Algorithms for the Constrained Perfect Phylogeny with Persistent Characters

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Abstract. The perfect phylogeny is one of the most used models in different areas of computational biology. In this paper we consider the problem of the Persistent Perfect Phylogeny (referred as P-PP) recently introduced to extend the perfect phylogeny model allowing persistent characters, that is characters can be gained and lost at most once. We define a natural generalization of the P-PP problem obtained by requiring that for some pairs (character, species), neither the species nor any of its ancestors can have the character. In other words, some characters cannot be persistent for some species. This new problem is called Constrained P-PP (CP-PP). Based on a graph formulation of the CP-PP problem, we are able to provide a polynomial time solution for the CP-PP problem for matrices having an empty conflict-graph. In particular we show that all such matrices admit a persistent perfect phylogeny in the unconstrained case. Using this result, we develop a parameterized algorithm for solving the CP-PP problem where the parameter is the number of characters. A preliminary experimental analysis of the algorithm shows that it performs efficiently and it may analyze real haplotype data not conforming to the classical perfect phylogeny model.

1 Introduction

The perfect phylogeny is one of the most investigated and used models in several applications where a coalescent model is required for analyzing genomic data. Conceptually the model is based on the infinite sites assumption, that is no character can mutate more than once in the whole tree. While this assumption is quite restrictive, the perfect phylogeny model turned out to be splendidly coherent within the haplotyping problem \cite{3,9}, where we want to distinguish the two haplotypes present in each individual when given only genotype data. More precisely, the interest here is in computing a set of haplotypes and a perfect phylogeny such that the haplotypes (i) label the vertices of the perfect phylogeny and (ii) explain the input set of genotypes. This context has been deeply studied in the last decade, giving rise to a number of algorithms \cite{1,5}.

In the general framework, the model is used to reconstruct the evolution of species (taxa) characterized by a set of binary characters that are gained and/or lost during the evolution. Characters can take only the states 0 or 1, usually interpreted as the presence or absence of the character. Restrictions on the type of changes from zero to one and vice versa lead to a variety of specific models \cite{6}.

Still, the perfect phylogeny model and the assumptions that have been central in the previous decades cannot be employed without adaptations or improvements. In fact, this model is too restrictive to explain the biological complexity of real data, where homoplasy events (such as recurrent mutations or back mutations) are present. Thus a central goal in this model is to extend its applicability, while retaining the computational efficiency. The problem of constructing phylogenies where the deviations from perfect phylogeny are small has been tackled for example in \cite{7} under the name of near perfect phylogeny. In particular, the near perfect phylogeny haplotyping problem has been explored in \cite{15}. Especially the impossibility of losing a character that has been previously acquired turned out to be too restrictive, resulting in more elaborated models, such as the notion of persistent character \cite{14} and the General Character Compatibility \cite{11}.
Following the research direction proposed in [14] to investigate the dynamics of protein interactions, the Persistent Perfect Phylogeny problem has been introduced [2] to address the computational problem of constructing a perfect phylogeny under the assumption that only a special type of back mutation may occur in the tree: a character may change state at most twice in the tree: once from 0 to 1, and (maybe) once from 1 to 0.

In the paper we consider a natural generalization of the P-PP problem, called Constrained P-PP problem (CP-PP), that is obtained by adding a constraint for some characters in the input data, given by the fact they cannot be persistent in some species. Then we explore algorithmic solutions for the CP-PP problem as well as for the restricted case of the P-PP problem.

Since our main aim is to find algorithmic solutions, following the approach in [2], we first explore a graph formulation of the CP-PP problem, called Red-black graph reduction based on the equivalence of P-PP to a problem of completing a matrix where each character $c$ has two columns $c^+, c^-$, with $c^+$ $(c^-)$ equal to 1 in a species $s$ in the matrix corresponds to the fact that $s$ has gained (lost) the character $c$. Based on the above graph formulation, we prove that there exists a class of binary matrices that always admit a positive solution for the P-PP problem, that is they admit a persistent perfect phylogeny. For this special case we also provide a polynomial algorithm that works for the general CP-PP problem. Based on this polynomial time algorithm we show that CP-PP is fixed parameter tractable in the number of characters and propose a branch and bound based algorithm, called Decide-pp-opt.

The algorithms and models discussed in the paper may have interesting applications in the construction of evolutionary trees based on the analysis of binary genetic markers, where variants of the perfect phylogeny have already been considered, such as in the study of evolution based on introns [14] or progression pathways using tumor markers or in discovering significant associations between phenotypes and single-nucleotide polymorphism markers [12] and also in haplotype analysis. In the paper we have run a preliminary experimental analysis aimed to show the applicability of our algorithm for the CP-PP model to deal with biological data (binary characters) incorporating recombination events. The results show that the algorithm performs efficiently on simulated matrices as well as on real data. The algorithm applied to haplotypes taken from the HapMap project is able to detect in binary matrices characters that may be persistent, whenever they do not obey the standard perfect phylogeny model.

Finally, we observe that the CP-PP problem (P-PP problem) is equivalent to cases of the General Character Compatibility problem (GCC) investigated in [11] whose complexity is still open. Thus our results also apply to those problems.

## 2 The persistent perfect phylogeny and the red-black graph reduction problem

In this section we present the persistent perfect phylogeny problem and its constrained version. We show that the CP-PP problem reduces to a graph problem, the red-black graph reduction problem: this result generalizes the Theorem [12] given in [2] to the constrained persistent perfect phylogeny problem.

In this paper the input is an $n \times m$ binary matrix $M$ whose columns are associated with the set $C = \{c_1, \ldots, c_m\}$ of characters and whose rows are associated with the set $S = \{s_1, \ldots, s_n\}$ of species. Then $M[i, j] = 1$ if and only if the species $s_i$ has character $c_j$, otherwise $M[i, j] = 0$. The gain of a character $c$ in a phylogenetic tree is represented by an edge labeled by the character $c^+$. In order to model the presence of persistent characters, the loss of a character $c$ in the tree is represented by an edge that is labeled by the negated character, labeled by $c^-$. Formally, we define the persistent perfect phylogeny model as follows [2][16].

**Definition 1 (Persistent Perfect Phylogeny).** Let $M$ be an $n \times m$ binary matrix. Then a persistent perfect phylogeny, in short p-pp, for $M$ is a rooted tree $T$ such that:

1. each node $x$ of $T$ is labeled by a vector $l_x$ of length $m$;
2. the root of $T$ is labeled by a vector of all zeroes, while for each node $x$ of $T$ the value $l_x[j] \in \{0, 1\}$ represents the state of character $c_j$ in tree $T$;
3. each edge $e = (u, v)$ is labeled by at least a character;
4. for each character $c_j$ there are at most two edges $e = (x, y)$ and $e' = (u, v)$ such that $l_x[j] \neq l_y[j]$ and $l_u[j] \neq l_v[j]$ (representing a change in the state of $c_j$). In that case $e, e'$ occur along the same path from the root of $T$ to a leaf of $T$; if $e$ is closer to the root than $e'$, then $l_x[j] = l_v[j] = 1$, $l_u[j] = l_y[j] = 1$ and the edge $e$ is labeled $c_j^+$, while $e'$ is labeled $c_j^-$;
5. each row $r$ of $M$ labels exactly one node $x$ of $T$. Moreover the vector $l_x$ is equal to the row $r$.

