RESEARCH

# Additional file 1: Supplementary Text: Implications of Non-uniqueness in Phylogenetic Deconvolution of Bulk DNA Samples of Tumors

Yuanyuan Qi[1], Dikshant Pradhan[2] and Mohammed El-Kebir[1*]

## Appendix A: Omitted Proofs

We start by defining #Mono-1-in-3SAT.

**Problem 1** (#Mono-1-in-3SAT [1]) Given a Boolean formula $\phi = \bigwedge_{j=1}^{q}(y_{j,1} \vee y_{j,2} \vee y_{j,3})$ in 3-conjunctive normal form (3-CNF) with $p$ variables $\{x_1, \ldots, x_p\}$ and $q$ clauses where each clause has exactly three positive or three negative literals, find a truth assignment $\theta : [p] \rightarrow \{0,1\}$ that satisfies each clause of $\phi$ with exactly one true literal.

Ref. [1] shows #P-completeness of #Mono-1-in-3SAT. Here, we show #P-completeness of #SubsetSum by giving a parsimonious polynomial-time reduction from #Mono-1-in-3SAT. We note that the same literal may appear multiple times in a clause. However, we may assume without loss of generality that for any $i \in [p]$, variable $x_i$ appears in at least one clause of $\phi$. To see why this is the case, observe that such unconstrained variables can be set either true or false, thus each resulting in a multiplicative factor of two on the number of solutions.

**(Main Text) Lemma 12** There exists a parsimonious reduction from #Mono-1-in-3SAT to #SubsetSum.

$$\phi = (x_1 \vee x_2 \vee x_3) \wedge (\neg x_2 \vee \neg x_3 \vee \neg x_4),$$

$$\theta = \{x_1 = false\,, x_2 = true, x_3 = false,\, x_4 = true\},$$

$$N = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \end{pmatrix}, M = \begin{pmatrix} 1 & 0 \\ 0 & 0 \\ 1 & 0 \\ 0 & 1 \\ 1 & 0 \\ 0 & 1 \\ 0 & 0 \\ 0 & 1 \end{pmatrix}, \qquad \begin{pmatrix} Q_2 \\ Q_3 \\ Q_6 \\ Q_7 \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 & 0 & 0 \end{pmatrix}.$$

**Figure S1 An example of reduction from** #Mono-1-in-3SAT **to** #SubsetSum. We show a truth assignment $\theta$ of the variables in #-Mono-1-in-3SAT problem instance $\phi$. Observe that each clause in $\phi$ is satisfied by exactly one literal. Moreover, we show the rows of $Q = [NM]$ corresponding to $\theta$.

*Proof* Let $\phi$ be a Boolean formula in 3-CNF with $p$ variables $\{x_1, \ldots, x_p\}$ and $q$ clauses where each clause has exactly three positive or three negative literals.

Given $\phi$, we construct a $2p \times (p+q)$ matrix $Q = [NM]$, whose first $p$ columns correspond to matrix $N = [n_{i,j}]$ and remaning $q$ columns correspond to matrix $M = [m_{i,j}]$, each having $2p$ rows. The idea is that each row $i \in [2p]$ of $Q$ uniquely corresponds to a literal, i.e. if $i$ is odd it corresponds to the positive literal $x_{(i+1)/2}$ and if $i$ is even it corresponds to the negative literal $\neg x_{i/2}$. The entries $n_{i,j}$ of matrix $N$ are defined as

$$n_{i,k} = \begin{cases} 1, & \lfloor \frac{i+1}{2} \rfloor = k, \\ 0, & \text{otherwise.} \end{cases}$$

To define matrix $M$, we introduce the function $g(j, y)$ which counts the number of occurrences of literal $y$ in clause $j$ of $\phi$. Using the function $g$, we define matrix $M = [m_{i,j}]$ as

$$m_{i,j} = \begin{cases} g(j, x_{(i+1)/2}), & \text{if } i \text{ is odd,} \\ g(j, \neg x_{i/2}), & \text{if } i \text{ is even.} \end{cases}$$

Observe that matrix $M$ provides a lossless encoding for $\phi$, and it is trivial to reconstruct $\phi$ from $M$. Moreover, observe that $Q$ can be obtained in polynomial time from $\phi$.

We obtain a SubsetSum instance from matrix $Q = [NM]$ as follows. First, observe that entries of $Q$ are in the set $\{0,1,2,3\}$. Thus, rows $\{1, 2, \ldots, 2p\}$ of $Q = [q_{k,i}]$ correspond to positive integers defined as $S =$

[*] Correspondence: melkebir@illinois.edu
[1] Department of Computer Science, University of Illinois at Urbana-Champaign, Champaign, IL 61801, USA
Full list of author information is available at the end of the article

$\{s_1, s_2, \ldots, s_{2p}\}$, where

$$s_k = \sum_{i=1}^{p+q} q_{k,i} \cdot 4^{p+q-i}, \qquad \forall k \in [2p].$$

We define the target sum as

$$t = \sum_{i=1}^{p+q} 4^{p+q-i}.$$

Clearly, $S$ and $t$ can be obtained in polynomial time from $\phi$. Fig. S1 shows an example of this reduction.

To prove correctness of this reduction, we start by showing that $(S, t)$ is a valid #SubsetSum instance. By construction, each integer $s_i$ is nonnegative. The remaining requirement is that for distinct rows $i \neq j$ it holds that $s_i \neq s_j$. Let $i, j \in [2k]$ such that $i \neq j$. The indices of the corresponding variables of these two literals are given by $\lfloor \frac{i+1}{2} \rfloor$ and $\lfloor \frac{j+1}{2} \rfloor$, respectively. We distinguish two cases. First, if $\lfloor \frac{i+1}{2} \rfloor \neq \lfloor \frac{j+1}{2} \rfloor$, then, by construction, $n_{i,\lfloor \frac{i+1}{2} \rfloor} \neq n_{j,\lfloor \frac{i+1}{2} \rfloor}$, i.e. the $\lfloor \frac{i+1}{2} \rfloor$-th digit of $s_i$ in the base 4 representation of the numbers differs from $s_j$, and hence $s_i \neq s_j$. Second, if $\lfloor \frac{i+1}{2} \rfloor = \lfloor \frac{j+1}{2} \rfloor = k$, assume without loss of generality that $i = 2k - 1$ and $j = 2k$. We have that $n_{i,l} = n_{j,l}$ for all $l \in [p]$. We claim that there is a clause $s \in [q]$ that contains at most one of $\{x_k, \neg x_k\}$. Suppose for a contradiction that no clause of $\phi$ contains at most one $\{x_k, \neg x_k\}$. If a clause of $\phi$ contains both $x_k$ and $\neg x_k$ then it violates the monochromaticity property of $\phi$. If no clause of $\phi$ contains either $x_k$ or $\neg x_k$ then $x_k$ is not a variable of $\phi$. Thus, there exists a clause $l \in [p]$ that contains at most one of $\{x_k, \neg x_k\}$. As such, for this clause $l$ we have $m_{i,l} \neq m_{i,l}$ and thus $s_i \neq s_j$. Hence, $(S, t)$ is a valid #SubsetSum instance.

To prove that this reduction is parsimonious, we need to prove that the number of solutions (witnesses) is preserved. We prove this by establishing a bijection between the set of satisfying truth assignments of $\phi$ and the set of subsets of $S$ that sum to the target sum $d$. Consider a satisfying assignment $\theta$ of $\phi$. We construct the corresponding subset $D$ of rows $\{1, \ldots, 2p\}$ of $Q$ as follows. For each variable $x_k$ (where $k \in [p]$), we include $s_{2k-1}$ in $D$ if $\theta(x_k) = 1$ and include $s_{2k}$ in $D$ otherwise. Let $d = \sum_{i \in D} s_i$. By construction, only one of $\{s_{2k-1}, s_{2k}\}$ is included in $D$. As such, the $k$-th digit of $d$ is 1, for all $k \in [p]$. Moreover, since exactly one literal of each clause is true, the $i$-th digit of $d$ is 1 for each $i \in \{p+1, \ldots, p+q\}$. Therefore $D$ is a subset of the rows of $Q$ such that $\sum_{i \in D} s_i = t$.

Consider a subset $D$ of $S$ such that $\sum_{i \in D} s_i = t$. Since the values of each entry in $Q$ are in the set $\{0, 1, 2, 3\}$, each row $i \in D$ describes a quaternary number. We claim that adding the quaternary numbers corresponding to $D$ will not introduce a carry. To see this, recall that $Q = [NM]$. For the $k$-th column of $N$ (where $k \in [p]$), the entry $n_{i,k}$ in row $i$ has value 1 if and only if $\lfloor \frac{i+1}{2} \rfloor = k$. This is only the case for $i = 2k - 1$ or $i = 2k$, and hence only two entries in each column $N$ are 1. For columns of $M$, the sum of the entries in $j$-th column is $\sum_{k \in [p]} [g(j, x_k) + g(j, \neg x_k)]$, i.e. the sum of the number of the occurrences of all literals in clause $j$. Since we only have three literals in each clause, this sum equals exactly 3. Therefore, no carry will happen in the addition under the quaternary representation, and since the $k$-th digit of $t$ under the quaternary representation is 1 for $1 \leq k \leq p$, only one of $\{s_{2k-1}, s_{2k}\}$ is in $D$. We construct an assignment $\theta$ of $\phi$, where we set $\theta(x_k) = 1$ if $s_{2k-1} \in D$ and set $\theta(x_k) = 0$ if $s_{2k} \in D$. Since for all $i \in \{p+1, \ldots, p+q\}$ the $i$-th digit of $t$ is 1, only one literal of each clause is true. Hence, $\theta$ is a satisfying assignment.

