]$ a cycle $\mathcal{C} = v_0 \to v_1 \to v_2 \to \ldots \to v_\ell = v_0$ containing an arc from X (wlog, assume that this arc is $v_0 \to_X v_1$). Wlog, we may assume that $\mathcal{C}$ is simple (otherwise, there exists a simple sub-cycle of $\mathcal{C}$ that contains

an arc from X). We distinguish two cases, depending on whether $v_0 \rightarrow_X v_1$ is the only arc in $D(\mathcal{C})$ or not.

First case: $v_0 \rightarrow v_1 \in X$ and for all i, $1 \leq i < \ell$, $v_i \rightarrow v_{i+1} \in F$ holds. In that case, we can directly use Lemma 6. Indeed, the path $v_1 \rightarrow v_2 \rightarrow \ldots \rightarrow v_\ell = v_0$ satisfies hypothesis H1 (by simplicity of $\mathcal{C}$), H2 (otherwise there would be a loop $v_0 \rightarrow v_0$ in X), H3 (since $v_\ell \rightarrow v_1 \in D$) and H4 (this is assumed in this first case). We also know, due to the fact that $v_0 \rightarrow_X v_1$, that $v_1 < v_\ell$. We can conclude that $v_1 \cdot v_1 + 1 \cdot \ldots \cdot v_\ell$ is an interval of π, so $v_1 <_\pi v_\ell = v_0$. This contradicts the fact that π is compatible with Π, since $v_0 <_\Pi v_1$.

Second case: Let $i_0 = 0, i_1, \ldots, i_{h-1}, i_h = \ell$ be the increasing sequence of indices such that $v_{i_j} \rightarrow v_{i_j+1} \in D$ for all j such that $0 \leq j < h$. Note that $h \geq 2$ and for all j, we have $v_{i_j} \in \Sigma$. Let us prove that for all $j < h$, the relation $v_{i_j} <_\pi v_{i_{j+1}}$ holds. The case where $i_{j+1} = i_j + 1$ is easy, since the arc $v_{i_j} \rightarrow_D v_{i_j+1}$ implies $v_{i_j} <_\Pi v_{i_{j+1}}$ (by construction of G_Π) and thus $v_{i_j} <_\pi v_{i_{j+1}}$, since π is compatible with Π. Now, assume there are several arcs between v_{i_j} and $v_{i_{j+1}}$, *i.e.* $i_{j+1} = i_j + m$ with $m \geq 2$. We use Lemma 6 with the path $\mathcal{P}$ in F given by $v_{i_j+1} \rightarrow v_{i_j+2} \rightarrow \ldots \rightarrow v_{i_j+m}$. Path $\mathcal{P}$ satisfies the hypotheses H1, H2, H3 and H4 of the lemma, thus one of the sequences $v_{i_j+1} \cdot (v_{i_j+1} + 1) \cdot \ldots \cdot v_{i_j+m}$ and $v_{i_j+m} \cdot (v_{i_j+m} + 1) \cdot \ldots \cdot v_{i_j+1}$ is an interval of π. Note that v_{i_j} is a distinct vertex from $v_{i_{j+1}}$ (since $h \geq 2$), and from other vertices in the set $\Sigma(\mathcal{P})$ as well (since each of them is the source of an arc from F in $\mathcal{C}$, whereas v_{i_j} is the source of an arc from D in $\mathcal{C}$). Consequently, v_{i_j} cannot appear in either of the intervals $v_{i_j+1} \cdot (v_{i_j+1} + 1) \cdot \ldots \cdot v_{i_j+m}$ and $v_{i_j+m} \cdot (v_{i_j+m} + 1) \cdot \ldots \cdot v_{i_j+1}$ of π. As v_{i_j} precedes v_{i_j+1} in Π (and thus in π), we have $v_{i_j} <_\pi v_{i'}$ for all $i' \in [i_j + 1, i_j + m]$, and particularly, $v_{i_j} <_\pi v_{i_{j+1}}$.

In conclusion, we have $v_{i_j} <_\pi v_{i_{j+1}}$ for all $j < h$ and $v_{i_h} = v_{i_0}$, a contradiction since there can be no cycle in the relation $<_\pi$. Hence, the subgraph $G_\Pi[W' \cup \Sigma]$ does not contain any conflict-cycle.

($\Leftarrow$) *(constructive proof)* We use the following method to construct a linearization π of Π containing all adjacencies of W', where the subgraph $G' = G_\Pi[W' \cup \Sigma]$, is assumed to contain no conflict-cycle. We denote by $V_1, \ldots V_k$ the strongly connected components of G', ordered by topological order (i.e., if $u, v \in V_i$, there exists a path from u to v ; moreover, if $u \in V_i$ and $v \in V_j$ and there exists a path $u \rightarrow^* v$ in G', then $i \leq j$). We sort the elements of each set $V_i \cap \Sigma$ in ascending order of integers, and obtain a sequence μ_i. The concatenation $\mu_1 \cdot \mu_2 \cdot \ldots$ gives π, a total order over Σ. We now check that π contains every adjacency in W' and is compatible with Π.