Let us state the main problems investigated in the paper.

The Persistent Perfect Phylogeny problem (P-PP): Given a binary matrix $M$, returns a p-pp tree for $M$ if such a tree exists.

A natural generalization of the P-PP problem is obtained by considering as input data a pair $(M, E^*)$, called constrained matrix where $M$ is a matrix over binary alphabet and $E^* = \{(i_1, j_1), \ldots, (i_k, j_k)\}$ is a set of 0-entries of $M$. Now a p-pp tree $T$ for matrix $M$ is consistent with $E^*$ if and only if $(i, j) \in E^*$ means that character $c_j$ is absent in species $s_i$ and cannot be gained and then lost in the species $s_i$ in tree $T$, that is $c_j$ is not persistent in species $s_i$.

The Constrained Persistent Perfect Phylogeny problem (P-PP): Given a constrained matrix $(M, E^*)$, returns a p-pp tree $T$ for $M$ if such a tree exists, such that tree $T$ is consistent with $E^*$.

Another fundamental observation is that we can restate the CP-PP problem as variant of the Incomplete Direct perfect Phylogeny [13].

Definition 2 (Extended Matrix). Let $(M, E^*)$ be an instance of the CP-PP problem. The extended matrix associated with $M$ is an $n \times 2m$ matrix $M_e$ over alphabet $\{0, 1, ?\}$ which is obtained by replacing each column $c$ of $M$ by a pair of columns $(c^+, c^-)$. Moreover for each row $s$ of $M$ if $M[s, c] = 1$, then $M_e[s, c^+] = 1$ and $M_e[s, c^-] = 0$, while if $M[s, c] = 0$ and $(s, c) \notin E^*$, then $M_e[s, c^+] = ?$ and $M_e[s, c^-] = ?$, otherwise $M_e[s, c^+] = 0$ and $M_e[s, c^-] = 0$.

In this case the characters $(c^+, c^-)$ are called conjugate. Informally, the assignment of the conjugate pair $(?, ?)$ in a species row $s$ for two conjugate characters $(c^+, c^-)$ means that character $c$ could be persistent in species $s$, i.e., it is first gained and then lost. On the contrary, the pair $(1, 0)$ means that character $c$ is only gained by the species $s$. Finally, the pair $(0, 0)$ means that character $c$ is never gained by the species $s$. A completion of a pair $(?, ?)$ associated to a species $s$ and characters $(c^+, c^-)$ of $M_e$ consists of forcing $M_e[c^+, s] = M_e[c^-, s] = 0$ or $M_e[c^+, s] = M_e[c^-, s] = 1$.

A (partial) completion $M_e$ is a completion of some of its conjugate pairs. A fundamental result states that $M$ admits a persistent phylogeny if and only if there exists a completion of $M_e$ admitting a directed perfect phylogeny [2]. Now, the same result holds when the input is a constrained matrix $(M, E^*)$. In fact, if $(M, E^*)$ admits a solution, it means that it is possible to build a p-pp tree $T$ where each $(i, j)$ in $E^*$ implies that $c_j$ is not persistent in species $s_i$ of tree $T$. As a consequence of this fact, there exists a completion of $M_e$ where $M_e[c_j^+, s_i] = M_e[c_j^-, s_i] = 0$. Moreover, by interpreting a conjugate pair of characters as characters of $M_e$ is immediate to verify that tree $T$ is a directed perfect phylogeny for $M_e$. Vice versa, given an extended matrix $M_e$ that admits a perfect phylogeny $T$, then it is possible to show that $T$ is a persistent phylogeny for $M$. This fact is an immediate consequence of definition 2 and the result in 2.

2.1 The conflict graph and red-black graph reduction

Let $M$ be a binary matrix. Given two characters $c_1$ and $c_2$, the configurations induced by the pair $(c_1, c_2)$ in matrix $M$ is the set of ordered pairs $(M[s, c_1], M[s, c_2])$ over all species $S$. Two characters $c_1$ and $c_2$ of $M$ are conflicting if and only if the configurations induced by such pair of columns is the set of all possible pairs $(0, 1), (1, 1), (1, 0)$ and $(0, 0)$. Notice that being in conflict is a symmetric relation, therefore we can define the conflict graph $G_c = (C, E_c \subseteq C \times C)$ of a matrix $M$, where a pair $(c_i, c_j) \in E_c$ if and only if $c_i$ and $c_j$ are conflicting in $M$. Notice that a conflict graph with no edges (called empty) does not necessarily imply the existence of a rooted perfect
phylogeny, because of the occurrence of the forbidden matrix with only the three configurations
\((1,1), (1,0)\) and \((1,0)\). However, by allowing a character to be persistent, the matrix admits a
rooted persistent perfect phylogeny. We also need some graph-theoretic definitions. A graph is
called edgeless if it has no edges. A connected component is called nontrivial if it has more than
one vertex.

|     | \(c_1\) | \(c_2\) | \(c_3\) | \(c_4\) | \(c_5\) |
|-----|--------|--------|--------|--------|--------|
| \(s_1\) | 0      | 0      | 0      | 1      | 0      |
| \(s_2\) | 0      | 0      | 1      | 1      | 1      |
| \(s_3\) | 0      | 1      | 1      | 0      | 0      |
| \(s_4\) | 1      | 1      | 0      | 0      | 0      |
| \(s_5\) | 1      | 1      | 1      | 0      | 1      |

\[
\begin{array}{ccccc}
C_1 & C_2 & C_3 & C_4 & C_5 \\
\end{array}
\]

Fig. 1. A matrix and its conflict graph

The first step is to simplify, if possible, the instance. In fact we can always remove duplicate
rows or columns. Moreover a character \(c\) is called universal if all species have \(c\), while \(c\) is called
void if no species has \(c\). Again, we can always start by removing void characters. In the rest of
the paper, by an extended matrix \(M_e\) we mean a matrix that may be partially or fully completed.

Besides the conflict graph, we introduce a second graph, called red-black graph and denoted by
\(G_{RB}\), which will be fundamental in our algorithm.

**Definition 3 (Red-black graph).** Let \(M_e\) be an extended matrix. Then the red-black graph
\(G_{RB} = (V, E)\) associated to \(M_e\) is the edge-colored graph where (i) the vertices are the species and
the conjugate pairs of \(M_e\) (that is for each two conjugate characters \(c^+\) and \(c^-\), only \(c\) is a vertex of
\(G_{RB}\)), (ii) a pair \((s, c)\) is a black edge iff the conjugate pairs \(c^+\) and \(c^-\) are still incomplete in matrix
\(M_e\) and \(M_e[s, c^+] = 1\) and \(M_e[s, c^-] = 0\), (iii) \((s, c)\) is a red edge iff \(M_e[s, c^+] = M_e[s, c^-] = 1\).

