The influence of mutation models in kinship likelihoods

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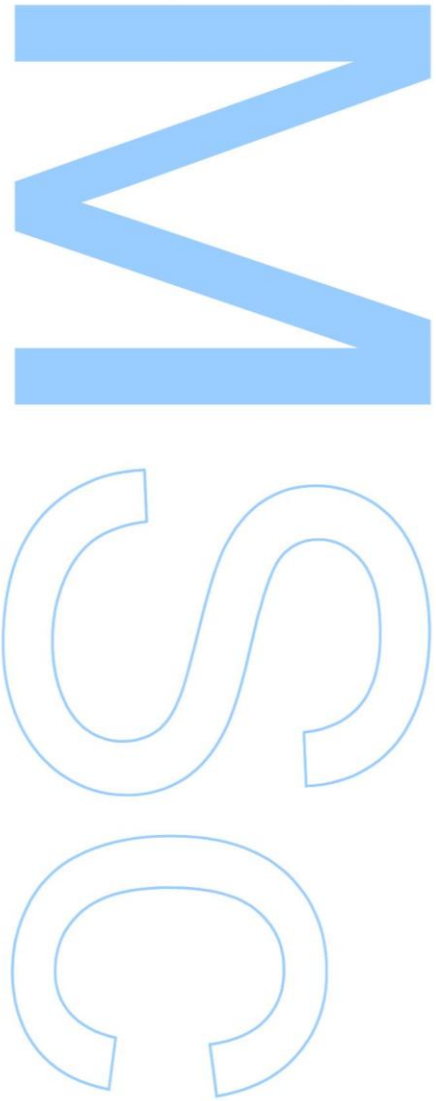

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Abstract

Different mutation models have been developed to consider the genotypic observations of parent(s)/offspring duos or trios, even though, for autosomal transmission, only Mendelian incompatibilities, not mutations, are able to be identified. The most commonly considered mutation models are the so-called “Equal”, “Proportional”, “Stepwise” and “Extended Stepwise”, all implemented in the software Familias.

In this work we simulated 100,000 families (in duos and trios) of Parent-Child, Full-siblings, and Half-siblings, as well as 100,000 profiles of Unrelated individuals, assuming a specific database for 17 autosomal STRs and probabilities of incompatibility inferred from the American Association of Blood Banks (AABB) report, 2008. 10 markers with fictitious allele frequencies were also considered. Using the R version of the software Familias, we calculated the likelihood ratios (LRs, where the probability of the genotypic configuration of the individuals assuming each of the pedigrees was compared with the probability of the same observations assuming unrelatedness, for each marker, considering each of the aforementioned models, as well as assuming the absence of mutation (Null model), and also increasing the integer-length mutation rate in the Extended Stepwise model parameters. In the case of full-siblings, the comparison assuming half-sibship as the alternative pedigree was also considered.

The results show that the use of the different mutation models and the increase in the considered mutation rate do not result in major differences in the LRs. The comparisons between the LRs obtained with the Null model and the others in cases with no incompatibilities show that the consideration of hidden mutations also does not have a major influence in the final result. Regarding the fictitious markers, no clear conclusions could be taken regarding the relationship between a marker’s allele frequencies’ configuration and its proneness to be influenced by the use of different mutation models or parameters. Future work could be developed to take a broader approach regarding the fictitious markers (more variability should be introduced) and the paternity cases where the putative father is a close relative of the real father.

Resumo

Vários modelos de mutação foram desenvolvidos para considerar as observações genotípicas de duos ou trios de pai(s)/filho(s), apesar de, na transmissão autossómica, apenas possam ser identificadas incompatibilidades Mendelianas, e não mutações. Os modelos de mutação mais comummente considerados são os chamados "Equal", "Proportional", "Stepwise" e "Extended Stepwise", todos eles implementados no *software* Familias.