Let $a \cdot (a+1) \in W'$. Vertices a and $a+1$ are in the same strong connected component V_i, because of the arcs $a \leftrightarrow a \cdot (a+1) \leftrightarrow a+1$. Those two elements are obviously consecutive in the corresponding μ_i, and appear as an adjacency in π. By contradiction, assume now that there exist two distinct elements $a, b \in \Sigma$ such that $a <_\pi b$ and $b <_\Pi a$. We denote by i and j the indices such that $a \in V_i$ and $b \in V_j$. Since $a <_\pi b$, we have $i \leq j$, and since $b <_\Pi a$, there exists a path $b \overset{P_1}{\rightarrow}{}^+_D a$ in (Σ, D). Therefore, in G', we have $i \geq j$. We thus deduce that $i = j$, and therefore a and b share the same strong connected component. This

means that there also exists a path P_2 from a to b in G'. Hence, we have a cycle $b \overset{P_1}{\to}{}^+ a \overset{P_2}{\to}{}^+ b$, which cannot be a conflict-cycle, thus those paths do not use any arc from X. The latter is in particular true along P_1, which implies $b < a$, since each arc $u \to v$ in $D - X$ is such that $u < v$. On the other hand, a appears before b in π, and therefore in μ_i, so $a < b$, a contradiction. Finally π is a feasible solution for MBL(Π), with at least $|W'|$ common adjacencies with the identity permutation Id_n.

Since all vertices in $W - W'$ count for unconserved adjacencies (and thus define $d_B(\pi, Id_n)$), from Theorem 5 we directly get the following corollary.

Corollary 7. *The value k of an optimal solution of* MBL*(Π) is the minimum number of vertices one needs to delete in W to remove all conflict-cycles from G_Π.*

5. Three Approximation Algorithms for MBL

5.1. Two Approximation Algorithms Based on Subset-FVS

Our previous result implies that we have reduced the problem MBL to a generalization of the well studied Feedback Vertex Set (FVS) problem, where only the conflict-cycles must be cut. In order to solve MBL, we use a (more general) variant of FVS, named Subset-FVS and studied by Even et al. [5], whose definition is the following:

Problem : Subset-FVS
Input : A directed graph $G = (V, E)$, a set $Y \subseteq V \cup E$, a weight map $w : V \to \mathbb{R}$.
Output : A set $V'' \subseteq V$ of minimum weight such that, with $V' = V - V''$, no cycle in $G[V']$ uses a vertex or an arc from Y.

In our paper, we are only interested in the restriction of Subset-FVS on adjacency-order graphs, where Y is the set of top-down arcs and w is such that only vertices in W can be deleted:

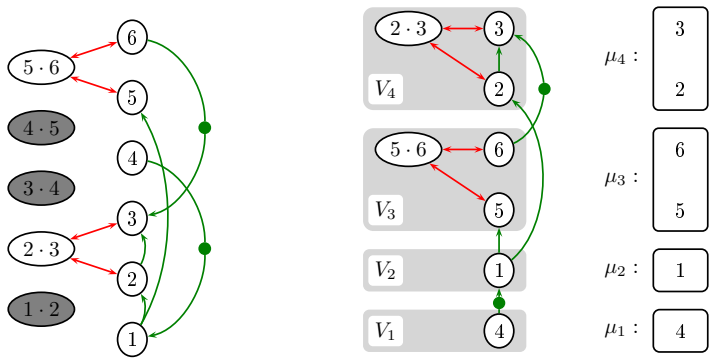
Problem : AOG-Subset-FVS
Input : An adjacency-order graph G_Π, $Y = X[G_\Pi]$, $w = w[G_\Pi]$
Output : A set W'' solution of Subset-FVS(G_Π, Y, w)

We note that any algorithm for Subset-FVS is also valid for AOG-Subset-FVS. Two approximation algorithms are given in [5] for Subset-FVS. The first one achieves an approximation ratio of $O(\log^2 |Y|)$, while the second algorithm achieves a ratio of $O\left(\min(\log(\tau^*)\log\log(\tau^*), \log(n)\log\log(n))\right)$, where τ^* is the value of the optimal *fractional* solution for the corresponding linear programming problem (thus τ^* is upper bounded by the optimal solution of Subset-FVS).

We use those approximation algorithms to solve MBL (see Algorithm 1, and Figures 4a and 4b for an example). We denote by SCC-sort() an algorithm that decomposes a graph into its strong connected components, and then topological sorts these components. Also, let sort() be an algorithm that sorts a set of integers according to the increasing order of its elements. Algorithm 1 is

Algorithm 1 $O(\log^2(|X|))$- and $O(\log(k)\log\log(k))$-approximation for MBL

Input: A directed acyclic graph $\Pi = (\Sigma, D)$
1. Create $G_\Pi = (V, E)$ the adjacency-order graph of Π;
2. $W'' \leftarrow$ AOG-Subset-FVS$(G_\Pi, X[G_\Pi], w[G_\Pi])$;
3. $W' \leftarrow W - W''$;
4. $(V_1, V_2, \ldots, V_h) \leftarrow$ SCC-sort$(G_\Pi[W' \cup \Sigma])$;
5. **For** $i \leftarrow 1$ **to** h;
6. $\quad \mu_i \leftarrow \text{sort}(V_i \cap \Sigma)$;
7. $\pi \leftarrow \mu_1 \cdot \mu_2 \cdot \ldots \cdot \mu_h$;
8. **return** π;



(a) Result of AOG-Subset-FVS: $W'' = \{1 \cdot 2, 3 \cdot 4, 4 \cdot 5\}$

(b) SCC-sort gives four components V_1, V_2, V_3 and V_4, and Algorithm 1 returns $\pi = 4 \cdot 1 \cdot 5 \cdot 6 \cdot 2 \cdot 3$

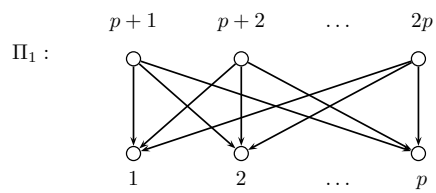
Figure 4: Key steps of Algorithm 1 on the example given in Fig. 2a

derived from the constructive proof of Theorem 5, and its correctness follows from Theorem 5 itself.