2.2 Realizing characters in a red-black graph

In the following we describe some completions of conjugate pairs of an extended matrix \(M_e\) that
can be expressed as graph operations over the red-black graph \(G_{RB}\) associated to the extended
matrix. Let \((c^+, c^-)\) be two conjugate characters of \(M_e\), and let \(C(c)\) be the connected component
of \(G_{RB}\) containing the vertex \(c\). Given a partially completed matrix or, equivalently, a red-black
graph, a character is in one of three possible states: inactive (the initial state of all characters),
active, and free. The realization of a character \(c\) in \(G_{RB}\) consists of the following steps:

1. if \(c\) is inactive and for all species \(s \in C(c)\), \(M_e[s, c^+] = M_e[s, c^-] \neq 0\) then:
   (a) for each species \(s \notin C(c)\), pose \(M_e[s, c^+] = M_e[s, c^-] = 0\);
   (b) for each species \(s \in C(c)\) if \((c, s)\) is not an edge of \(G_{RB}\), add a red edge \((c, s)\) and complete
      \(M_e\) by posing \(M_e[s, c^+] = M_e[s, c^-] = 1\);
   (c) remove from \(G_{RB}\) all black edges \((c, s)\) and label \(c\) active.
2. else if \(c\) is active and \(c\) is connected by red edges to all species in \(C(c)\), then:
   (a) all such red edges are deleted from \(G_{RB}\) and \(c\) is labeled free;

In some cases \((c\) is free, or \(c\) is active but there exists a species \(s \in C(c)\) that is not connected to
\(c\) by a red edge, or \(c\) is inactive but persistent for a species \(s \in C(c)\), i.e. \(M_e[s, c^+] = M_e[s, c^-] = 0\)
none of the stated conditions hold, therefore the realization is impossible. Notice that realizing
a character corresponds to a partial completion of the matrix \(M_e\) that is called the canonical
completion of \(c\) in \(M_e\), which in turn corresponds to the construction of a standard tree, as follows.
Definition 4 (Standard tree). Let $M_e$ be an extended matrix, then a standard $p$-pp solving $M_e$ has the following additional properties:

1. some edge $e = (v, w)$ may not be labeled by any character. In this case $l_v = l_w$;
2. no internal node has more than one child that is a leaf;
3. each leaf is incident on an unlabeled edge;
4. each species labels a leaf $x$ of $T$ and the parent of $x$ in $T$;
5. each internal node $x$ is labeled with the set $S(x)$ of species and with the set $C(x)$ of characters appearing in the subtree $T(x)$ of $T$ rooted at $x$;
6. some nodes $x$ are also labeled by a red-black graph $G_{RB}(x)$ defined as follows. The graph associated to the root $r$ is the red-black graph associated to the extended matrix $M_e$ and where all vertices are inactive. Each other node $x$ might be labeled by the connected components of the red-black graph having species and characters of tree $T(x)$ and obtained from graph $G_{RB}(r)$ realizing in sequence all characters (active or inactive) labeling the edges on the path from $r$ to $x$ in $T$.
7. Each internal node $x$ is labeled with the conflict graph $G_c(x)$ computed on the submatrix of $M_e$ induced by the columns and rows in $C(x)$ and $S(x)$.
8. Each subtree rooted at a node $y$ of $T$ whose parent $x$ is labeled by the red-black graph $G_{RB}(x)$ has species $S(y)$ and characters $C(y)$ such that $S(y) \cup C(y)$ is a union of connected components of $G_{RB}(x)$.
9. Let $x$ be a node such that the red-black graph $G_{RB}(x)$ has connected components $C_1, \ldots, C_k$ with $k > 1$ (i.e., $G_{RB}$ is disconnected). Then $x$ has $k$ children $x_1, \ldots, x_k$, where $S(x_i) \cup C(x_i) = C_i$ and each edge $(x, x_i)$ are not labeled by any character.

It is easy to show that given a generic $p$-pp tree solving a matrix $M_e$, we can modify it to satisfy the properties from 1 to 7 of a standard tree. In fact, these properties are obtained by adding a labeling of nodes and leaves of the tree (see 4-5-6-7) or are obtained by assuming that there are not any identical rows (see 2) or by adding additional edges (see 3). Consequently, when proving that a $p$-pp tree is standard, we need to prove that properties 8-9 hold under the assumption that the tree is in the form specified by properties 1-7.

Fig. 2. Figures (a) and (b) illustrates the realization of a character in a red-black graph associated to an extended matrix. The canonical completion of the extended matrix after the graph operations is shown for the characters $c_4$ (a) and $c_3$ (b).

The following property of a standard tree is central in characterizing matrices $M_e$ that do not have a solution.

Property 5. Let $T$ be a standard tree for an extended matrix $M_e$ and let $x$ be a node of $T$. Then the red-black graph $G_{RB}(x)$ that labels $x$ does not contain an induced simple path starting from a species vertex and consisting of four red edges (such an induced graph is called red $\Sigma$-graph).
Since a red-black graph $G_{RB}$ implicitly induces a submatrix $M_1$ of $M$ whose rows and columns are the species and characters of $G_{RB}$, we can define the the conflict graph induced by $G_{RB}$ as the conflict graph on such submatrix $M_1$. Observe that for every descendant $x$, of node $x$, then by Definition 4 of standard tree, there will be a connected component of $G_{RB}(x)$ whose species are exactly those of $T(x)$. Moreover, given an internal node $x$ of a tree $T$, the label sequence of $x$ is the sequence of characters of the edges on the unique path from the root of $T$ to $x$. Then we associate to $x$ the matrix $M_c(x)$ that is the partially completion of $M_c$ according to the label sequence of $x$ where only the rows and columns corresponding to vertices of $G_{RB}(x)$ are retained.

**Property 6.** Let $G_{RB}(x)$ be the red-black graph associated to a node $x$, let $c$ be any character of $G_{RB}(x)$, let $c^+$ be the edge of $T$ labeled by $c^+$ and let $c^−$ be the edge of $T$ labeled by $c^−$ (if it exists). By construction of the red-black graph, only three cases are possible:

1. $c$ is inactive, all edges of $G_{RB}(x)$ that are incident on $c$ are black, and $c^+$ does not belong to the label sequence of $x$;
2. $c$ is active, all edges of $G_{RB}(x)$ that are incident on $c$ are red, moreover $c^+$ belongs to the label sequence of $x$, but $c^−$ does not;
3. $c$ is free, $c$ is an isolated vertex of $G_{RB}(x)$.

Using the stated properties we can prove the characterization stated in Theorem 12 used to test the existence of a solution of the CD-PP problem. We discover that the Theorem builds upon an analogous characterization for the P-PP problem, stating that an extended matrix $M_e$ has a perfect phylogeny (i.e., a pp tree) if and only if it has a standard tree. Moreover a standard tree represents a canonical completion of all characters of the matrix, i.e. the realization of a sequence of all characters, called $c$-reduction that leads to an edgeless red-black graph (see Definition 9 given below).

**Lemma 7.** Let $M_e$ be an extended matrix admitting a perfect phylogeny. Then there exists a perfect phylogeny $T$ realizing $M_e$ such that for each node $x$ of $T$ and for each character $c_1$, if $c_1$ is adjacent to two species $s_1, s_2$ in $G_{RB}(x)$, then $s_1, s_2$ are either both in $T(x)$ or none of them is in $T(x)$, where $G_{RB}(x)$ is the red-black graph obtained by realizing the label sequence of $x$ from the red-black graph associated to $M_e$.

Now Lemma 4 is used to prove the following lemma, first proved in [2], showing that when an extended matrix admits a solution, than it must have a standard tree. Moreover its proof establishes a correspondence between a standard tree and the red-black graphs associated to nodes. More precisely, given a standard tree $T$, such a tree represents the canonical completion of $M_e$ that we obtain by visiting tree $T$ and realizing characters of visited edges of tree $T$ in the red-black graph for $M_e$. Then, when reaching a node $x$ of $T$ by visiting tree $T$, the red-black graph $G_{RB}(x)$ represents the species and characters that still have to be completed in the extended matrix.