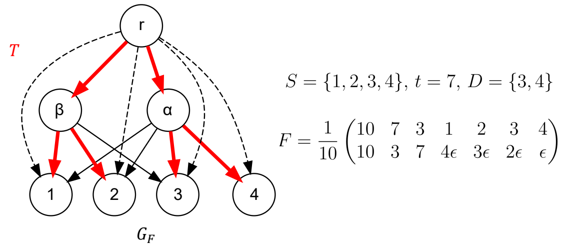

T
r
β
α
1
2
3
4
$G_F$
$S = \{1, 2, 3, 4\}$, $t = 7$, $D = \{3, 4\}$
$F = \frac{1}{10} \begin{pmatrix} 10 & 7 & 3 & 1 & 2 & 3 & 4 \\ 10 & 3 & 7 & 4\epsilon & 3\epsilon & 2\epsilon & \epsilon \end{pmatrix}$

**Figure S2 An example reduction from a #SubsetSum instance to #PPM.** A solution to the SubsetSum problem instance $(S, t)$ and its corresponding spanning arborescence $T$ of ancestry graph $G_F$.

Obviously, the construction of $D$ given $\theta$ and the construction of $\theta$ given $D$ are inverses of each other. Therefore, if we view the constructions as functions, they are bijections between the solution spaces. This proves that the reduction is parsimonious. □

**(Main Text) Lemma 13** There exists a parsimonious reduction from #SubsetSum to #PPM restricted to $m = 2$ samples.

*Proof* El-Kebir et al. [2] showed the NP-completeness of PPM even when $m = 2$ by reduction from SubsetSum. Here, we will show that this reduction is parsimonious by defining a bijection between the solution space of a SubsetSum instance and the solution space of the corresponding PPM instance. From this result it will immediately follow that the number of solutions is preserved.

Let $(S, t)$ be an instance of SubsetSum, where $S = \{s_1, s_2, \ldots, s_d\}$ is the set of numbers and $t$ is the target sum. Suppose $s_1 < s_2 < \ldots < s_d$ without loss of generality. Let

$$F = \frac{1}{e}\begin{pmatrix} e & t & e-t & s_1 & \cdots & s_d \\ e & e-t & t & s_d\epsilon & \cdots & s_1\epsilon \end{pmatrix},$$

where $e = \sum_{s \in S} s$, and $0 < \epsilon < \frac{1}{e}$. Clearly, $F$ can be obtained in polynomial time, and is a valid instance of PPM. Let $G_F = (V, E)$ be the ancestry graph for $F$, whose vertices $r, \alpha, \beta, v_1, v_2, \ldots, v_d$ correspond to the columns of $F$.

Now consider a subset $D \subseteq S$ whose sum $\sum_{s_i \in D} s_i$ equals the target value $t$. Given $D$, we construct a spanning arborescence $T(D) = (V, E')$ of $G_F$, where

$$E' = \{(\alpha, v_i) \mid s_i \in D\} \cup \{(\beta, v_i) \mid s_i \notin D\} \cup \{(r, \alpha), (r, \beta)\}.$$

For any $i$, vertex $v_i$ is connected to either $\alpha$ or $\beta$, and $\alpha$ and $\beta$ are both connected to $r$. Therefore, each vertex is reachable from $r$. Since $|E'| = |D| + |S - D| + 2 = d + 2$ and $|V| = d + 3$, $T$ is an arborescence over $V$. Now we need to show that $T$ is a spanning arborescence of $G_F$ and it suffices to show $E' \subseteq E$. First, $(r, \alpha), (r, \beta)$ are obviously included in $E$. Since $\sum_{s_i \in D} s_i = t$ and $s_i > 0$ for all $i \in [d]$, it holds that $s_i \leq t$. Thus, $f_{1,v_i} \leq f_{1,\alpha}$ if $s_i \in D$. Wit a similar argument, we can show that $f_{1,v_i} \leq f_{1,\beta}$ if $s_i \notin D$. Since $0 < t < e$ and $e, t$ are integers, we have that $t \geq 1, e - t \geq 1$. Since $f_{2,v_i} = s_i\epsilon < s_i/e < 1$, we have $\{(\alpha, v_i) | s_i \in D\} \cup \{(\beta, v_i) | s_i \notin D\} \subseteq E$, and thus $E' \subseteq E$. To show that $T(D)$ is a solution to the PPM, we need to show that $T(D)$ also satisfies (SC). Since $T(D)$ has only three non-leaf vertices $\{r, \alpha, \beta\}$, it suffices to verify (SC) at these three vertices. Obviously, (SC) holds for $r$. Since

$$f_{1,\alpha} = \frac{t}{e} = \frac{\sum_{s_i \in D} s_i}{e} = \sum_{s_i \in D} f_{1,v_i}$$

and

$$f_{2,\alpha} \geq \frac{1}{e} > \frac{\sum_{i \in [d]} s_i}{e}\epsilon = \sum_{i \in [d]} f_{2,v_i} > \sum_{s_i \in D} f_{2,v_i},$$

(SC) holds for $\alpha$. Similarly, we can show that (SC) holds for $\beta$. Therefore, $T(D)$ is a valid solution to the instance $F$ of PPM.

Consider a spanning arborescence $T = (V, E')$ of $G_F$ that satisfies (SC). The edge set $E' \subseteq E$ satisfies the following:

(i) $(r, \alpha), (r, \beta) \in E'$.
Since $f_{2,\alpha} \geq \frac{1}{e} > \frac{\sum_{i \in [d]} s_i}{e}\epsilon = \sum_{i \in [d]} f_{2,v_i} > f_{2,v_i}$, it holds that $(v_i, \alpha) \notin E$ for any $i \in [d]$. Similarly, $(v_i, \beta) \notin E$ for any $i \in [d]$. Therefore, $\alpha, \beta$ can only be reachable from $r$.

(ii) $(r, v_i) \notin E'$ for any $i \in [d]$.
Since $(r, \alpha), (r, \beta) \in E'$ and $F_{1,\alpha} + F_{1,\beta} = F_{1,r}$, adding any $(r, v_i)$ will violate (SC) at $r$.

(iii) For any distinct $i, j \in [d]$, it holds that $(v_i, v_j) \notin E$.
Suppose $i > j$, then $f_{1,v_i} > f_{1,v_j}$ and $f_{2,v_i} < f_{2,v_j}$. Therefore, $(v_i, v_j) \notin E$.

(iv) Either $(\alpha, v_i)$ or $(\beta, v_i)$ is in $E'$ for any $i \in [d]$.
In (ii) and (iii), we have shown that $v_i$ is not a child of $r$, or a child of any other $v_j$ (where $j \neq i$). Therefore, $v_i$ can only be reached from $r$ through $\alpha$ or $\beta$.

Fig. S2 shows an example. Let $D(T) = \{s_i \mid (\alpha, v_i) \in E'\}$. By (SC), we have that $\sum_{s_i \in D} s_i \leq t$ and $\sum_{s_i \notin D(T)} s_i \leq e - t$. Since $\sum_{s_i \in D(T)} s_i + \sum_{s_i \notin D(T)} s_i = \sum_{s_i \in S} s_i = e$, both inequalities are tight, i.e. $\sum_{s_i \in D(T)} s_i = t$ and $\sum_{s_i \notin D(T)} s_i = e - t$. Therefore, $D(T)$ is a solution to SubsetSum.

The construction of $T$ given $D$ and the construction of $D$ given $T$ are inverses of each other. If we view the constructions as functions, they are bijections between the solution spaces. This in turn shows that the number of solutions (witnesses) is preserved. Obviously, the reduction can be performed in polynomial time. Therefore, this reduction is parsimonious. □

## Appendix B: Supplementary Results

We have the following additional figures and tables in the supplement.

- Fig. S3 illustrates how an ancestry graph is derived from a frequency matrix.
- Fig. S4 shows the solution space of lung cancer patient CRUK0012 with $m = 2$ samples and $n = 5$ mutation clusters.
- Fig. S5 shows the six solutions of instance #81 with $n = 7$ mutations and $m = 5$ samples.
- Fig. S6 illustrates the distribution of samples drawn by PhyloWGS for all $n = 7$ instances.
- Fig. S7 illustrates the distribution of samples drawn by Canopy for all $n = 7$ instances.
- Fig. S8 illustrates the distribution of samples drawn by rejection sampling for all $n = 7$ instances.
- Tables S1-S2 list the real data results obtained from a lung cancer cohort [3].
- Table S3 lists the parameters and results of all simulation instances where $n = 3$.
- Table S4 lists the parameters and results of all simulation instances where $n = 5$.