Depending on the algorithm used for AOG-Subset-FVS, Algorithm 1 can be either an exponential-time exact algorithm, an $O(\log^2|X|)$-approximation or an $O(\log(k)\log\log(k))$-approximation (where $|X|$ is the number of arcs $u \to v$ in $\Pi = (\Sigma, D)$ with $u > v$, and k the optimal value of our problem). Note that the two latter ratios are incomparable, since we may have $|X| \approx nk$ or $k \approx n|X|$, as can be seen in Fig. 5a and Fig. 5b.

5.2. An $(m^2 + 4m - 4)$-approximation Algorithm

In this section, we assume that the partial order Π is generated from m gene maps. Recall that a gene map is a totally ordered sequence of blocks, each of which is an unordered set of markers. We exploit this supplementary information to obtain an $(m^2 + 4m - 4)$-approximation algorithm for AOG-



(a) With Π_1: $|X| = p^2 \ >> \ k = 1$

$\Pi_2 :\ 1 \to 3 \to \ldots \to (2p-1) \to 2 \to 4 \to \ldots \to (2p)$

(b) With Π_2: $|X| = 1 \ << \ k = 2p-1$

Figure 5: Comparing $|X|$ (number of arcs $u \to v$ in Π such that $v < u$) to k (optimal breakpoint distance to the identity)

Subset-FVS, and therefore a new approximation algorithm, having the same ratio, for MBL. Before giving the algorithm, we first introduce a few definitions

Definitions. A path $u \xrightarrow{R}{}^*_D v$ in (Σ, D) is said to be a *shortcut* of a conflict-cycle $\mathcal{C}$ (see Fig. 6), if:

- $u, v \in \Sigma(\mathcal{C})$ (we write P and Q the paths such that $\mathcal{C} = u \xrightarrow{P}{}^+ v \xrightarrow{Q}{}^+ u$),
- cycle $\mathcal{C}' = u \xrightarrow{P}{}^+ v \xrightarrow{R}{}^*_D u$ is a conflict-cycle,
- $W(Q) \neq \emptyset$ (using the shortcut removes at least one adjacency).

We say that a conflict-cycle is *minimal* if it has no shortcut. With the following property, we ensure that removing minimal conflict-cycles is enough to remove all conflict-cycles.

Property 8. *If an adjacency-order graph contains a conflict-cycle, it also contains a minimal conflict-cycle.*

Proof. Take a non-minimal conflict-cycle $\mathcal{C}$. If $\mathcal{C}$ is simple, we use the shortcut to create a conflict-cycle $\mathcal{C}'$ with $|W(\mathcal{C}')| < |W(\mathcal{C})|$. Otherwise, if $\mathcal{C}$ is not simple, there exists a vertex u such that $\mathcal{C} = u \xrightarrow{P}{}^+ u \xrightarrow{Q}{}^+ u$, and one of P and Q, say P, uses at least one arc of X. Thus P is a conflict-cycle, with $|W(P)| \leq |W(\mathcal{C})|$, and $|\ell(\mathcal{C}')| < |\ell(\mathcal{C})|$. In both cases, we create a conflict-cycle $\mathcal{C}'$ with either $|W(\mathcal{C}')| < |W(\mathcal{C})|$, or $|W(\mathcal{C}')| = |W(\mathcal{C})|$ and $|\ell(\mathcal{C}')| < |\ell(\mathcal{C})|$. If $\mathcal{C}'$ is not a minimal conflict-cycle, we can replace $\mathcal{C}$ by $\mathcal{C}'$ and iterate this process: it necessarily ends ($\ell(\mathcal{C})$ and $|W(\mathcal{C})|$ must remain positive integers), and reaches a minimal conflict-cycle.

□

In a cycle $\mathcal{C}$, we call *joint* a vertex $e \in \Sigma$ whose incident arcs in $\mathcal{C}$ belong to $D(\mathcal{C})$ and to $F(\mathcal{C})$. Alternatively, there exist vertices e^D and e^F such that

i. either both arcs $e^D \to_D e$, $e \to_F e^F$ appear in $\mathcal{C}$, or

ii. both arcs $e^F \to_F e$, $e \to_D e^D$ appear in $\mathcal{C}$.

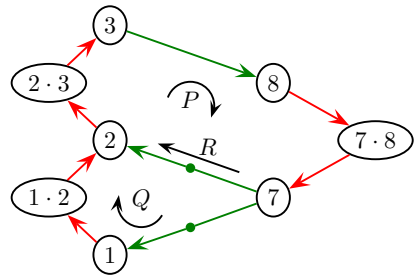


Figure 6: Cycle $\mathcal{C} = 2 \xrightarrow{P} {}^*7 \xrightarrow{Q} {}^*2$ is a conflict-cycle (it contains $7 \to 1 \in X$). The length-1 path R forms a shortcut for $\mathcal{C}$ (with $\mathcal{C}' = 2 \xrightarrow{P} {}^*7 \xrightarrow{R} {}^*2$, $\mathcal{C}'$ is a conflict-cycle, and $W(Q) = \{1 \cdot 2\}$). So $\mathcal{C}'$ is the only minimal conflict-cycle.