Neste trabalho simulamos 100,000 famílias (em duos e trios) de Pai-Filho, Irmãos, Meios-irmãos, bem como 100,000 perfis de indivíduos não-relacionados, assumindo uma base de dados específica com 17 microssatélites autossómicos e probabilidades de incompatibilidade inferidas do relatório de 2008 da American Association of Blood Banks (AABB). 10 marcadores com frequências alélicas fictícias foram também considerados.

Usando a versão R do *software* Familias, calculamos as razões de verosimilhança (LRs), onde a probabilidade da configuração genotípica dos indivíduos assumindo cada um dos *pedigrees* foi comparado com a probabilidade dessas mesmas observações assumindo que os indivíduos não são relacionados, para cada marcador. Considerando cada um dos modelos acima mencionados, bem como assumindo ausência de mutação (modelo Nulo) e também aumentando a taxa de mutação entre repetições completas, nos parâmetros do modelo Extended Stepwise. No caso dos Irmãos, foi também feita a comparação assumindo Meios-irmãos como a hipótese alternativa.

Os resultados mostram que o uso de diferentes modelos de mutação e o aumento da taxa de mutação considerada não resultam em grandes diferenças nos LRs. As comparações entre os LRs obtidos com o modelo Nulo e os restantes, em casos sem incompatibilidades, mostram que a consideração de mutações silenciosas também não tem um grande impacto no resultado final. Relativamente aos marcadores fictícios, não puderam ser retiradas conclusões claras quanto à relação entre a configuração das frequências alélicas de um marcador e a sua propensão para ser influenciado pelo uso de diferentes modelos de mutação ou parâmetros. Poderá ser desenvolvido trabalho futuro para alargar a abordagem aos marcadores fictícios (deverá ser introduzida maior variabilidade) e aos casos de paternidade em que o suposto pai é um parente próximo do pai verdadeiro.

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Introduction

1.1. Forensic Genetics

Forensic Genetics is an applied science which has been described as "the application of genetics to human and non-human material (in the sense of a science with the purpose of studying inherited characteristics for the analysis of inter- and intra-specific variations in populations) for the resolution of legal conflicts" (Carracedo, 1998).

Unlike many other forensic sciences, Forensic Genetics is capable of producing evidence which is not evaluated in a purely empirical way, but framed within population genetics theory. A solid theoretical basis, substantial validation and continuous quality assurance practices, along with vast peer-reviewed literature, differentiate Forensic Genetics from other forensic sciences (Amorim & Budowle, 2017, p. 4). It does not rely on the assumption of discernible uniqueness, according to which any two marks that are indistinguishable must have been produced by the same agent, since every object must leave unique traces (Saks and Koehler, 2005), instead basing its conclusions on Probability Theory.

The work of a forensic geneticist focuses on either interpretation of mixtures (Gill *et al.*, 1998), which is especially relevant in rape cases (see Weir *et al.*, 1997), or kinship evaluation (including identification), which will be the focus of this work.

1.2. Kinship Evaluation

1.2.1. Applications

DNA profiling provides a reliable means to establish or discard biological relationships between individuals, whether in a criminal or civil context. In a criminal context, kinship testing mostly serves identification purposes, using biological traces from the perpetrators found in crime scenes or on the victims, such as saliva in sexual assault cases (Williams *et al.*, 2015)., and paternity testing, namely in late reported cases of rape resulting in pregnancy – such cases might also involve interpretation of mixtures, when identifying the fetus' genotype from abortion material, which is a mixture of the mother's and the fetus' genotypes.

In the civil framework of kinship evaluations, paternity testing is the most frequent analysis, with hundreds of thousands of tests being performed per year (AABB, 2008). Other commonly tested kinships include sibship and half-sibship (Thomson *et al.*, 2001;

Mayor & Balding, 2006) when the parent(s) in doubt isn't (aren't) available for testing. Kinship tests may also be performed in the context of: (a.) identification of victims of mass disasters (see Hsu *et al.*, 1999; Calacal *et al.*, 2005 for examples), (b.) identification of ancient human remains — such as the famous case of identification of the remains of the Romanov family through mitochondrial DNA sequencing, Short Tandem Repeat analysis and PCR cloning (Gill *et al.*, 1994) —, (c.) proving biological relationships in cases of inheritance claims, or (d.) resolution of immigration cases, such as the first kinship test using DNA fingerprinting (Jeffreys *et al.,* 1985).