- Table S5 lists the parameters and results of all simulation instances where $n = 7$.
- Table S6 lists the parameters and results of all simulation instances where $n = 9$.
- Table S7 lists the parameters and results of all simulation instances where $n = 11$.
- Table S8 lists the parameters and results of all simulation instances where $n = 13$.
- Table S9 lists the parameters and results of rejection sampling over all $n = 7$ simulation instances.

**Table S1 Non-uniqueness of solutions in a multi-region lung cancer cohort of 100 patients [3].** Table shows the patient identifier, the number $n$ of mutation clusters, the number $m$ of samples, the number of solutions in the solution space when removing no samples, one sample and two samples, and finally the number of solutions reported in Ref. [3]. Patients where our enumeration algorithm found no solutions are indicated with *. Patients where no solutions were reported in Ref. [3] are indicated with **.

| patient | clusters $n$ | samples $m$ | 0 removed samples | 1 removed sample | 2 removed samples | solutions reported in [3] |
|---|---|---|---|---|---|---|
| CRUK0001 | 7 | 3 | 0* | 24 | 3936 | 1 |
| CRUK0002 | 8 | 3 | 6 | 84 | 53248 | 1 |
| CRUK0003 | 8 | 5 | 86 | 238 | 1680 | 1 |
| CRUK0004 | 7 | 4 | 30 | 102 | 735 | 2 |
| CRUK0005 | 6 | 4 | 2 | 10 | 48 | 2 |
| CRUK0006 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0007 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0008 | 5 | 2 | 4 | 60 | N/A | 1 |
| CRUK0009 | 8 | 4 | 4 | 14 | 1920 | 1 |
| CRUK0010 | 4 | 2 | 2 | 12 | N/A | 1 |
| CRUK0011 | 8 | 3 | 27 | 768 | 49152 | 3 |
| CRUK0012 | 5 | 2 | 6 | 135 | N/A | 2 |
| CRUK0013 | 9 | 5 | 480 | 2343 | 2343 | 8 |
| CRUK0014 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0015 | 4 | 2 | 2 | 12 | N/A | 1 |
| CRUK0016 | 8 | 2 | 0* | 3941 | N/A | 1 |
| CRUK0017 | 8 | 4 | 0* | 28 | 336 | 1 |
| CRUK0018 | 8 | 4 | 4 | 56 | 1920 | 1 |
| CRUK0019 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0020 | 4 | 2 | 2 | 27 | N/A | 1 |
| CRUK0021 | 4 | 2 | 2 | 16 | N/A | 1 |
| CRUK0022 | 5 | 2 | 3 | 90 | N/A | 2 |
| CRUK0023 | 10 | 4 | 54 | 1680 | 29400 | 2 |
| CRUK0024 | 8 | 4 | 12 | 192 | 1280 | 1 |
| CRUK0025 | 7 | 3 | 18 | 84 | 4116 | 2 |
| CRUK0026 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0027 | 5 | 2 | 4 | 60 | N/A | 1 |
| CRUK0028 | 5 | 2 | 4 | 60 | N/A | 2 |
| CRUK0029 | 9 | 6 | 108 | 1224 | 11920 | 1 |
| CRUK0030 | 4 | 3 | 2 | 3 | 16 | 1 |
| CRUK0031 | 7 | 3 | 21 | 140 | 3887 | 2 |
| CRUK0032 | 13 | 4 | 636 | 75790 | 19649968 | 1 |
| CRUK0033 | 2 | 2 | 1 | 1 | N/A | 1 |
| CRUK0034 | 7 | 3 | 6 | 420 | 9702 | 1 |
| CRUK0035 | 5 | 4 | 1 | 8 | 45 | 1 |
| CRUK0036 | 7 | 4 | 2 | 12 | 140 | 1 |
| CRUK0037 | 10 | 5 | 828 | 14774 | 75660 | 17 |
| CRUK0038 | 4 | 2 | 2 | 12 | N/A | 2 |
| CRUK0039 | 8 | 3 | 3 | 288 | 36864 | 1 |
| CRUK0040 | 2 | 2 | 2 | 2 | N/A | 1 |
| CRUK0041 | 3 | 4 | 1 | 4 | 4 | 1 |
| CRUK0043 | 2 | 2 | 1 | 2 | N/A | 1 |
| CRUK0044 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0045 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0046 | 5 | 4 | 5 | 14 | 19 | 2 |
| CRUK0047 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0048 | 4 | 3 | 4 | 4 | 15 | 1 |
| CRUK0049 | 6 | 2 | 10 | 294 | N/A | 4 |
| CRUK0050 | 3 | 5 | 2 | 2 | 2 | 1 |

**Table S2 Non-uniqueness of solutions in a multi-region lung cancer cohort of 100 patients [3].** Table shows the patient identifier, the number $n$ of mutation clusters, the number $m$ of samples, the number of solutions in the solution space when removing no samples, one sample and two samples, and finally the number of solutions reported in Ref. [3]. Patients where our enumeration algorithm found no solutions are indicated with *. Patients where no solutions were reported in Ref. [3] are indicated with **.

| patient | clusters $n$ | samples $m$ | 0 removed samples | 1 removed sample | 2 removed samples | solutions reported in [3] |
|---|---|---|---|---|---|---|
| CRUK0051 | 5 | 3 | 2 | 12 | 105 | 1 |
| CRUK0052 | 5 | 3 | 2 | 8 | 90 | 1 |
| CRUK0054 | 3 | 2 | 1 | 2 | N/A | 1 |
| CRUK0055 | 2 | 1 | 1 | N/A | N/A | 0** |
| CRUK0056 | 4 | 3 | 1 | 3 | 18 | 1 |
| CRUK0057 | 4 | 2 | 1 | 18 | N/A | 1 |
| CRUK0061 | 2 | 2 | 1 | 1 | N/A | 1 |
| CRUK0062 | 15 | 7 | 160 | 19500 | 289500 | 1 |
| CRUK0063 | 8 | 5 | 65 | 847 | 1330 | 2 |
| CRUK0064 | 5 | 2 | 2 | 72 | N/A | 1 |
| CRUK0065 | 14 | 6 | 3280 | 8710 | 173712 | 1 |
| CRUK0066 | 8 | 4 | 5 | 28 | 672 | 1 |
| CRUK0067 | 5 | 2 | 5 | 90 | N/A | 2 |
| CRUK0068 | 10 | 4 | 328 | 1485 | 20160 | 3 |
| CRUK0069 | 12 | 5 | 1464 | 565216 | 3411072 | 1 |
| CRUK0070 | 10 | 5 | 56 | 2136 | 160800 | 2 |
| CRUK0071 | 10 | 6 | 180 | 540 | 7200 | 1 |
| CRUK0072 | 6 | 3 | 3 | 25 | 552 | 1 |
| CRUK0073 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0074 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0075 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0076 | 9 | 4 | 157 | 504 | 17010 | 4 |
| CRUK0077 | 7 | 4 | 35 | 328 | 1155 | 2 |
| CRUK0078 | 6 | 3 | 1 | 40 | 552 | 1 |
| CRUK0079 | 6 | 4 | 8 | 25 | 120 | 1 |
| CRUK0080 | 4 | 4 | 1 | 1 | 6 | 1 |
| CRUK0081 | 3 | 2 | 1 | 4 | N/A | 1 |
| CRUK0082 | 6 | 5 | 2 | 85 | 137 | 1 |
| CRUK0083 | 8 | 4 | 10 | 56 | 1152 | 1 |
| CRUK0084 | 6 | 4 | 8 | 40 | 332 | 2 |
| CRUK0085 | 10 | 4 | 48 | 8160 | 750000 | 1 |
| CRUK0086 | 3 | 3 | 1 | 2 | 3 | 1 |
| CRUK0087 | 3 | 3 | 1 | 2 | 2 | 1 |
| CRUK0088 | 3 | 2 | 2 | 5 | N/A | 1 |
| CRUK0090 | 2 | 2 | 1 | 2 | N/A | 1 |
| CRUK0094 | 6 | 4 | 14 | 122 | 224 | 2 |
| CRUK0095 | 4 | 3 | 6 | 6 | 17 | 2 |
| CRUK0096 | 5 | 7 | 1 | 2 | 15 | 1 |
| CRUK0097 | 4 | 2 | 2 | 12 | N/A | 1 |
| CRUK0098 | 4 | 3 | 2 | 2 | 16 | 1 |
| CRUK0099 | 5 | 4 | 3 | 4 | 15 | 2 |
| CRUK0100 | 8 | 3 | 60 | 315 | 26880 | 3 |

**Table S3 Result for $n = 3$ instances**. From left to right, we list the instance identifier, the number $m$ of samples, the number of solutions, the number of spanning arborescences in the ancestry graph of the instance, the ratio between the solutions and spanning arborescences and the median edge recall.