Consequently, two types of joints are identified: a joint is of type *(i.)* (resp. *(ii.)*) if it marks the end of a subpath with arcs from D (resp. from F) and the beginning of a subpath with arcs from F (resp. from D). In both cases, $e^F = e \cdot (e+1)$ or $e^F = (e-1) \cdot e$.

We say that e is a *low joint* if $e^F = e \cdot (e+1)$ (intuitively, e is at the bottom of a subpath with arcs from F, independently of its type).

Given a vertex $w \in W(\mathcal{C})$, we say that e is the *low joint associated to* w in $\mathcal{C}$, if the cycle $\mathcal{C}$ uses one of the paths $w \to_F^* e$ or $e \to_F^* w$ (e is either the first low joint after w in $\mathcal{C}$, or the last one before w).

Recall that Π is created from gene maps, numbered from 1 to m. From these gene maps, we can deduce two properties: (1) if there is an arc between u and v in Π, then u and v appear in consecutive blocks of the same gene map, and (2) if u and v appear in the same gene map, but in different blocks, then there exists a path $u \to^+ v$ or $v \to^+ u$ in Π.

For each $u \in \Sigma$, we denote $I(u) \subset \{1, \ldots, m\}$ the numbers of the gene maps in which u appears (u appears in at least one gene map, so $I(u) \neq \emptyset$). For each arc $u \to_D v$ of D, we denote $\eta(u \to_D v)$ the number of a gene map in which u and v appear in consecutive blocks. Then $\eta(u \to_D v) \in I(u) \cap I(v)$. Given a cycle $\mathcal{C}$, we extend the notation η to each of its joints e: $\eta(e) = \eta(e^D \to e)$ if e is of type *(i)*; and $\eta(e) = \eta(e \to e^D)$ otherwise.

We also extend I to paths: given a path $P = u_0 \to u_1 \to \ldots \to u_\ell$, we write

$$I(P) = \bigcup_{\substack{0 \le i \le \ell \\ u_i \in \Sigma}} I(u_i)$$

Algorithm. Algorithm 2 is an $(m^2 + 4m - 4)$-approximation for AOG-Subset-FVS. Used as a subroutine in Algorithm 1, it gives us an $(m^2 + 4m - 4)$-approximation for the MBL problem (see Corollary 17).

The approximation ratio is thoroughly analyzed in the next section; this analysis can be briefly summarized as follows. The first step is to bound the

Algorithm 2 $(m^2 + 4m - 4)$-approximation for AOG-Subset-FVS

Input: An adjacency-order graph $G_\Pi = (V, E), X[G_\Pi], w[G_\Pi]$
1. $W'' \leftarrow \emptyset$;
2. **while** there exists a minimal conflict-cycle $\mathcal{C}$ in $G_\Pi[V - W'']$;
3. $\quad L \leftarrow$ the set of low joints of $\mathcal{C}$;
4. $\quad W'' \leftarrow W'' \cup \{e^F \ : \ e \in L\}$;
5. **return** W'';

number of low joints that can appear in some minimal conflict-cycle by $O(m)$, see Lemma 12 for a more precise bound. Then, we show that for any adjacency $w \in W$, at most $2m$ minimal conflict-cycles using w can appear during step 2 of Algorithm 2: by Lemma 14, there cannot be more than two low joints, associated to w in different cycles, appearing in the same gene map. Hence we can bound the number of vertices deleted by Algorithm 2 for a given vertex $w \in W$ by $O(m^2)$. This is the object of Theorem 16, which gives the precise value of the approximation ratio of Algorithm 1: $m^2 + 4m - 4$.

5.3. Approximation Ratio Analysis

Lemma 9. *Let $e \to f$ be an arc of D, and let $u \in \Sigma$ such that $\eta(e \to f) \in I(u)$. Then one of the paths $e \to^* u$ or $u \to^* f$ appears in the graph (Σ, D).*

Proof. The three markers u, e and f appear in the same gene map numbered $\eta(e \to f)$. If u appears in a block strictly following e, then there exists a path $e \to^* u$ in Π, and thus in the graph (Σ, D). Else, since the block of e strictly precedes the block of f, u also appears strictly before f in this gene map, so there exists a path $u \to^* f$ in Π(and thus in the graph (Σ, D)).

□

Bounding the number of joints in a minimal conflict-circle.

Lemma 10. *Let $\mathcal{C}$ be a minimal conflict-cycle where three vertices $u, e, f \in \Sigma(\mathcal{C})$ are such that (see Fig. 7):*

- $\mathcal{C} = u \xrightarrow{P_1}{}^+ e \to_D f \xrightarrow{P_2}{}^+ u$
- *Each of the paths P_1 and P_2 uses at least one vertex from W and at least one arc from D.*

Then $\eta(e \to_D f) \notin I(u)$.