**Lemma 8.** Let $M_e$ be an extended matrix admitting a p-pp tree. Then, there exists a completion of $M_e$ that is realized by a standard tree $T$.

Consider an extended matrix $M_e$ that has been completed and $M_e$ admits a standard tree $T$. Let us consider the sequence of character corresponding to a depth-first visit of $T$ and the corresponding red-black graph $G_{RB}$ obtained from $G_{RB}$ by realizing all characters in the visit. First of all, notice that $G_{RB}$ cannot contain any black edges, for otherwise we would immediately contradict the hypothesis that $T$ solves $M_e$. Moreover we can prove that $G_{RB}$ cannot contain any red edge $(c, s)$. Assume to the contrary that such an edge exists. Since $T$ solves $M_e$, the path of $T$ from the root to the leaf labeled by $s$ contains the edge labeled by $c^+$ and the one labeled by $c^−$. Let $(x, y)$ be the edge labeled by $c^−$. By point 9 of Definition 4 the red-black graph $G_{RB}(y)$ is connected, therefore all red edges connecting $c$ and a leaf of $T(y)$ are deleted. Since $s$ is a leaf of $T(y)$, the red edge $(c, s)$ is deleted.
Definition 9. Let $G_{RB}$ be a red-black graph for an extended matrix $M_e$ and let $R$ be a sequence of characters such that each negative character $c^-$ appears after the corresponding positive character $c^+$, and all characters of $G_{RB}$ appear in $R$. Then $R$ is a successful $c$-reduction of $G_{RB}$ if and only if all single character realization of $R$ are possible and the graph reduced by $R$ has no edge. Then we say that $M_e$ is solvable.

Lemma 10. Let $T$ be a standard tree that solves a matrix $M$ and let $V$ be the sequence of characters labeling the edges of $T$ according to a depth-first visit. Then $V$ is a successful $c$-reduction of $M_e$.

By Lemma 10 a standard tree is represented by a canonical completion of all characters, i.e. a $c$-reduction that leads to an edgeless red-black graph. Now we can show that having such a edgeless red-black graph is not only a necessary but a sufficient condition for having a canonical completion admitting a tree.

We have shown that an extended matrix admits a persistent phylogeny if and only if it has a directed perfect phylogeny. Since the matrices admitting a perfect phylogeny are those that do not contain a forbidden submatrix [8], we know that an extended matrix admits a persistent phylogeny if and only if there exists a completion such that no forbidden matrix induced by two negated characters, two positive characters, or one of each kind, is induced by the completion. Let us show that having an edgeless red-black graph due to a successful reduction implies that the associated canonical completion $M'$ of $M_e$ has no forbidden matrix. First, observe that no forbidden matrix between two positive characters in $M'$ is possible, since completing or realizing two characters $c_1^+$ and $c_2^+$ that are in the same connected component of the red-black implies a containment relation between the two characters (note that two characters in disjoint components of the red-black graph cannot be connected during the successful $c$-reduction). Finally, observe that the only way to have red-edges in a reduced graph is with a path of length four in the graph, i.e., the red $\Sigma$-graph, corresponding to the forbidden matrix induced by negative characters. Notice that if a red-black graph has only red edges and a red $\Sigma$-graph is forbidden, then the graph must be edgeless.

Theorem 11. Let $M$ be a binary matrix and let $M_e$ be the extended matrix associated with $M$ such that its associated red-black graph admits a successful $c$-reduction. Then $M_e$ is solvable by a standard tree.

Lemmas 11 and 10 allow to generalize the Theorem initially proved in [2] for the P-PP problem.

Theorem 12. Let $M_e$ be an instance of the CP-PP problem. Then $M_e$ is solvable if and only if there exists a successful $c$-reduction for the red-black graph $G_{RB}$ associated to $M_e$.

Therefore we only need to find a successful $c$-reduction; if none exists, then the initial instance has no solution. Finally, observe that the property 8 and 9 of a standard tree imply that we need to find a successful $c$-reduction for each connected component of the red-black graph, and any concatenation of those successful $c$-reductions on a single component gives a successful $c$-reduction for the whole graph.

3 Solving the CP-PP problem in polynomial time on matrices with empty conflict graphs

In the following, by using properties of the red-black graph, we show that a persistent perfect phylogeny always exists for a matrix $M$ that has an empty conflict graph. The main characterization given by Theorem 12 is used to solve the CP-PP problem, since we design a procedure that finds a successful $c$-reduction of the red-black graph associated to the extended matrix for $M$.

Given $M$ a binary matrix, the partial order graph for $M$ is the partial order $P$ obtained by ordering columns of $M$ under the $<$ relation which is defined as follows: character $c < c'$ if and only if $M[s,c] \leq M[s,c']$ for each species $s$, otherwise we say that $c$ and $c'$ are not comparable. Moreover, we build a graph $G = (V,E)$, called adjacency graph for $M$: $V$ is the set of columns of
Let \((u, v)\) be an edge of \(G\) if and only if \(u, v\) are adjacent, i.e. there is a species \(s\) that is adjacent to both \(u\) and \(v\) in the red-black graph for the extended matrix \(M_e\) associated with \(M\). Then the following result holds.

**Lemma 13.** Let \(M\) be a binary matrix with an empty conflict graph. Assume that the extended matrix associated with \(M\) induces a connected red-black graph and let \(P\) be the partial order graph for \(M\). Let \(C_M\) be the set of maximal elements in \(P\). Then \(C_M\) consists of elements that are pairwise adjacent in the adjacency graph.

**Lemma 14.** Let \(M\) be a binary matrix that has an empty conflict graph. Let \(G_{RB}\) be the red-black graph for the extended matrix associated with \(M\). The realization of two characters \(a\) and \(b\) that are adjacent in the adjacency graph for \(M\) produces at most two red disjoint components, one with only vertex \(a\) and the other with only vertex \(b\).

The above Lemma 14 combined with Lemma 13 implies that maximal characters can be realized in an arbitrary order and are crucial to prove the following Theorem.

**Theorem 15.** Let \(M\) be a binary matrix that has an empty conflict graph. Then \(M\) admits a persistent perfect phylogeny \(T\) and there exists a polynomial time algorithm to compute \(T\).

If we consider a constrained matrix \((M, E^*)\) where \(E^* \neq \emptyset\) and having an empty conflict graph, the CP-PP problem might not have a solution for \((M, E^*)\) since some characters cannot be realized. In fact, if all characters are not persistent, we obtain the classical perfect phylogeny problem, and even this problem might not have a solution when the conflict graph is empty, since the matrix \((M, E^*)\) could contain the forbidden matrix. However, Lemmas 13 and Theorem 12 allow to prove the correctness of the following procedure that can be used to solve the CP-PP in polynomial time in the case of empty conflict graph. In fact, the two Lemmas hold also for constrained matrices \((M, E^*)\) (see proof in the Appendix).

**Procedure Solve-CP-PP-empty-conflict\((M, E^*)\)**

*Input:* a constrained binary matrix \((M, E^*)\) that has an empty conflict graph.

*Output:* a realization \(S_c\) of characters to successfully reduce graph \(G_{RB}\).