| # | samples $m$ | solutions | spanning arborescences | ratio | median recall |
|---|---|---|---|---|---|
| 2 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 1 | 2 | 0.500000 | 1.000 |
| | 5 | 1 | 2 | 0.500000 | 1.000 |
| | 10 | 1 | 2 | 0.500000 | 1.000 |
| 8 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |
| 12 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |
| 15 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |
| 30 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |
| 39 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |
| 50 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |
| 104 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |
| 119 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |
| 129 | 1 | 2 | 2 | 1.000000 | 0.750 |
| | 2 | 2 | 2 | 1.000000 | 0.750 |
| | 5 | 1 | 1 | 1.000000 | 1.000 |
| | 10 | 1 | 1 | 1.000000 | 1.000 |

**Table S4 Result for $n = 5$ instances**. From left to right, we list the instance identifier, the number $m$ of samples, the number of solutions, the number of spanning arborescences in the ancestry graph of the instance, the ratio between the solutions and spanning arborescences and the median edge recall.

| $\#$ | samples $m$ | solutions | spanning arborescences | ratio | median recall |
|---|---|---|---|---|---|
| 3 | 1 | 15 | 24 | 0.625000 | 0.500 |
| | 2 | 6 | 12 | 0.500000 | 0.750 |
| | 5 | 4 | 6 | 0.666667 | 0.625 |
| | 10 | 1 | 2 | 0.500000 | 1.000 |
| 5 | 1 | 16 | 24 | 0.666667 | 0.500 |
| | 2 | 5 | 6 | 0.833333 | 0.750 |
| | 5 | 5 | 6 | 0.833333 | 0.750 |
| | 10 | 2 | 2 | 1.000000 | 0.875 |
| 9 | 1 | 21 | 24 | 0.875000 | 0.500 |
| | 2 | 3 | 6 | 0.500000 | 0.750 |
| | 5 | 9 | 24 | 0.375000 | 0.500 |
| | 10 | 2 | 6 | 0.333333 | 0.875 |
| 18 | 1 | 21 | 24 | 0.875000 | 0.500 |
| | 2 | 5 | 6 | 0.833333 | 0.750 |
| | 5 | 6 | 8 | 0.750000 | 0.750 |
| | 10 | 2 | 3 | 0.666667 | 0.875 |
| 37 | 1 | 24 | 24 | 1.000000 | 0.500 |
| | 2 | 6 | 6 | 1.000000 | 0.750 |
| | 5 | 6 | 6 | 1.000000 | 0.750 |
| | 10 | 2 | 2 | 1.000000 | 0.875 |
| 45 | 1 | 12 | 24 | 0.500000 | 0.625 |
| | 2 | 3 | 16 | 0.187500 | 0.750 |
| | 5 | 5 | 24 | 0.208333 | 0.750 |
| | 10 | 2 | 18 | 0.111111 | 0.875 |
| 62 | 1 | 18 | 24 | 0.750000 | 0.500 |
| | 2 | 5 | 6 | 0.833333 | 0.750 |
| | 5 | 6 | 6 | 1.000000 | 0.750 |
| | 10 | 2 | 2 | 1.000000 | 0.875 |
| 66 | 1 | 11 | 24 | 0.458333 | 0.500 |
| | 2 | 4 | 12 | 0.333333 | 0.750 |
| | 5 | 2 | 6 | 0.333333 | 0.875 |
| | 10 | 2 | 6 | 0.333333 | 0.875 |
| 69 | 1 | 22 | 24 | 0.916667 | 0.500 |
| | 2 | 4 | 6 | 0.666667 | 0.625 |
| | 5 | 7 | 8 | 0.875000 | 0.750 |
| | 10 | 2 | 3 | 0.666667 | 0.875 |
| 71 | 1 | 11 | 24 | 0.458333 | 0.750 |
| | 2 | 4 | 18 | 0.222222 | 0.750 |
| | 5 | 2 | 24 | 0.083333 | 0.875 |
| | 10 | 1 | 18 | 0.055556 | 1.000 |

**Table S5 Result for $n = 7$ instances**. From left to right, we list the instance identifier, the number $m$ of samples, the number of solutions, the number of spanning arborescences in the ancestry graph of the instance, the ratio between the solutions and spanning arborescences and the median edge recall.

| # | samples $m$ | solutions | spanning arborescences | ratio | median recall |
|---|---|---|---|---|---|
| 7 | 1 | 432 | 720 | 0.600000 | 0.500 |
|  | 2 | 94 | 120 | 0.783333 | 0.500 |
|  | 5 | 24 | 60 | 0.400000 | 0.667 |
|  | 10 | 6 | 24 | 0.250000 | 0.833 |
| 10 | 1 | 28 | 720 | 0.038889 | 0.667 |
|  | 2 | 17 | 720 | 0.023611 | 0.667 |
|  | 5 | 4 | 144 | 0.027778 | 0.833 |
|  | 10 | 3 | 144 | 0.020833 | 0.833 |
| 12 | 1 | 315 | 720 | 0.437500 | 0.333 |
|  | 2 | 43 | 120 | 0.358333 | 0.500 |
|  | 5 | 12 | 80 | 0.150000 | 0.750 |
|  | 10 | 6 | 48 | 0.125000 | 0.833 |
| 23 | 1 | 79 | 720 | 0.109722 | 0.500 |
|  | 2 | 18 | 360 | 0.050000 | 0.667 |
|  | 5 | 10 | 180 | 0.055556 | 0.750 |
|  | 10 | 3 | 90 | 0.033333 | 0.833 |
| 30 | 1 | 293 | 720 | 0.406944 | 0.500 |
|  | 2 | 70 | 120 | 0.583333 | 0.667 |
|  | 5 | 22 | 24 | 0.916667 | 0.667 |
|  | 10 | 6 | 6 | 1.000000 | 0.833 |
| 43 | 1 | 618 | 720 | 0.858333 | 0.333 |
|  | 2 | 54 | 720 | 0.075000 | 0.500 |
|  | 5 | 21 | 360 | 0.058333 | 0.667 |
|  | 10 | 6 | 216 | 0.027778 | 0.833 |
| 49 | 1 | 398 | 720 | 0.552778 | 0.333 |
|  | 2 | 37 | 270 | 0.137037 | 0.500 |
|  | 5 | 2 | 24 | 0.083333 | 0.917 |
|  | 10 | 1 | 24 | 0.041667 | 1.000 |
| 61 | 1 | 328 | 720 | 0.455556 | 0.500 |
|  | 2 | 106 | 240 | 0.441667 | 0.500 |
|  | 5 | 19 | 30 | 0.633333 | 0.667 |
|  | 10 | 3 | 8 | 0.375000 | 0.833 |
| 66 | 1 | 101 | 720 | 0.140278 | 0.500 |
|  | 2 | 14 | 240 | 0.058333 | 0.667 |
|  | 5 | 6 | 120 | 0.050000 | 0.833 |
|  | 10 | 2 | 48 | 0.041667 | 0.917 |
| 81 | 1 | 297 | 720 | 0.412500 | 0.500 |
|  | 2 | 50 | 240 | 0.208333 | 0.667 |
|  | 5 | 6 | 48 | 0.125000 | 0.833 |
|  | 10 | 2 | 24 | 0.083333 | 0.917 |

**Table S6 Result for $n = 9$ instances**. From left to right, we list the instance identifier, the number $m$ of samples, the number of solutions, the number of spanning arborescences in the ancestry graph of the instance, the ratio between the solutions and spanning arborescences and the median edge recall.

| # | samples $m$ | solutions | spanning arborescences | ratio | median recall |
|---|---|---|---|---|---|
| 0 | 1 | 1472 | 40320 | 0.036508 | 0.500 |
| | 2 | 36 | 1920 | 0.018750 | 0.750 |
| | 5 | 7 | 360 | 0.019444 | 0.875 |
| | 10 | 5 | 360 | 0.013889 | 0.875 |
| 5 | 1 | 10445 | 40320 | 0.259053 | 0.375 |
| | 2 | 2200 | 5040 | 0.436508 | 0.500 |
| | 5 | 4 | 16 | 0.250000 | 0.875 |
| | 10 | 3 | 12 | 0.250000 | 0.875 |
| 18 | 1 | 6180 | 40320 | 0.153274 | 0.500 |
| | 2 | 1450 | 5040 | 0.287698 | 0.500 |
| | 5 | 13 | 60 | 0.216667 | 0.750 |
| | 10 | 9 | 48 | 0.187500 | 0.750 |
| 24 | 1 | 4776 | 40320 | 0.118452 | 0.375 |
| | 2 | 522 | 10080 | 0.051786 | 0.500 |
| | 5 | 36 | 1440 | 0.025000 | 0.625 |
| | 10 | 12 | 960 | 0.012500 | 0.750 |
| 27 | 1 | 3755 | 40320 | 0.093130 | 0.500 |
| | 2 | 382 | 7560 | 0.050529 | 0.625 |
| | 5 | 16 | 864 | 0.018519 | 0.750 |
| | 10 | 6 | 360 | 0.016667 | 0.875 |
| 31 | 1 | 8183 | 40320 | 0.202951 | 0.375 |
| | 2 | 600 | 13440 | 0.044643 | 0.500 |
| | 5 | 19 | 288 | 0.065972 | 0.750 |
| | 10 | 6 | 180 | 0.033333 | 0.875 |
| 32 | 1 | 14760 | 40320 | 0.366071 | 0.375 |
| | 2 | 1196 | 3360 | 0.355952 | 0.500 |
| | 5 | 56 | 720 | 0.077778 | 0.625 |
| | 10 | 18 | 120 | 0.150000 | 0.688 |
| 48 | 1 | 9436 | 40320 | 0.234028 | 0.375 |
| | 2 | 1906 | 10080 | 0.189087 | 0.375 |
| | 5 | 36 | 240 | 0.150000 | 0.625 |
| | 10 | 9 | 48 | 0.187500 | 0.750 |
| 56 | 1 | 10122 | 40320 | 0.251042 | 0.375 |
| | 2 | 1234 | 2016 | 0.612103 | 0.500 |
| | 5 | 66 | 120 | 0.550000 | 0.750 |
| | 10 | 6 | 16 | 0.375000 | 0.875 |
| 70 | 1 | 22151 | 40320 | 0.549380 | 0.375 |
| | 2 | 3364 | 10080 | 0.333730 | 0.375 |
| | 5 | 13 | 80 | 0.162500 | 0.750 |
| | 10 | 7 | 48 | 0.145833 | 0.875 |

**Table S7 Result for $n = 11$ instances**. From left to right, we list the instance identifier, the number $m$ of samples, the number of solutions, the number of spanning arborescences in the ancestry graph of the instance, the ratio between the solutions and spanning arborescences and the median edge recall.