Proof. By contradiction, assume that $\eta(e \to_D f) \in I(u)$. Then, by Lemma 9, there exists a path R in D connecting either e to u or u to f. In the first case, we write $P = P_1$ and $Q = e \to_D f \xrightarrow{P_2}{}^+ u$, and in the second, $P = P_2$ and $Q = u \xrightarrow{P_1}{}^+ e \to_D f$, so that there exists a cycle $\mathcal{C}' = u \xrightarrow{P}{}^+ e \xrightarrow{R}{}^* u$ (resp., $\mathcal{C}' = f \xrightarrow{P}{}^+ u \xrightarrow{R}{}^* f$). Since $\mathcal{C}$ is a minimal conflict-cycle then R cannot be a

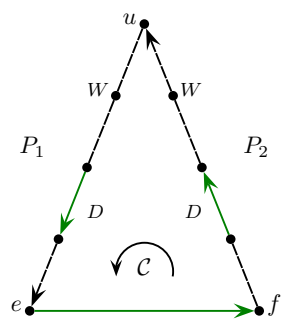


Figure 7: A cycle satisfying the conditions of Lemma 10 (dotted lines represent paths)

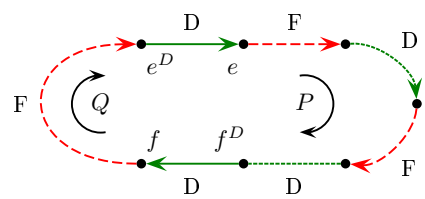


Figure 8: Illustration of Lemma 11, with $\lambda = 6$. Here $e_s = e^D$, $e_t = e$, $f_s = f^D$, $f_t = t$.

shortcut, and with $W(Q)$ not being empty, cycle $\mathcal{C}'$ cannot be a conflict-cycle. Hence, no arc in $D(\mathcal{C}')$ appears in X.

Let $a = \min(\Sigma(\mathcal{C}'))$ and $b = \max(\Sigma(\mathcal{C}'))$. For all $c \in \{a, \dots, b-1\}$, we can apply Lemma 3 on $\mathcal{C}'$, where only proposition (ii) can be true. Hence, $\mathcal{C}'$ contains every arc $c+1 \to_F c\cdot(c+1)$, $c\cdot(c+1) \to_F c$ between b and a. Moreover, none of these arcs can appear in R, so they all come from path P.

But P also contains at least one arc from D: let $a' \to_D b'$ be such an arc. By definition of a and b, we have $(a', b') \in \{a, \dots, b\}$. The path P is part of a simple cycle, so it can enter and leave only once each vertex. This implies $a' \notin \{a+1, \dots b\}$ and $b' \notin \{a, \dots, b-1\}$, so $a' = a$ and $b' = b$. Thus P contains every arc of the cycle $a \to_D b \to_F^* a$, which contradicts the fact that $\mathcal{C}$ is simple. □

Lemma 11. *Let $\mathcal{C}$ be a minimal conflict-cycle, with $\lambda \geq 5$ joints. Let e and f be two non consecutive joints of $\mathcal{C}$. Then $\eta(e) \neq \eta(f)$.*

Proof. We write e_s, e_t, f_s, f_t the four vertices of Σ such that $\{e_s, e_t\} = \{e, e^D\}$, $\{f_s, f_t\} = \{f, f^D\}$, and $\mathcal{C}$ uses both arcs $e_s \to e_t$ and $f_s \to f_t$ (see Fig. 8). We write P and Q the paths such that:

$$\mathcal{C} = e_s \to e_t \xrightarrow{P}{}^* f_s \to f_t \xrightarrow{Q}{}^* e_s.$$

Since e and f are not consecutive joints, both paths P and Q use an arc from F (and a vertex from W). Moreover, since there are at least five joints, one of P and Q has a joint as an inner vertex. Wlog, let this path be P. Thus P uses an arc from D.

We denote by Q' the path $f_s \to f_t \xrightarrow{Q}{}^* e_s$, which also contains an arc from D. Hence the cycle $\mathcal{C} = f_s \xrightarrow{Q'}{}^* e_s \to e_t \xrightarrow{P}{}^* f_s$ satisfies the conditions of Lemma 10: $\eta(e) \notin I(f_s)$. This proves the lemma, since $\eta(f) \in I(f_s)$.

□

Lemma 12. *Let $\mathcal{C}$ be a minimal conflict-cycle with λ joints. Let P be a path in F between two consecutive joints in $\mathcal{C}$, and P' be the path P where both ends are removed. Then $\lambda \leq 2(m - |I(P')|) + 4$.*

Proof. If $\lambda \leq 4$, the lemma is proved, so we can assume there are at least five joints.

Wlog, we assume that e_2 and e_3 are the two consecutive joints linked by P. Let $u \in \Sigma(P')$. Vertex u appears between joints e_2 and e_3, so we can use Lemma 10 with u, e_i and e_i^D for all $i \notin \{1, 2, 3, 4\}$. Indeed, paths P_1 and P_2 contain respectively $u \to_F^+ e_3 \to_D^+ e_4$ and $e_1 \to_D^+ e_2 \to_F^+ u$, so they both use an arc from D, an arc from F, and a vertex from W. Hence, for all $i \in \{5, \ldots, \lambda\}$, we have $\forall u \in \Sigma(P')$, $\eta(e_i) \notin I(u)$, so $\eta(e_i) \notin I(P')$.