- Build the partial order \(P\) for \(M\); let \(G_{RB}\) be the red-black graph for the extended matrix for \(M\).
- let \(C_M\) be the set of all maximal elements in \(P\) that are in the same connected component of the red-black graph \(G_{RB}\); then realize in an arbitrary order those characters in \(C_M\) that can be realized. Repeat the step till all characters have been realized. Otherwise, return *no solution*.

Now, the correctness of the algorithm for the CP-PP problem is again a consequence of the fact that maximal characters can be realized in an arbitrary order and the fact that maximal characters are realized before characters they include by the \(<\)-relation. This fact relies on the observation that if \(c < c'\) and \(c'\) is not persistent in a species \(s\), then also \(c\) is not persistent in the same species. In fact, if \(c'\) occurs in the p-pp tree after \(c\) then, assuming that \(c\) is persistent in a species \(s\), also \(c\) must be persistent in the same species, since \(c'\) occurs before the negated character \(c^-\). Otherwise, if \(c'\) occurs in the tree before \(c\), then all species below \(c^+\) and the negated character \(c^-\) are also in \(c\), thus forbidding to have \(c\) persistent in the same species of \(c\). The correctness of the algorithm is proved in the Appendix.

## 4 An optimized algorithm

In this section we propose an algorithm for the CP-PP problem called **Decide-pp-opt** that is based on the procedure **Solve-CP-PP-empty-conflict\((M)\)**. Just as the algorithm in [2], **Decide-pp-opt** reduces an instance \(M\) of P-PPH to an instance \(M_e\) of the IP-PPH problem. In fact, we know that \(M_e\) admits a pph tree \(T\) if and only if \(T\) is a solution of matrix \(M\). Then, by Theorem 12 \(M_e\) admits a pph tree \(T\) if and only if there exists a successful \(c\)-reduction of the red-black graph...
for $M_r$. The algorithm in [2] explores all permutations of the set $C$ of characters of $M_r$ in order to find one that is a successful c-reduction, if it exists. On the other hand, **Decide-pp-opt** builds a decision tree, where each edge represents a character and each path of the tree from the root to a leaf is a permutation $I(C')$ of a subset $C'$ of the set $C$ of characters such that the realization of $I(C')$ makes the conflict-graph induced by the red-black graph empty. Thus **Decide-pp-opt** strongly relies on the polynomial time solution of the P-PP problem in the case the conflict-graph is empty. The algorithm works in a branch and bound like manner, in the sense that if a branch of the decision tree ending in node $x$ does not lead to a solution, then the decision tree below $x$ is discarded. More precisely, each branch ending in node $x$ gives a partial permutation $\pi$ that consists of all characters labeling the path from root $r$ to node $x$. A partial completion $M_x$ is computed by realizing characters provided by the partial permutation $\pi$. Whenever $M_\pi$ contains the forbidden matrix, then the branch ending in $x$ does not lead to a solution, and $x$ is labeled as a fail node. The algorithm either finds the first permutation of characters that provides a successful c-reduction of the red-black graph for the extended matrix, if it exists, or will decide that the matrix does not admit a pph tree by visiting the whole decision tree.

Let us describe the recursive procedure **Decide-pp-opt** which is initial invoked as **Decide-pp-opt** $(M, M_r, r, \{r\})$, where $r$ is the root of the decision tree and the visited tree is the set $\{r\}$.

**Algorithm Decide-pp-opt**($M, M', x, T$)

*Input*: a binary constrained matrix $(M, E^*)$ of size $n \times m$, the set $E^*$ of constraints, a partial depth-first visit tree $T'$ of the decision tree $T$ and a leaf node $x$ of $T$, a partial completion $M'$ of the extend matrix $M_e$ obtained by the realization of the characters labeling a path $\pi$ from $r$ to node $x$ of the tree $T'$;

*Output*: the tree $T'$ extended with the depth-first visit of $T$ from node $x$. The procedure eventually outputs a successful c-reduction $r$ or fails to find such a successful c-reduction.

- Step 1: if the edge incident to node $x$ is labeled $c$ and $c$ is admissible, then realize $c$ in $G_{RB}$ and complete the pair of columns $(c, c')$ in $M'$. If the matrix $M'$ has a forbidden matrix, then label $x$ as a fail node. If $x$ is a leaf node, then mark $x$ as a successful node and output the permutation labeling the path from the root $r$ of tree $T$ and the leaf $x$ of $T'$.
- Step 2: compute the conflict graph $G_c$ for the matrix $M$, updated after the realization of the characters along the path $\pi$ from the root $r$ to node $x$ (i.e. $M$ is obtained after eliminating the rows that correspond to species-nodes that are singletons in $G_{RB}$).
- Step 3: if the conflict graph $G_c$ is empty, then apply the polynomial-time algorithm for an empty conflict graph and return a successful c-reduction, if it exists. Else for each node $x_i$ that is a child of node $x$ in tree $T'$ and is labeled by a non-active character in $G_{RB}$, apply Decide-pp-opt($M, M', x_i, T' \cup \{x_i\}$).

Notice that testing whether a character may be realized in a connected component of the red-black graph $G_{RB}$ requires time that is linear in the number of species of the component. Clearly, the algorithm requires to compute the connected components of $G_{RB}$, which can be done in time $O(f(n, m))$, where $f(n, m)$ is polynomial in the size of graph $G_{RB}$. Consequently, the time required to evaluate a single path of the tree is $O(f(n, m)m)$, since the path may have $m$ characters to be realized and completed. The total number of explored paths is clearly equal to the number of permutations of set $C$ of characters on the input matrix, in the worst case.

5 Experimental analysis

We have implemented the algorithm **Decide-pp-opt** and tested it over simulated data produced by the tool ms by Hudson [10] and on real data coming from the International HapMap project, a multi-country research to identify and catalog genetic similarities and differences in human beings [4]. The main goal of these preliminary experiments has been to test the average running time when the number of rows and columns increase, since we wanted to test the applicability of the method on matrices of given sizes. The experimental analysis on real haplotype data aims to
investigate the use of the persistent model to detect haplotypes data that cannot be explained by the perfect phylogeny model but can exhibit persistent characters.

We have implemented the algorithm in C++ and the experiments have been run on a standard Windows workstation with 4 GB of main memory.

The results of a first experiment are reported in Table 1. The table reports the computation time to solve sets of 50 matrices for each dimension 50 × 15—i.e., 50 species and 15 characters—100 × 15, 200 × 15, and 500 × 15 with a recombination rate 1/15. The sets contain only matrices that are solved within five minutes. Clearly, the number of unsolved matrices increases with the size of the input matrices but also with the number of conflicts that are present in the conflict graph.

The table also reports the results obtained by comparing the execution times of the exact algorithm given in [2] (Decide-pp) with the optimized algorithm on sets of matrices with a fixed number of columns and different numbers of rows. Since Decide-pp works on unconstrained matrices, we have not introduced any constraints in the input matrices. The Decide-pp-opt algorithm is able to find a solution for all matrices in contrast to the Decide-pp algorithm that in some cases takes more than 10 minutes to find a solution for a single matrix.

The average execution time to solve 10 matrices with a single conflict is of 0.031s, 0.047s, 0.093s for matrices of size 100x15, 200x15, 500x15 respectively.