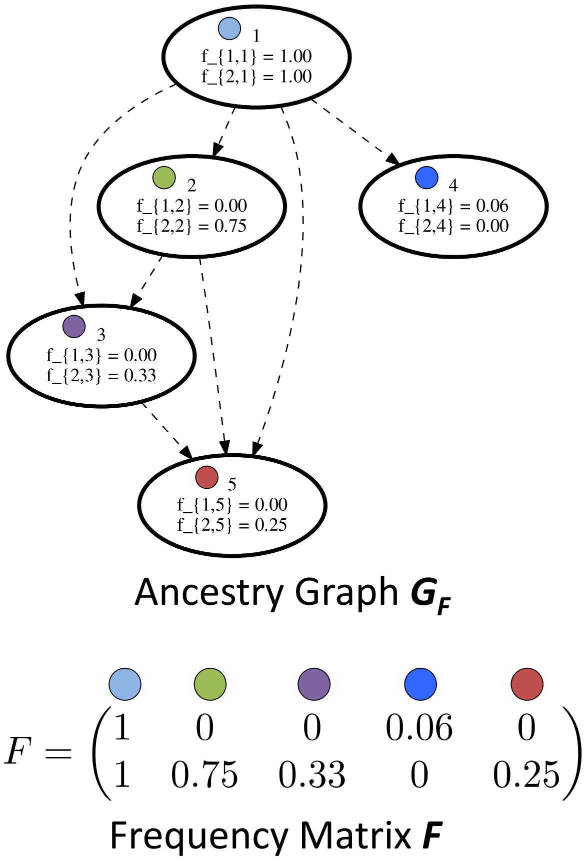
| # | samples $m$ | solutions | spanning arborescences | ratio | median recall |
|---|---|---|---|---|---|
| 24 | 1 | 74138 | 3628800 | 0.020430 | 0.400 |
| | 2 | 11301 | 1451520 | 0.007786 | 0.400 |
| | 5 | 4 | 2160 | 0.001852 | 0.900 |
| | 10 | 2 | 1296 | 0.001543 | 0.950 |
| 27 | 1 | 211022 | 3628800 | 0.058152 | 0.400 |
| | 2 | 9456 | 544320 | 0.017372 | 0.500 |
| | 5 | 46 | 12096 | 0.003803 | 0.700 |
| | 10 | 3 | 2592 | 0.001157 | 0.900 |
| 35 | 1 | 13338 | 3628800 | 0.003676 | 0.500 |
| | 2 | 3350 | 3628800 | 0.000923 | 0.600 |
| | 5 | 10 | 108000 | 0.000093 | 0.850 |
| | 10 | 3 | 72000 | 0.000042 | 0.900 |
| 69 | 1 | 224451 | 3628800 | 0.061853 | 0.400 |
| | 2 | 3898 | 120960 | 0.032226 | 0.600 |
| | 5 | 15 | 3840 | 0.003906 | 0.800 |
| | 10 | 5 | 1920 | 0.002604 | 0.900 |
| 83 | 1 | 129706 | 3628800 | 0.035743 | 0.400 |
| | 2 | 936 | 414720 | 0.002257 | 0.600 |
| | 5 | 104 | 40320 | 0.002579 | 0.600 |
| | 10 | 4 | 4320 | 0.000926 | 0.900 |
| 89 | 1 | 4249 | 3628800 | 0.001171 | 0.500 |
| | 2 | 547 | 1814400 | 0.000301 | 0.700 |
| | 5 | 4 | 15120 | 0.000265 | 0.900 |
| | 10 | 3 | 12960 | 0.000231 | 0.900 |
| 109 | 1 | 546559 | 3628800 | 0.150617 | 0.400 |
| | 2 | 78547 | 362880 | 0.216454 | 0.500 |
| | 5 | 48 | 480 | 0.100000 | 0.800 |
| | 10 | 7 | 64 | 0.109375 | 0.900 |
| 115 | 1 | 288866 | 3628800 | 0.079604 | 0.300 |
| | 2 | 6428 | 241920 | 0.026571 | 0.400 |
| | 5 | 6 | 192 | 0.031250 | 0.900 |
| | 10 | 6 | 512 | 0.011719 | 0.900 |
| 129 | 1 | 522216 | 3628800 | 0.143909 | 0.400 |
| | 2 | 103994 | 725760 | 0.143290 | 0.400 |
| | 5 | 60 | 640 | 0.093750 | 0.750 |
| | 10 | 12 | 96 | 0.125000 | 0.800 |
| 139 | 1 | 729024 | 3628800 | 0.200899 | 0.400 |
| | 2 | 84747 | 725760 | 0.116770 | 0.400 |
| | 5 | 10 | 432 | 0.023148 | 0.850 |
| | 10 | 8 | 216 | 0.037037 | 0.850 |

**Table S8 Result for $n = 13$ instances**. From left to right, we list the instance identifier, the number $m$ of samples, the number of solutions, the number of spanning arborescences in the ancestry graph of the instance, the ratio between the solutions and spanning arborescences and the median edge recall.

| # | samples $m$ | solutions | spanning arborescences | ratio | median recall |
|---|---|---|---|---|---|
| 3 | 1 | 9863339 | 479001600 | 0.020591 | 0.250 |
| | 2 | 409393 | 47900160 | 0.008547 | 0.417 |
| | 5 | 252 | 194400 | 0.001296 | 0.667 |
| | 10 | 4 | 11520 | 0.000347 | 0.917 |
| 12 | 1 | 1118667 | 479001600 | 0.002335 | 0.250 |
| | 2 | 14892 | 19958400 | 0.000746 | 0.583 |
| | 5 | 16 | 138240 | 0.000116 | 0.833 |
| | 10 | 6 | 40320 | 0.000149 | 0.917 |
| 15 | 1 | 867056 | 479001600 | 0.001810 | 0.417 |
| | 2 | 26834 | 114048000 | 0.000235 | 0.500 |
| | 5 | 42 | 2419200 | 0.000017 | 0.750 |
| | 10 | 4 | 829440 | 0.000005 | 0.917 |
| 19 | 1 | 7318619 | 479001600 | 0.015279 | 0.333 |
| | 2 | 120419 | 65318400 | 0.001844 | 0.500 |
| | 5 | 60 | 97200 | 0.000617 | 0.750 |
| | 10 | 6 | 38880 | 0.000154 | 0.917 |
| 25 | 1 | 78781 | 479001600 | 0.000164 | 0.500 |
| | 2 | 2488 | 119750400 | 0.000021 | 0.667 |
| | 5 | 44 | 1244160 | 0.000035 | 0.750 |
| | 10 | 3 | 345600 | 0.000009 | 0.917 |
| 40 | 1 | 9300931 | 479001600 | 0.019417 | 0.250 |
| | 2 | 436744 | 47900160 | 0.009118 | 0.333 |
| | 5 | 352 | 40320 | 0.008730 | 0.667 |
| | 10 | 12 | 4800 | 0.002500 | 0.833 |
| 43 | 1 | 33809749 | 479001600 | 0.070584 | NA |
| | 2 | 575588 | 29030400 | 0.019827 | 0.333 |
| | 5 | 152 | 69120 | 0.002199 | 0.667 |
| | 10 | 7 | 5760 | 0.001215 | 0.917 |
| 45 | 1 | 28053 | 479001600 | 0.000059 | 0.583 |
| | 2 | 1592 | 108864000 | 0.000015 | 0.667 |
| | 5 | 20 | 2646000 | 0.000008 | 0.833 |
| | 10 | 2 | 1620000 | 0.000001 | 0.958 |
| 56 | 1 | 23086684 | 479001600 | 0.048198 | NA |
| | 2 | 2235187 | 79833600 | 0.027998 | 0.333 |
| | 5 | 280 | 57600 | 0.004861 | 0.667 |
| | 10 | 12 | 3840 | 0.003125 | 0.833 |
| 84 | 1 | 27236653 | 479001600 | 0.056861 | NA |
| | 2 | 8623319 | 479001600 | 0.018003 | 0.333 |
| | 5 | 156 | 3600 | 0.043333 | 0.667 |
| | 10 | 12 | 768 | 0.015625 | 0.833 |