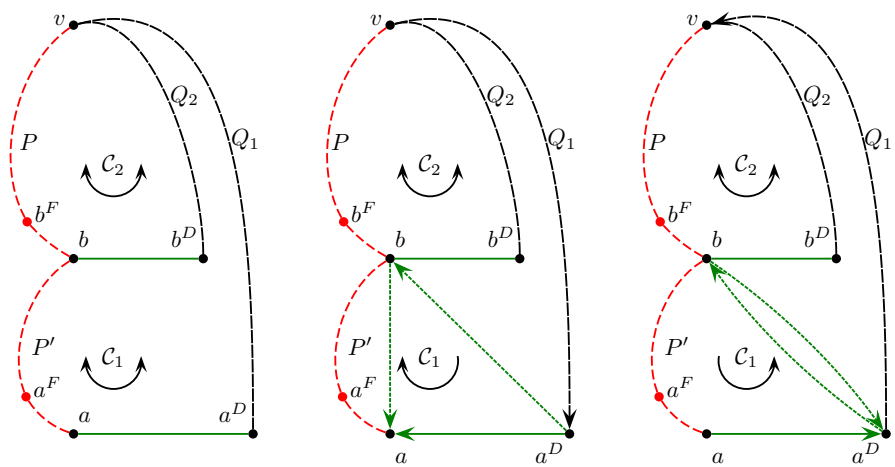
By Lemma 11, the cycle $\mathcal{C}$ cannot have more than two joints with the same value of η, since three joints cannot be pairwise consecutive when $\lambda \geq 5$. Thus we have $\lambda - 4 \leq 2|\{1, \ldots, m\} - I(P')| = 2(m - |I(P')|)$.

□

Bounding the number of cycles considered in Algorithm 2.

Lemma 13. *Let $w = v \cdot (v+1) \in W$, $\mathcal{C}_1$ and $\mathcal{C}_2$ be two cycles being considered during step 2 of Algorithm 2 ($\mathcal{C}_1$ being considered before $\mathcal{C}_2$), such that $w \in W(\mathcal{C}_1) \cap W(\mathcal{C}_2)$. Denote by a the low joint associated to w in $\mathcal{C}_1$, b the one associated to w in $\mathcal{C}_2$. Then either*
(1) $\eta(a) \neq \eta(b)$, or
(2) $\eta(a) = \eta(b)$, a is of type ii*, and a^D and b appear in the same block of the gene map $\eta(a)$.*

Proof. Vertices a and b are low joints associated to $w = v \cdot (v+1)$, so $a \leq v$ and $b \leq v$. Vertex $a^F = a \cdot (a+1)$ when $\mathcal{C}_1$ is being considered so it cannot appear in $\mathcal{C}_2$. Thus $a < b$, and consequently b^F appears in the path $a \to_F^* w$ or $w \to_F^* a$. In $\mathcal{C}_2$, we write P the path linking w and b in F, and Q_2 the path linking b^D and w in $F \cup D$ (see Fig. 9a). Depending on the type of b, we have



(a) Decomposition of $\mathcal{C}_1$ and $\mathcal{C}_2$ into arc and paths.

(b) First case (joint a is of type i)

(c) Second case (joint a is of type ii)

Figure 9: Path decomposition of $\mathcal{C}_1$ and $\mathcal{C}_2$ and case study for Lemma 13.

i $\mathcal{C}_2 = w \overset{Q_2}{\to}{}^* b^D \to_D b \overset{P}{\to}{}^* w$, or

ii $\mathcal{C}_2 = w \overset{P}{\to}{}^* b \to_D b^D \overset{Q_2}{\to}{}^* w$.

In $\mathcal{C}_1$, we write P' the path linking b and a in F, and Q_1 the path linking a^D and w in $F \cup D$. Thus, depending on the type of a, we have

i $\mathcal{C}_2 = w \overset{Q_1}{\to}{}^* a^D \to_D a \overset{P'}{\to}{}^* b \overset{P}{\to}{}^* w$, or

ii $\mathcal{C}_2 = w \overset{P}{\to}{}^* b \overset{P'}{\to}{}^* a \to_D a^D \overset{Q_2}{\to}{}^* w$.

Note that P can be followed in different ways in $\mathcal{C}_1$ and $\mathcal{C}_2$. We do not distinguish this case in the notations, since paths in F can always be followed in both ways.

We suppose, by contradiction, that $\eta(a) = \eta(b)$.

First case: a is a joint of type (i.). We use Lemma 9 with b and $a^D \to a$: there exists a path R in (Σ, D) from b to a or from a^D to b (see Fig. 9b). If $R = b \to^* a$, we define $\mathcal{C}' = a \overset{P'}{\to}{}^* b \overset{R}{\to}{}^* a$, then $\mathcal{C}'$ is a conflict-cycle (this is due to Lemma 3: $\mathcal{C}'$ cannot contain $a^F \to a$ but visits the vertices a and $a+1$, hence it contains an arc from X). Moreover, $W(\mathcal{C}') \subsetneq W(\mathcal{C}_1)$, hence $\mathcal{C}_1$ cannot be a minimal conflict-cycle. Similarly, if $R = a^D \to^* b$, then $\mathcal{C}' = b \overset{P}{\to}{}^* w \overset{Q_1}{\to}{}^* a^D \overset{R}{\to}{}^* b$ is a conflict-cycle and $\mathcal{C}_1$ is not a minimal conflict-cycle. Thus this first case is a contradiction to the fact that $\eta(a) = \eta(b)$.

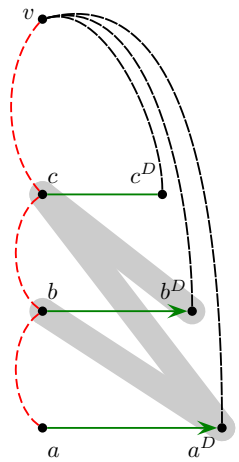


Figure 10: Illustration of Proof of Lemma 14. Vertices appearing in the same block of the gene map η are marked in gray.