In order to test the performance of the algorithm for large matrices in terms of number of species we have processed a set of 20 matrices, 10 of size 1000 × 30 and 10 of size 1000 × 40, with conflict graphs having a number of conflicts (edges) between 40 and 236. We fixed a maximum time (900 seconds), after which the execution is stopped. In all cases the simulation terminates without finding a solution, i.e. all matrices do not admit a p-pp tree. Therefore those instances are likely to be the worst cases for our algorithm, since the entire search tree is explored. Considering the set of matrices of size 1000 × 30, in 40% of tested cases the simulation is stopped since the maximum time is elapsed. In the remaining 60% of the cases the simulation halts before the timeout. In particular, in 10% of cases we obtain a result in a time between 10 and 15 minutes, and in 50% of cases the result is given in less than 3 minutes. Considering the set of matrices of size 1000 × 40, in 50% of tested cases the execution is stopped because the timeout is reached. In the remaining 50% the result is given in a time between 3 and 6 minutes, with an average time of 216 seconds.

Finally, the algorithm has been tested on real data coming from the International HapMap project. The data are classified by type of population. In our case, we used data from the set ASW (African ancestry in Southwest USA). Each individual is described by the two haplotypes (in our application the two haplotypes correspond to two different species, i.e. two different rows of the matrix). The data set consists of binary matrices of dimensions 10 × 10, 26 × 15, 26 × 25, and 26 × 30. For each group we considered 10 matrices. In all cases the matrices do not admit perfect phylogeny, and the number of conflicts changes from a minimum of 4 to a maximum of 138. Increasing the size of the matrix, and therefore the number of conflicts, the percentage of matrices that admit persistent perfect phylogeny decreases. More in detail, 80% of the tested matrices of size 10 × 10 admits solution, only 20% of the tested matrices of size 26 × 15 admits solution, and none of the sets 26 × 25, and 26 × 30 admits solution. The results confirm the conjecture that haplotype data may be related by the persistent phylogeny in case they cannot be explained by the perfect model. Moreover, the results on simulated and real data show the good performance in terms of...
time for matrices of a certain size even in the case that no solution is given, i.e. the searching space increases. This behavior is due to the fact that the algorithm includes a test to bound a path whenever the path does not lead to a solution, since we test whether a partial completion includes the forbidden matrix.

A final experiment an interesting case where we have matrices of size 30 x 60 with 4 or 5 conflicts (hence those matrices do not admit a perfect phylogeny). On those matrices Decide-pp have always reached the 15-minute timeout without computing a solution. On the other hand, imposing that a few (less than 10) characters cannot be persistent allows Decide-pp-opt to find a solution in a few seconds. This experiment shows that introducing some constraints can help in finding a solution, hence a feasible strategy to determine if a matrix has a persistent phylogeny is to introduce some random constraints. We are currently planning an extension of Decide-pp-opt that introduce some deterministic constraints, based on an analysis of the initial conflict graph, to speed up the computation.

6 Conclusions and open problems

In this paper we have investigated the CP-PP problem, which is the general problem of computing a persistent perfect phylogeny for binary matrices where some characters may be forced not to be persistent. The case where all characters may be persistent is called P-PP problem. The computational complexity of this problem is still open, except when the output is a specific tree, that is, a branch or a path. In order to find algorithmic solutions of the CP-PP problem we proved that, similarly to the P-PP problem [2], CP-PP can be reduced to a problem, called Red-black graph reduction problem, of emptying a graph with a sequence of operations on characters. This formulation of the problem allows us to find a polynomial time solution for matrices whose conflict graph is empty. Based on this result we propose a fixed parameter algorithm (the parameter is the number of characters) that uses a branch-and-bound technique to reduce the computation time.

An experimental analysis over simulated matrices and on binary matrices representing real haplotypes shows that the algorithm is able to process the majority of matrices with 40 characters, 1000 species, and no solution in a few minutes (clearly, for all those cases the algorithm determines that no solution exists—those instances are usually the hardest for our approach), while being very fast on matrices with 1000 species and 15–20 characters that admit a solution.

Finally, we observe that the CP-PP problem (P-PP problem) is equivalent to cases of the General Character Compatibility problem (GCC) investigated in [11], when states are over set \{0, 1, 2\} and when, for each generalized character \(\alpha\), \(\alpha(s) \in \{\{1\}, \{0\}, \{0, 2\}\}\) (respectively, \(\alpha(s) \in \{\{0\}, \{0, 2\}\}\) for the P-PP case ) for each species \(s\) and \(T_\alpha = 0 \rightarrow 1 \rightarrow 2\). It is interesting to note that the computational complexity of the cases of the GCC problem that are equivalent to P-PP and CP-PP, i.e. cases 5 and 6 of Table 1 in [11], is still open, while only partial results are obtained when the solution is constrained to be a branch or a path (see the Appendix). Thus the results we give in the paper also apply to those cases.

6.1 Acknowledgements

The authors would like to thank Rob Gysel for pointing out the connection of the persistent perfect phylogeny with the GCC problem. Anna Paola Carrieri also thanks Dan Gusfield for useful discussions on the problem.

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Appendix

Proof of Lemma 7

Proof. Assume to the contrary that no such tree exists. More precisely, we will consider, among all realizations of $M_e$, a tree $T$ with an edge $e = (u, x)$ that is closest to the root among all edges contradicting the lemma, that is $s_1 \in T(x), s_2 \notin T(x)$. Clearly $e$ is labeled by $c^+$ or $c^-$. Let $y$ be the least common ancestor of $s_1$ and $s_2$. Since $s_2 \notin T(x)$, $y$ must be an ancestor of $x$.

By cases (1) and (2) of Prop. 6, since $c_1$ has incident edges from $s_1$ and $s_2$ in $G_{RB}(x)$, both edges $(c_1, s_1), (c_1, s_2)$ are black or red. Assume they are both black in graph $G_{RB}(x)$: thus they must be black also in graph $G_{RB}(y)$. For this reason, note that $c_1$ is adjacent to $s_1$ and $s_2$ also in graph $G_{RB}(y)$ as they are adjacent after the realization of the characters in the label sequence of $x$.

Since both $s_1$ and $s_2$ have the character $c_1$, the edge $e_1$ of $T$ labeled by $c_1$ must lie on the common portion of the paths from the root to both $s_1$ and $s_2$ that is $c_1$ lies on the path from the root to node $y$ (as $y$ is the least common ancestor of $s_1$ and $s_2$). Therefore both edges $(c_1, s_1), (c_1, s_2)$ are red in graph $G_{RB}(y)$ (by definition of graph associated to a node), contradicting the previous assumption. Thus assume that $(c_1, s_1), (c_1, s_2)$ are red in $G_{RB}(x)$.

By case 2 of Prop. 6, $x$ precedes the edge $e_1 = (v, z)$ that is labeled by $c_1^-$, as $c_1^+$ belongs to the label sequence of $x$, but $c_1^-$ does not. Two cases are possible. If $c_1^+$ belongs to the label sequence for $y$, since both $s_1$ and $s_2$ do not have character $c_1$ but are descendant of $y$, they must also be two descendants of $z$ and a fortiori of $x$, a contradiction of the initial assumption. Thus, assume that $c_1^-$ does not belong to the label sequence of $y$.

Thus there exists an edge $(u', v')$ labeled $c_1^+$ that occurs along the path from node $y$ to $u$. In the graph $G_{RB}(v')$, $c_1$ is connected to $s_1$ and $s_2$ with red edges, for otherwise the same property would not hold for $G_{RB}(v')$. Since we have asked for a vertex $x$ that is the closest to the root for which this Lemma does not hold, the Lemma does hold for all vertices on the path from the root to $u$. Consequently, $s_1$ and $s_2$ are both descendants of $u$, contradicting the hypothesis that $y$ is the lca of $s_1$ and $s_2$.