**Table S9 Rejection sampling results for $n = 7$ instances.** From left to right, we list the instance identifier, the number $m$ of samples, the number of solutions (satisfying (SC)), the number of spanning arborescences in the ancestry graph of the instance, the ratio between the solutions and spanning trees, the total number of samples (trials) used by the rejection sampling algorithm, the fraction of accepted samples (successful trials). Observe that 'success ratio' $\approx$ 'solution ratio'.

| # | samples $m$ | solutions | spanning arborescences | solution ratio | trials | success ratio |
|---|---|---|---|---|---|---|
| 7 | 1 | 432 | 720 | 0.600 | 16585 | 0.603 |
| | 2 | 94 | 120 | 0.783 | 12753 | 0.784 |
| | 5 | 24 | 60 | 0.400 | 24821 | 0.403 |
| | 10 | 6 | 24 | 0.250 | 40859 | 0.245 |
| 10 | 1 | 28 | 720 | 0.039 | 256090 | 0.039 |
| | 2 | 17 | 720 | 0.024 | 419637 | 0.024 |
| | 5 | 4 | 144 | 0.028 | 358360 | 0.028 |
| | 10 | 3 | 144 | 0.021 | 481517 | 0.021 |
| 12 | 1 | 315 | 720 | 0.438 | 23109 | 0.433 |
| | 2 | 43 | 120 | 0.358 | 28009 | 0.357 |
| | 5 | 12 | 80 | 0.150 | 67803 | 0.147 |
| | 10 | 6 | 48 | 0.125 | 78530 | 0.127 |
| 23 | 1 | 79 | 720 | 0.110 | 90828 | 0.110 |
| | 2 | 18 | 360 | 0.050 | 197369 | 0.051 |
| | 5 | 10 | 180 | 0.056 | 180518 | 0.055 |
| | 10 | 3 | 90 | 0.033 | 300223 | 0.033 |
| 30 | 1 | 293 | 720 | 0.407 | 24665 | 0.405 |
| | 2 | 70 | 120 | 0.583 | 17204 | 0.581 |
| | 5 | 22 | 24 | 0.917 | 10942 | 0.914 |
| | 10 | 6 | 6 | 1.000 | 10000 | 1.000 |
| 43 | 1 | 618 | 720 | 0.858 | 11606 | 0.862 |
| | 2 | 54 | 720 | 0.075 | 132441 | 0.076 |
| | 5 | 21 | 360 | 0.058 | 169685 | 0.059 |
| | 10 | 6 | 216 | 0.028 | 354898 | 0.028 |
| 49 | 1 | 398 | 720 | 0.553 | 18115 | 0.552 |
| | 2 | 37 | 270 | 0.137 | 73073 | 0.137 |
| | 5 | 2 | 24 | 0.083 | 120731 | 0.083 |
| | 10 | 1 | 24 | 0.042 | 239816 | 0.042 |
| 61 | 1 | 328 | 720 | 0.456 | 21939 | 0.456 |
| | 2 | 106 | 240 | 0.442 | 22626 | 0.442 |
| | 5 | 19 | 30 | 0.633 | 15896 | 0.629 |
| | 10 | 3 | 8 | 0.375 | 26864 | 0.372 |
| 66 | 1 | 101 | 720 | 0.140 | 71260 | 0.140 |
| | 2 | 14 | 240 | 0.058 | 171753 | 0.058 |
| | 5 | 6 | 120 | 0.050 | 199703 | 0.050 |
| | 10 | 2 | 48 | 0.042 | 239576 | 0.042 |
| 81 | 1 | 297 | 720 | 0.412 | 24528 | 0.408 |
| | 2 | 50 | 240 | 0.208 | 49137 | 0.204 |
| | 5 | 6 | 48 | 0.125 | 79423 | 0.126 |
| | 10 | 2 | 24 | 0.083 | 120821 | 0.083 |



$$F = \begin{pmatrix} 1 & 0 & 0 & 0.06 & 0 \\ 1 & 0.75 & 0.33 & 0 & 0.25 \end{pmatrix}$$

**Figure S3 Example ancestry graph.** Frequency matrix $F$ corresponds to a simulated $n = 5$ instance (#9) and has $m = 2$ samples. The corresponding ancestry graph $G_F$ illustrates the potential parental relationships.

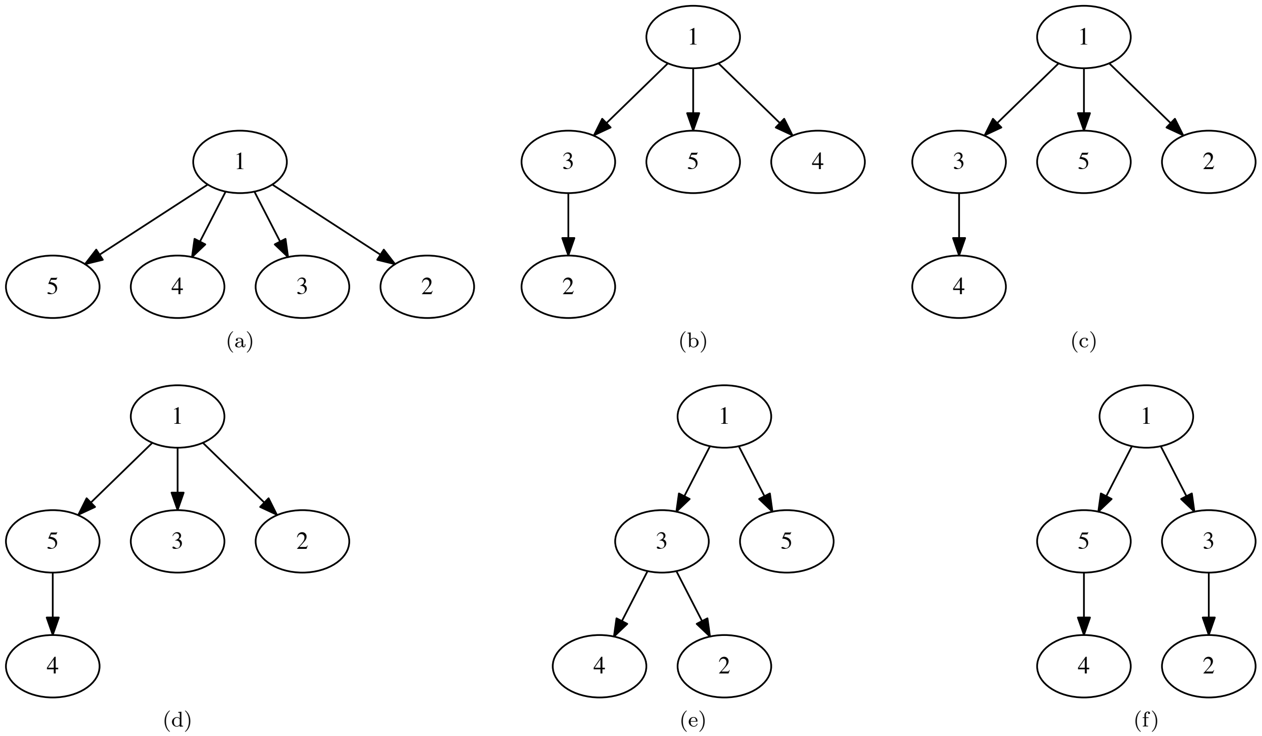


**Figure S4 Patient CRUK0012 with $m = 2$ samples and $n = 5$ mutation clusters has six possible trees.** Jamal-Hanjani et al. [3] reported two trees, which correspond to (e) and (f). The solution space contains four more trees that were not reported in [3].