Second case: a is a joint of type (ii.). We distinguish three sub-cases 2.1, 2.2 and 2.3 where, respectively, the path $b \xrightarrow{R}{}^* a^D$ exists in (Σ, D), the path $a^D \xrightarrow{R}{}^* b$ exists in (Σ, D), and a^D and b are incomparable in D (see Fig. 9b).

2.1 $R = b \rightarrow^* a^D$. We consider $\mathcal{C}' = b \xrightarrow{R}{}^* a^D \xrightarrow{Q_1}{}^* w \xrightarrow{P}{}^* b$. If Q_1 contains an arc from X, $\mathcal{C}'$ is a conflict-cycle. Otherwise, the only marked arc in $\mathcal{C}_1$ is necessarily $a \rightarrow_X a^D$, so $a > a^D$. Hence the path R in D uses at least one marked arc (since $b > a > a^D$), so $\mathcal{C}'$ is again a conflict-cycle. In both cases, it contradicts the fact that $\mathcal{C}_1$ is a minimal conflict-cycle.

2.2 $R = a^D \rightarrow^* b$. We consider $\mathcal{C}' = b \xrightarrow{P'}{}^* a \rightarrow a^D \xrightarrow{R}{}^* b$. If $a^D < a$, then $a \rightarrow a^D$ is in X, so $\mathcal{C}'$ is a conflict-cycle. Otherwise, since $\mathcal{C}_1$ is simple, $a^D > b > a$, R contains an arc from X, and $\mathcal{C}'$ is also a conflict-cycle. Again, $\mathcal{C}_1$ cannot be a minimal conflict-cycle.

2.3 a^D and b are incomparable in (Σ, D). Since they appear in the same gene map numbered $\eta(a) = \eta(b)$, they appear in the same block of this map.

□

Lemma 14. *Let $w = v \cdot (v+1) \in W$, $\mathcal{C}_1$, $\mathcal{C}_2$ and $\mathcal{C}_3$ three cycles being considered during step 2 of Algorithm 2 (in this order), such that $w \in W(\mathcal{C}_1) \cap W(\mathcal{C}_2) \cap W(\mathcal{C}_3)$. Denote respectively by a, b and c the low joints associated to w in $\mathcal{C}_1$, $\mathcal{C}_2$ and $\mathcal{C}_3$. Then we cannot have $\eta(a) = \eta(b) = \eta(c)$.*

Proof. Assume that $\eta = \eta(a) = \eta(b) = \eta(c)$. Then we use Lemma 13 with $(\mathcal{C}_1, \mathcal{C}_2)$, $(\mathcal{C}_1, \mathcal{C}_3)$ and $(\mathcal{C}_2, \mathcal{C}_3)$ successively, thus (see Fig. 10) :

- a^D and b appear in the same block of gene map η,
- a^D and c appear in the same block of gene map η,
- b^D and c appear in the same block of gene map η.

So, b and b^D both come from the same block of gene map η, which contradicts $\eta(b) = \eta$ (in the gene map $\eta(b)$, b and b^D appear in consecutive blocks).

□

Computing the Approximation Ratio.

Lemma 15. *Let $w \in W$ and let $\mathbb{C}$ be the set of all cycles considered during step 2 of Algorithm 2 going through w. Then the cardinality of the set of low joints in cycles of $\mathbb{C}$ is upper bounded by $m^2 + 4m - 4$.*

Proof. We write $w = v\cdot(v+1) \in W$, and $\mathbb{C} = \{\mathcal{C}_1, \ldots, \mathcal{C}_q\}$ the set of the q cycles considered, in this order, by Algorithm 2. In each cycle $\mathcal{C}_h$, $1 \leq h \leq q$, w can be associated to a low joint v_h and to the corresponding deleted vertex $w_h = v_h^F = v_h\cdot(v_h+1)$. We write P_h the path $w_h \rightarrow_F^* w$ or $w \rightarrow_F^* w_h$ in $\mathcal{C}_h$, and λ_h the number of joints of $\mathcal{C}_h$. Thus $\frac{\lambda_h}{2}$ is the number of low joints (and the number of deleted vertices) in this cycle.

Since w_h is deleted while $\mathcal{C}_h$ is being considered, for all $1 \leq h < h' \leq q$, $w_h \notin W(\mathcal{C}_{h'})$, and $v_h < v_{h'} \leq v$. Indeed, for any $u \in \{v_{h'}, \ldots, v\}$, the vertex $u\cdot(u+1)$ belongs to $W(\mathcal{C}_{h'})$, and $v_h, v_{h'} \leq v$. Finally, the path P_h uses each $v_{h'}$, $1 \leq h < h' \leq q$.

Consider now the list $(\eta(v_{h+1}), \eta(v_{h+2}), \ldots, \eta(v_q))$. Using Lemma 14, the same value cannot appear more than twice in this list, so it contains at least $\left\lceil \frac{q-h}{2} \right\rceil$ different values. The first consequence is $q \leq 2m$ (with $h = 0$, all values are in a set of size m). And since for all $h' \in \{h+1, \ldots, q\}$, $\eta(v_{h'}) \in I(P_h)$, we have $|I(P_h)| \geq \left\lceil \frac{q-h}{2} \right\rceil$.