Proof of Lemma 8

Proof. Consider the tree $T$ realizing $M_e$ that satisfies Lemma 7. It is immediate to modify $T$ in such a way that it has properties 1-7 of definition of a standard tree. Let $e = (u, x)$ be an edge labeled by $c^+$ or $c^-$, and let $S(x), C(x)$ be respectively the species and the characters of $T(x)$. Notice that an immediate consequence of Lemma 7 is that the set of species that are in the same connected component $C$ of graph $G_{RB}(u)$ is either contained in $T(x)$ or disjoint from $T(x)$. Therefore $T(x)$ is the union of some connected components of $G_{RB}(u)$. It is easy to show that properties 8-9 of a standard tree holds for $T$.

Proof of Lemma 10

Proof. By definition of standard tree and of depth-first visit, each negative character $c^-$ is preceded in $V$ by $c^+$. Therefore we only have to prove that all all single character reductions of $V$ are possible and the graph reduced by $V$ has no edge.

Let us prove the lemma by induction on the number $n$ of nodes of $T$. Clearly the lemma holds when $n = 1$, that is the tree consists of a single leaf, therefore assume that the lemma holds for all tree with at most $n$ nodes.

If $G_{RB}$ is disconnected, then it is easy to show that visiting separately and successively each subtree of a standard tree $T$ is equivalent to visiting all of $T$, from which the lemma easily follows.

Assume now that $G_{RB}$ is connected, therefore the root $r$ of $T$ has only a child $x$. Let $e = (r, x)$ be the only edge of $T$ incident on $r$ and let $c$ be the character labeling $e$. Since $x$ is the only child of $r$, $V$ consists of the edge $e$ followed by the depth-first visit of $T(x)$.

By definition of standard tree (point 6), $G_{RB}(x)$ is obtained from $G_{RB}$ by realizing character $c$. Consequently $T(x)$ solves the graph $G_{RB}(x)$ and, by inductive hypothesis, the lemma holds for $T(x)$. Moreover $T(x)$ contains no black edges incident on $c$, as they all have been removed when
realizing $c$. All other edges of $G_{RB}$ are removed by realizing the characters in the depth-first visit of $T(e)$, therefore no edge remains from $G_{RB}$ after realizing $V$. □

**Proof of Theorem of [11]**

Proof. Let $M$ be the completion of matrix $M_e$ obtained from a successful c-reduction of the red-black graph for $M_e$. In the following we show that $M$ has no forbidden matrix. This fact will prove that $M$ admits a pp tree. Let $G_R$ be the red-black obtained after the realization of the characters of the successful c-reduction. Assume to the contrary that $M$ has two characters $c, c_1$ that induce a forbidden matrix $F$, and let $s_1, s_2, s_3$ be the species of $M$ having the configuration $(1,1), (1,0)$ and $(0,1)$ in $F$, respectively.

We must consider the following cases.

Case 1. Assume that the forbidden matrix is induced by two negated characters. This fact implies that $G_R$ will have an induced $\Sigma$-graph, thus contradicting the fact that $G_R$ is edgeless.

Case 2. Assume that the forbidden matrix is induced by two positive characters.

Then $c, c_1$ must be in the same connected component of the red-black graph before their realization, as species $s_1$ is connected to both characters (we do not know if $s_1$ is connected by a black or red edge). Now, the realization of $c$ produces the red edge $(c, s_3)$, since $M_e[s_3, c] = ?$. Then $M[e[s_3, c]] = 1$ in the completion $M$, a contradiction with the assumption.

Case 3. Assume that the forbidden matrix is induced by a positive and negated character.

Assume that $c$ is the negated character. Since $c$ and $c_1$ share a species in the forbidden matrix $F$, it means that $c$ and $c_1$ are in the same connected component of the red-black graph when $c_1$ and $c$ are realized in the graph. Since $(0,1)$ is given in the matrix $F$ in row $s_3$, by definition of realization of $c_1$, it must be that $M[e[s_2, c_1]] = 1$ and $M[e[s_2, c_1]] = 1$ as $M_e[s_2, c_1] = 0$. But this is a contradiction.

□

**Proof of Lemma [13]**

Proof. Let $a, b$ be an arbitrary pair of elements that are in set $C_M$. Since the red-black is connected, there exists a path $\pi$ connecting the two vertices $a$ and $b$. Then by induction on the number $k$ of internal vertices of the smallest path that connects $a$ to $b$ we show that $(a, b)$ is an edge of the adjacency graph $G$. Assume first that $k = 1$. Then assume that $(a, c), (c, b)$ are edges of the shortest path $\pi$ connecting the two vertices $a$ and $b$.

Assume on the contrary that there is no edge $(a, b)$ in the adjacency graph. The following cases must be considered. Assume that $c$ is not comparable with both $a$ and $b$. Since $c$ adjacent with $a$ it follows that there exists a species $s$ such that $s$ contains $a$ but not $c$ and similarly there exists a species $s'$ such that $s'$ contains $c$, but not $a$. But this fact would imply that $(a, c)$ is an edge of the conflict graph which is a contradiction. For the same reason $c$ must be comparable with $b$. Assume that $c$ is comparable with $b$ and $a$ in $P$. Since $a, b \in C_M$, it holds that $c < b$ and $c < a$. But this fact would imply that $a, b$ are adjacent in graph $G$ as they share a common species. Then assume that $k = n > 1$. Clearly, $G$ must have edge $(a, c)$ where $c$ is the vertex adjacent to $a$ on the path having $k$ internal vertices. Since the path connecting $c$ and $b$ has $k - 1$ internal vertices, by induction it holds that also edge $(c, b)$ is in graph $G$. Consequently, there exists a path with 1 vertex in the red-black graph connecting $a$ and $b$. By induction, we show that $(a, b)$ must be an edge of the graph $G$, as required.

□

**Proof of Lemma [14]**

Proof. Take two characters $a$ and $b$ that are consecutive in the graph $G_{RB}$.

Then two cases are possible. Case 1: assume that $a < b$ or $b < a$. Then the realization of $a$ and $b$ produces a unique red graph that is connected, otherwise there exists a species to which $a$ is connected but $b$ is not and vice-versa, which contradicts the containment relation between the two characters. This fact proves the lemma.

Case 2: if $a$ and $b$ are not comparable, then there exists a species $s$ such that $a$ connected to $s$ but $b$ is not connected to $s$, and vice-versa there exists a species $s'$ such that $b$ is connected
to \( s' \), but \( a \) is not. Then there does not exist a specie \( x \) of graph \( G_{RB} \) that is not connected to both \( a \) and \( b \). In fact, if on the contrary, such a specie exists, then the pair \((a, b)\) induces the four gametes and thus \((a, b)\) is an edge of the conflict graph, contradicting the fact that it is empty. Consequently, if specie \( x \) does not exist, then the realization of \( a \) and \( b \) induces two red disjoint components thus proving the lemma.

\[
\square
\]

**Theorem 16.** Let \((M, E^*)\) be a binary matrix that has an empty conflict graph. Then there exists a polynomial time algorithm to build the p-pp tree for \( M \) and if \( E^* \) is empty then \( M \) admits a solution.