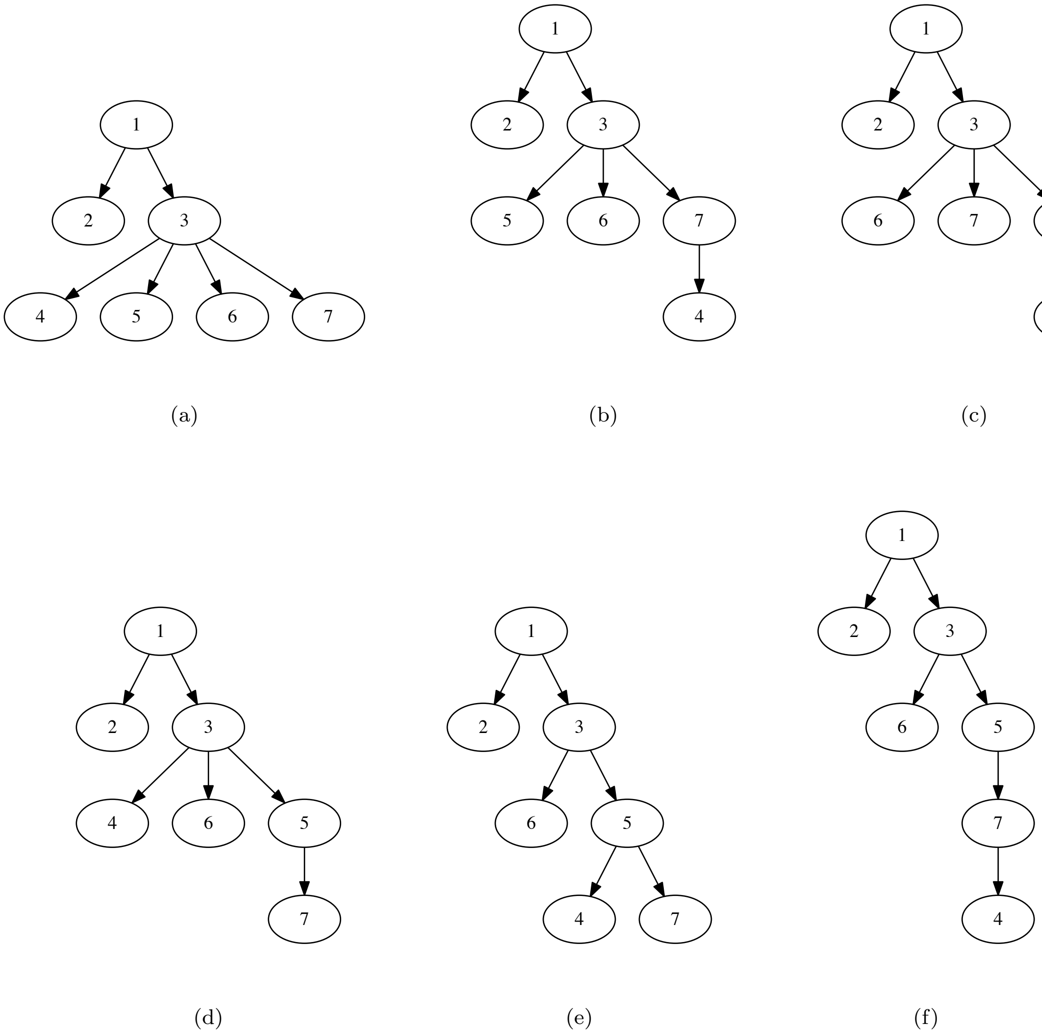


**Figure S5 Instance #81 with $n = 7$ mutations and $m = 5$ samples has six solutions.** Solution (A) is the true solution. All 7500 samples generated by PhyloWGS correspond to (F). Canopy generated a total of 387 samples corresponding to three different trees. Two out of the three trees were incorrect (307 samples), the remaining 80 samples correspond to (A). Our rejection sampling procedure generated 10000 samples corresponding to each of the six trees in roughly equal proportions.

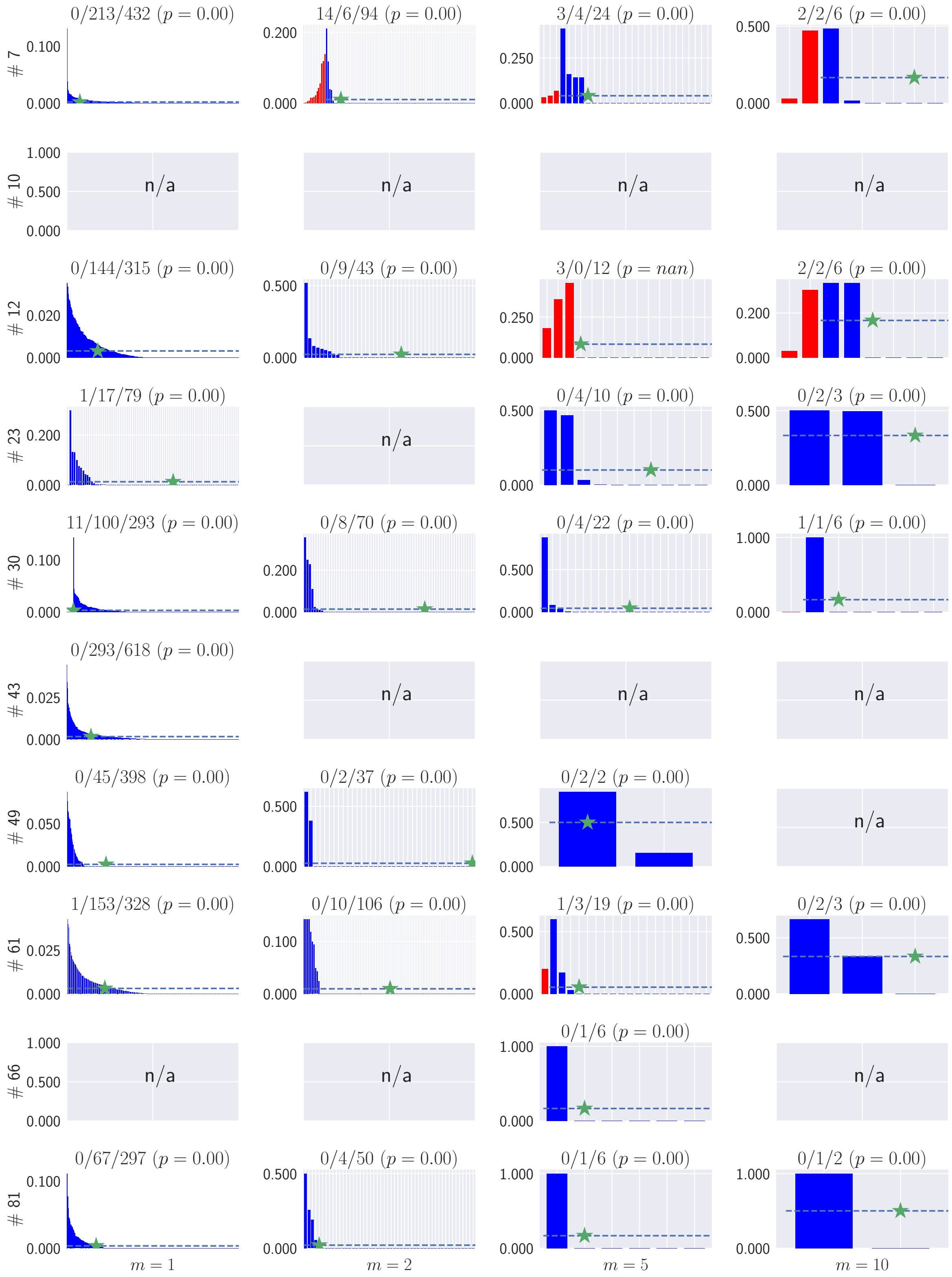


**Figure S6 PhyloWGS results.** Each plot shows the relative frequency of correct solutions (satisfying (SC)) output by PhyloWGS (blue bars), with the simulated solution indicated by '$\star$'. Red bars correspond to incorrect solutions (violating (SC)). Dashed line indicates the expected relative frequency in the case of uniformity. The title of each plot lists the number of incorrect solutions, the number of recovered correct solutions, the total number of correct solutions and the $p$-value of the chi-squared test of uniformity. PhyloWGS did not generate any trees without clustered mutations for the instances marked by 'n/a'.