Using Lemma 12 for all h, we obtain $\lambda_h \leq 2(m - |I(P_h)|) + 4$. We can thus bound the number of low joints in $\mathcal{C}_h$:

$$\frac{\lambda_h}{2} \leq \frac{2(m - |I(P_h)|) + 4}{2} = m - |I(P_h)| + 2 \leq m - \left\lceil \frac{q-h}{2} \right\rceil + 2$$

By Lemma 11, we also have that, for $m \geq 2$, $\lambda_h \leq 2m$. Let L_w be the

number of low joints in the cycles going via w:

$$\begin{aligned}
L_w &= \sum_{h=1}^{q} \frac{\lambda_h}{2} \\
&\leq \sum_{h=1}^{q} \min\left(m, m - \left\lceil \frac{q-h}{2} \right\rceil + 2\right) \\
&\leq \sum_{d=0}^{q-1} \min\left(m, m - \left\lceil \frac{d}{2} \right\rceil + 2\right) \\
&\leq \left(\sum_{d=0}^{2m-1} m - \left\lceil \frac{d}{2} \right\rceil + 2\right) - 4 \\
&\leq \left(\sum_{i=0}^{m-1} (m-i+2) + (m-i+1)\right) - 4 \\
&\leq 2m^2 - m(m-1) + 3m - 4 \\
&\leq m^2 + 4m - 4
\end{aligned}$$

thus $L_w \leq m^2 + 4m - 4$, which proves Lemma 15.

□

Theorem 16. *Algorithm 2 is an* $(m^2 + 4m - 4)$*-approximation of* AOG-Subset-FVS*, where* m *is the number of gene maps used to create the input graph.*

Proof. Correctness of Algorithm 2 follows from Corollary 7, since Algorithm 2 removes at least one vertex from each conflict-cycle. Let $W^o = \{w_1^o, \ldots, w_k^o\}$ be an optimal solution of size k. For each w_i^o, $1 \leq i \leq k$, Algorithm 2 deletes at most m^2+4m-4 adjacencies of W (by Lemma 15). Since every cycle considered by the algorithm goes through some w_i^o, the total size of the output solution is at most $k(m^2 + 4m - 4)$.

□

Corollary 17. *Using Algorithm 2 as an approximation for* AOG-Subset-FVS *in Algorithm 1 yields an* $(m^2 + 4m - 4)$*-approximation for the* MBL *problem.*

6. Conclusion

In this paper, we revisited the MBL problem with the aim of providing correct algorithms as replacement for those proposed in [6, 4], which were based on an inaccurate statement. We proposed a new graph G_Π to represent the conflicts between the given partial order Π and the reference genome Id_n, we characterized the cycles containing these conflicts, we showed how the MBL problem reduces to solving the AOG-Subset-FVS problem in G_Π, and we proposed three approximation algorithms. These algorithms allow us to approach a

given, practical instance of MBL from different viewpoints, by choosing the appropriate algorithm depending on the data at hand (i.e., whether the instance is created from few gene maps) and on the parameter evaluation (k and $|X|$). We also pointed out that MBL is **APX**-hard ; following this line, it would be interesting to know whether there exists a constant-ratio approximation algorithm for MBL (which would classify MBL as **APX**-complete). Another challenging question is whether MBL is Fixed-Parameter Tractable, notably when the parameter is the number m of gene maps that were used to construct the partial order Π.

References

[1] P. Alimonti and V. Kann. Hardness of approximating problems on cubic graphs. In G. C. Bongiovanni, D. P. Bovet, and G. Di Battista, editors, *CIAC*, volume 1203 of *LNCS*, pages 288–298. Springer, 1997.

[2] G. Blin, E. Blais, D. Hermelin, P. Guillon, M. Blanchette, and N. El-Mabrouk. Gene maps linearization using genomic rearrangement distances. *Journal of Computational Biology*, 14(4):394–407, 2007.

[3] L. Bulteau, G. Fertin, and I. Rusu. Revisiting the minimum breakpoint linearization problem. In J. Kratochvíl, A. Li, J. Fiala, and P. Kolman, editors, *TAMC*, volume 6108 of *Lecture Notes in Computer Science*, pages 163–174. Springer, 2010.

[4] X. Chen and Y. Cui. An approximation algorithm for the minimum breakpoint linearization problem. *IEEE/ACM Trans. Comput. Biology Bioinform.*, 6(3):401–409, 2009.

[5] G. Even, J. Naor, B. Schieber, and M. Sudan. Approximating minimum feedback sets and multi-cuts in directed graphs. In E. Balas and J. Clausen, editors, *IPCO*, volume 920 of *Lecture Notes in Computer Science*, pages 14–28. Springer, 1995.

[6] Z. Fu and T. Jiang. Computing the breakpoint distance between partially ordered genomes. *J. Bioinformatics and Computational Biology*, 5(5):1087–1101, 2007.

[7] C. Papadimitriou and M. Yannakakis. Optimization, approximation, and complexity classes. *J. Comput. Syst. Sci.*, 43(3):425–440, 1991.

[8] I.V. Yap, D. Schneider, J. Kleinberg, D. Matthews, S. Cartinhourb, and S.R. McCouch. A graph-theoretic approach to comparing and integrating genetic, physical and sequence-based maps. *Genetics*, 165(4):2235–2247, 2003.

[9] C. Zheng, A. Lenert, and D. Sankoff. Reversal distance for partially ordered genomes. In *ISMB (Supplement of Bioinformatics)*, pages 502–508, 2005.

[10] C. Zheng and D. Sankoff. Genome rearrangements with partially ordered chromosomes. In L. Wang, editor, *COCOON*, volume 3595 of *Lecture Notes in Computer Science*, pages 52–62. Springer, 2005.