**Proof.** Clearly, the algorithm for an empty conflict graph described in the paper works in polynomial time in the size of the input matrix \( M \). In the following we show that the algorithm outputs a sequence \( r \) that is a successful \( c \)-reduction of graph \( G_{RB} \). In the following we assume that a maximal character \( c \) can be realized before a character \( c' \) such that \( c' < c \) in a successful \( c \)-reduction.

In particular, in the case that of the P-PP problem a solution always exists. In fact at each iteration all characters may be realized and in the following we show that no red sigma-graph is induced at any iteration of the algorithm, till the red-black graph is edgeless. By Lemma 13 the set \( C_M \) of \( P \) forms a clique. Then by Lemma 14 these characters can be realized in an arbitrary order without inducing a \( \Sigma \)-graph in the red-black graph. More precisely, by Lemma 14 after the realization of set \( C_M \), each character in \( C_M \) is connected to red-edges and the red components induced by a single character in \( C_M \) are disjoint. Observe that at a second iteration of step 1, a maximal element \( c \) is contained in a maximal element \( c_m \) of the first iteration of step 1.

In the following we show that after the realization of elements in \( C_M \), the red-black graph consists of disjoint components and each maximal element \( c \) that is in the poset \( P \) after the removal of \( C_M \) is in one of such disjoint connected components and it is a universal characters or the component has a unique maximal character in \( C_M \) that is free. In the first case, no red-edge is induced by the realization of \( c \), while in the second case, the red-edges of the component induced by an element in \( C_M \) are removed. Consequently, it follows that by the application of Lemma 14 and Lemma 13 no red sigma-graph is induced in the new iteration of the algorithm.

Let \( e \) be an element such that \( c < c_m \). Assume that \( S_1 = S(c_n)/S(c_m) \) and \( S_2 = S(c_m)/S(c_n) \). Clearly \( S_1 \) and \( S_2 \) are disjoint sets and since \( S(c) \subseteq S(c_m) \), it holds that \( S(c)/S(c_m) \subseteq S_2 \). Now, we have three cases: (1) there exists a specie \( s \in S_2 \) such that \( s \) is not in \( S(c) \) and a specie \( s_1 \in S_2 \) such that \( s_1 \) is in \( S(c) \), or (2) all species in \( S_2 \) are not in \( S(c) \) or (3) all species in \( S_2 \) are in \( S(c) \). Assume that case 1) holds. Then, if there exists a specie \( s' \) that is of \( c_n \) and \( c_m \) and \( s' \) has character \( c \), it holds that \( c \) is free in such a component. Assume now that case 2) holds. Then \( c \) is connected to a specie \( c_n \) and \( c_m \). It follows that \( c \) is universal for the connected component consisting of the specie \( c_n \) and \( c_m \) to which \( c \) is connected. Assume now that case 3) holds. Again this case shows that \( c \) is universal for the connected component to which \( c \) belongs.

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We shows that the CP-PP problem is equivalent to a case of the General Character Compatibility (GCC) whose computational complexity is still open and similarly we show the connection of the restricted P-PP problem with the GCC one.

In the General Character Compatibility problem, the input is a set \( S \) of species. Observe that a set of species \( S \) is defined by means of a set of generalized characters. A generalized character \( \hat{\alpha} \) consists of a pair \( (\alpha, T_\alpha) \) where \( \alpha: S \rightarrow 2^{Q_\alpha} \) (\( Q_\alpha \) is the set of states for \( \hat{\alpha} \)), and \( T_\alpha = (V(T_\alpha), E) \) is a rooted character tree with nodes bijectively labeled by the elements of \( Q_\alpha \).

Then a the solution of the GCC problem is a rooted tree \( T = (V, E) \) and a state-assignment function \( c \) that assigns to each vertex \( v \in V(T) \) and generalized character \( \hat{\alpha} \) a state, in such a way that \( c(v, \hat{\alpha}) \in Q_\alpha \) such that the following fact holds.

1. For each specie \( s \in S \) there is a vertex \( v_s \) of tree \( T \) such that \( c(v_s, \hat{\alpha}) \in \alpha(s) \) for each \( \hat{\alpha} \).
2. For every $\hat{\alpha} \in C$ and state $i \in Q_{\alpha}$, the set of vertices of $T$ where $\hat{\alpha}$ assumes value $i$ is a connected component of $T$.

3. For every $\hat{\alpha} \in C$, the tree $T(\alpha)$ is an induced subtree of $T_{\alpha}$, where $T(\alpha)$ is obtained from $T$ by labeling the nodes of $T$ only with their $\alpha$-states (as chosen by function $c$), and then contracting edges having the same $\alpha$-state at their endpoints.

In the following we show that the P-PP problem is equivalent to the GCC problem where $\alpha(s) \in \{\{1\}, \{0, 2\}\}$ for each species $s$ and moreover $T_{\alpha} = 0 \to 1 \to 2$.

We can show that state 2 in the GCC problem is equivalent to the fact that a character is persistent that is, it is in state 0 (lost) but it has been in state 1 before (gain). Given an instance of the GCC problem where for each generalized character $\hat{\alpha}$ it holds that $\alpha(s) \in \{\{1\}, \{0, 2\}\}$ for each species $s$ and $T_{\alpha} = 0 \to 1 \to 2$, we can associate a matrix $M$ that is an instance of the P-PP problem as follows: we assign a column $c_j$ in $M$ to each generalized character $\hat{\alpha}_j$ and a row for each species $s \in S$, where $M[s, c_j] = 0$ if and only if $\hat{\alpha}_j(s) \in \{0, 2\}$, otherwise $M[s, c_j] = 1$. Given a solution $T_{pp}$ of the PP-problem, it is easy to verify that the underlying unlabeled tree $T$ together with the function $c$ such that for each vertex $v$ and vector $l_v$, it holds that $l_v[i] = c(v, \hat{\alpha}_i)$, if $\hat{\alpha}_i$ is in state 0 or 1 for the first time, otherwise if $l_v[i] = 0$ for the second time, then $c(v, \hat{\alpha}_i) = 2$ is a solution of the associated GCC problem instance. Consequently, GCC reduces to the P-PP-problem.

The vice versa, that is the P-PP-problem reduces to GCC, is easily proved as follows. For each species $s$ of the GCC problem where for each generalized character $\hat{\alpha}_j$ of the tree $T$ we can label only one edge $(u, v)$ of the tree with a character $c_j^u$ or $c_j^v$, more precisely, when then the state of the generalized character $\hat{\alpha}_j$ changes from 0 to 1 in $l_u$ and $l_v$, and respectively, from 1 to 2 in $l_u$ and $v$ in the tree $T$. In fact, the set of vertices with a common state $c(v, \hat{\alpha}_j) = k$ for a character $\hat{\alpha}_j$ must be a connected component. Now, when $k \in \{1\}$ (or $k \in \{2\}$), the connected component induced by vertices $v$ labeled $k$ by the $c$ function represents the subtree of tree $T_{pp}$ rooted in the end of the edge labeled $c_j^u$ (or $c_j^v$, respectively).

Using the above result, assuming that some characters may have only state 0 in a given species, it is easy to show that the CP-PP problem is equivalent to the GCC in the case that $\alpha(s) \in \{\{1\}, \{0\}, \{0, 2\}\}$ for each species $s$ and $T_{\alpha} = 0 \to 1 \to 2$. 

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