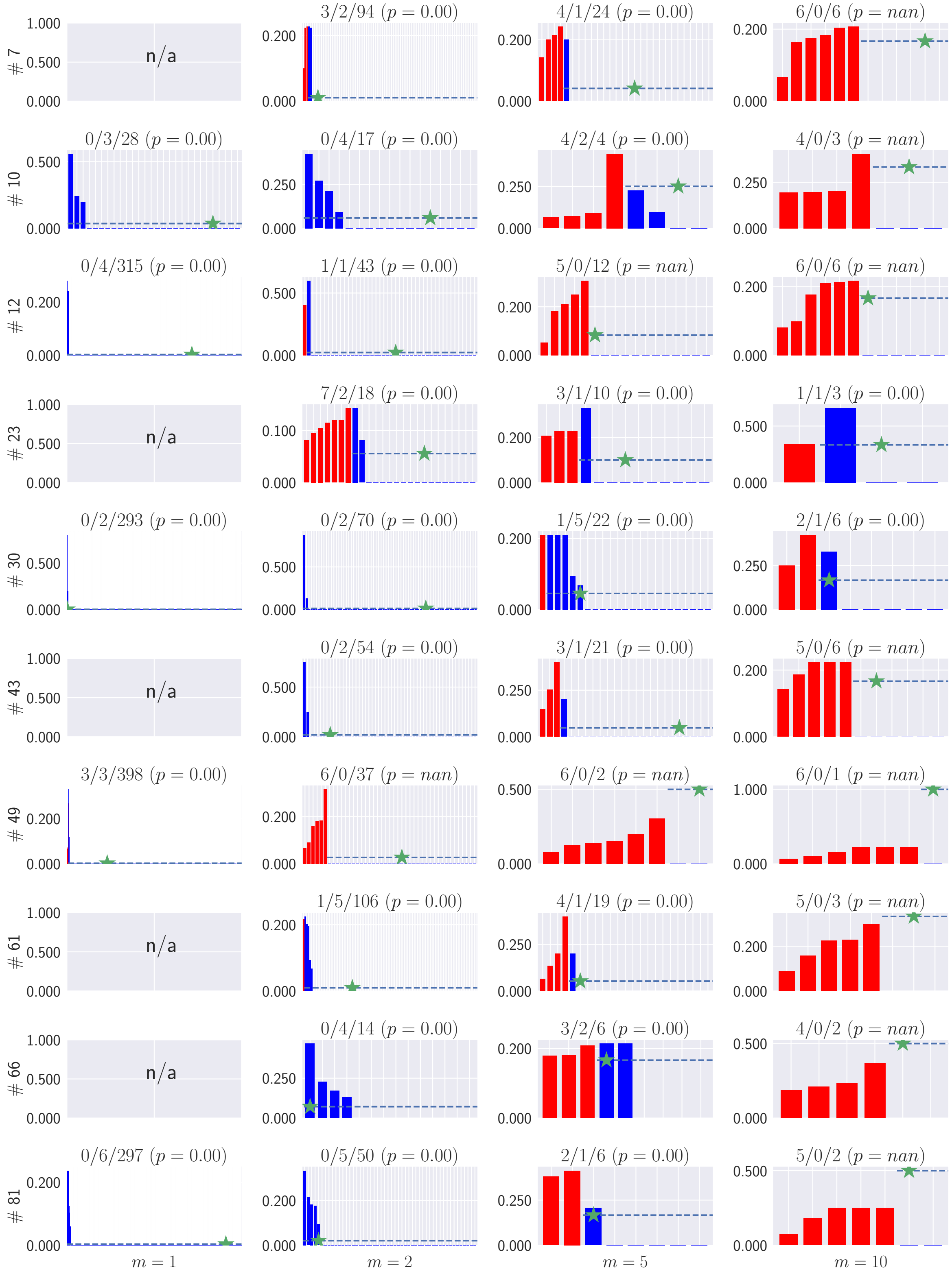


**Figure S7 Canopy results.** Each plot shows the relative frequency of correct solutions (satisfying (SC)) output by Canopy (blue bars), with the simulated solution indicated by '⋆'. Red bars correspond to incorrect solutions (violating (SC)). Dashed line indicates the expected relative frequency in the case of uniformity. The title of each plot lists the number of incorrect solutions, the number of recovered correct solutions, the total number of correct solutions and the $p$-value of the chi-squared test of uniformity. Canopy did not generate any trees without clustered mutations for the instances marked by 'n/a'.

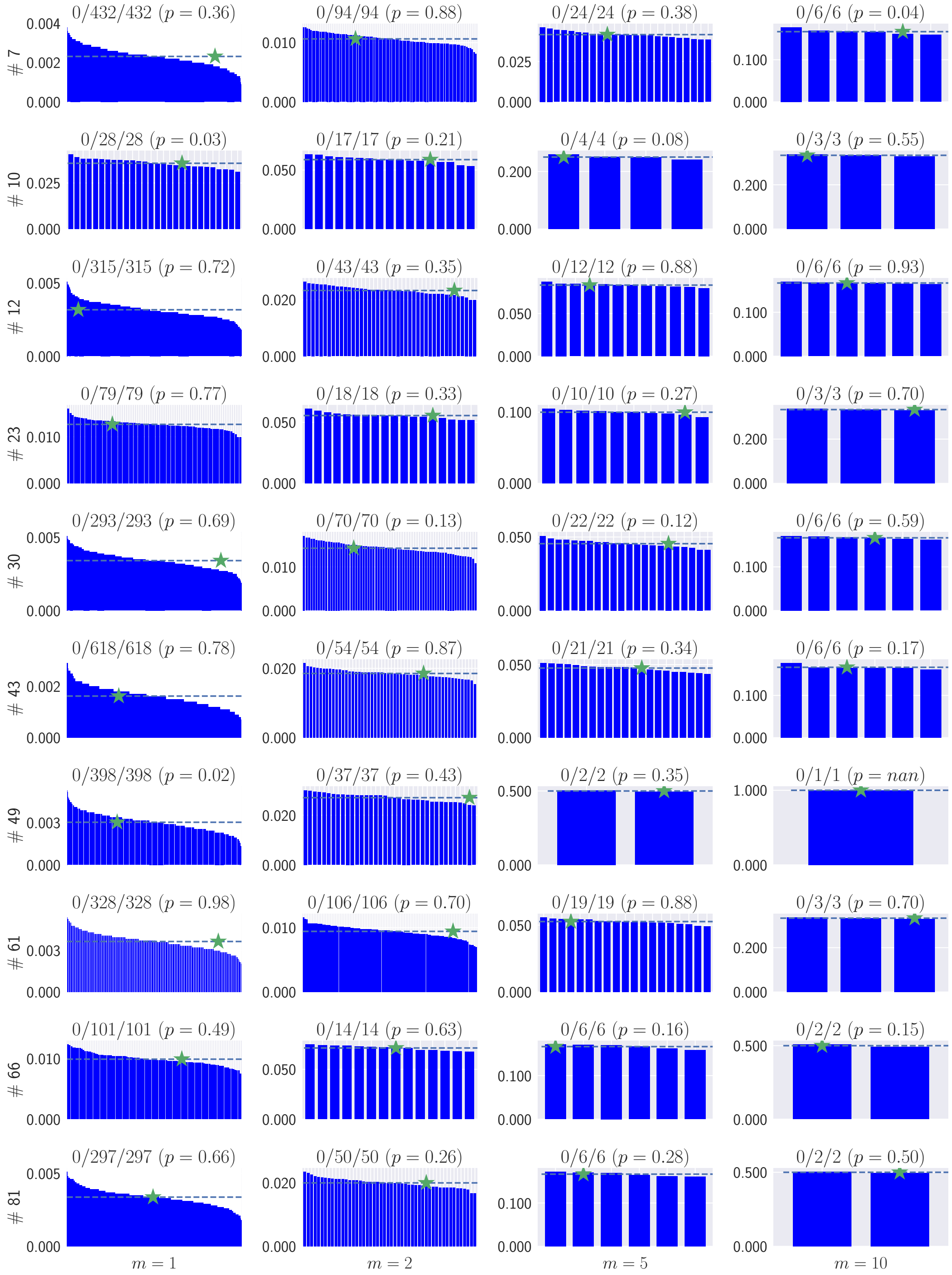


**Figure S8 Rejection sampling results.** Each plot shows the relative frequency of correct solutions (satisfying (SC)) output by our rejection sampling procedure (blue bars), with the simulated solution indicated by '⋆'. Dashed line indicates the expected relative frequency in the case of uniformity. The title of each plot lists the number of recovered correct solutions, the total number of correct solutions and the $p$-value of the chi-squared test of uniformity.

**Author details**
[1]Department of Computer Science, University of Illinois at Urbana-Champaign, Champaign, IL 61801, USA. [2]Department of Bioengineering, University of Illinois at Urbana-Champaign, Champaign, IL 61801, USA.

**References**

1. Creignou, N., Hermann, M.: On #P completeness of some counting problems. Research Report RR-2144, INRIA (1993). https://hal.inria.fr/inria-00074528
2. El-Kebir, M., Satas, G., Oesper, L., Raphael, B.J.: Inferring the Mutational History of a Tumor Using Multi-state Perfect Phylogeny Mixtures. Cell Systems **3**(1), 43–53 (2016)
3. Jamal-Hanjani, M., Wilson, G.A., McGranahan, N., Birkbak, N.J., Watkins, T.B.K., Veeriah, S., Shafi, S., Johnson, D.H., Mitter, R., Rosenthal, R., Salm, M., Horswell, S., Escudero, M., Matthews, N., Rowan, A., Chambers, T., Moore, D.A., Turajlic, S., Xu, H., Lee, S.M., Forster, M.D., Ahmad, T., Hiley, C.T., Abbosh, C., Falzon, M., Borg, E., Marafioti, T., Lawrence, D., Hayward, M., Kolvekar, S., Panagiotopoulos, N., Janes, S.M., Thakrar, R., Ahmed, A., Blackhall, F., Summers, Y., Shah, R., Joseph, L., Quinn, A.M., Crosbie, P.A., Naidu, B., Middleton, G., Langman, G., Trotter, S., Nicolson, M., Remmen, H., Kerr, K., Chetty, M., Gomersall, L., Fennell, D.A., Nakas, A., Rathinam, S., Anand, G., Khan, S., Russell, P., Ezhil, V., Ismail, B., Irvin-sellers, M., Prakash, V., Lester, J.F., Kornaszewska, M., Attanoos, R., Adams, H., Davies, H., Dentro, S., Taniere, P., O'Sullivan, B., Lowe, H.L., Hartley, J.A., Iles, N., Bell, H., Ngai, Y., Shaw, J.A., Herrero, J., Szallasi, Z., Schwarz, R.F., Stewart, A., Quezada, S.A., Le Quesne, J., Van Loo, P., Dive, C., Hackshaw, A., Swanton, C., TRACERx Consortium: Tracking the Evolution of Non-Small-Cell Lung Cancer. New England Journal of Medicine **376**(22), 2109–2121 (2017)