Besides these human-centered applications, kinship tests can also be performed using non-human DNA, such as, for example, canine DNA (van Asch *et al.*, 2009). Non-human DNA can be used to solve judicial disputes of undue appropriation, as described by Lirón *et al.*, 2003, through parentage testing in cattle, it can act as evidence to link suspects to a given crime scene, as shown by Menotti-Raymond *et al.*, 2009, using domestic cat hair to implicate a murder suspect. Identity testing using non-human DNA might also be useful to confirm (or exclude) a given specimen as the perpetrator of an attack (see Tsuji *et al*., 2008 and Frosch *et al.* 2011 for examples).

Throughout this work, we will focus on human paternity, sibship and half-sibship evaluations, which means the databases and STRs kits considered are based in human forensic markers, even though the theoretical and statistical approach is analogous for non-human material.

1.2.2. Types of markers

Depending on the type of analysis to be performed and its objective, multiple types of DNA polymorphisms may be used in forensic and/or population genetics. These polymorphisms can be divided into two main groups — bi-allelic and multi-allelic polymorphisms.

Bi-allelic markers are *loci* which present two possible variants and, therefore, three possible genotypes. These markers include Single Nucleotide Polymorphisms and Insertion/Deletion Polymorphisms. Multi-allelic markers have multiple variants per *locus* (and, therefore, a multitude of possible genotypes). It is worth to note that neither one of these types of markers are exclusively bi-allelic – there are multi-allelic Single Nucleotide and Insertion/Deletion Polymorphisms, although the vast majority of them are indeed bi-allelic. The most commonly used multi-allelic markers in Forensic Genetics are Short Tandem Repeats.

1.2.2.1. Single Nucleotide Polymorphisms (SNPs)

SNPs are single-base sequence variations between individuals, located in specific physical locations in the genome. They are the most common human polymorphism, with millions of occurrences throughout the genome — they have been estimated to occur at 1 in every 1,000-2,000 bases (Sachidanandam *et al.*, 2001). These markers are usually considered unique polymorphic events, due to their low mutation rates, in the order of magnitude of 10^{-8} (Nachman & Crowell, 2000). SNPs can be used for identity testing/individual identification and to infer lineages, ancestry, or even phenotypes (Budowle & Van Daal, 2008).

1.2.2.2. Insertion/Deletion Polymorphisms (Indels)

Another type of bi-allelic markers are Indels, which are characterized by insertions or deletions of one or multiple nucleotides in the genome. Over 2,000 insertion/deletion polymorphisms have been characterized throughout the human genome (Weber *et al.*, 2002). Most have allele-length differences of up to 4 nucleotides, but some rare cases may even have differences of hundreds of kilobase pairs (Lupski e*t al.*, 1996). Indels can also be used for identity testing — for example, a multiplex assay with 38 non-coding bi-allelic autosomal Indels has been developed by Pereira *et al.*, 2009, which produces random match probabilities within the orders of magnitude of 10^{-14} to 10^{-15}. They have also proven to be particularly useful for ancestry inference, as shown in Pereira *et al.*, 2012.

However, since the low polymorphism of bi-allelic markers leads to a greater probability that two individuals share identical alleles by chance, both Indels and the aforementioned SNPs should be taken with caution in the inclusion of an alleged father (Pinto *et al*., 2013; Amorim & Pereira, 2005).

1.2.2.3. Short Tandem Repeats (STRs)

STRs, or microsatellites, are multi-allelic markers consisting of a number of repetitions of a certain nucleotide sequence. Their core repeat region is usually between 1bp and 6bp long, with the most preferred in Forensic Genetics usually having core repeats of 4–5bp. Depending on the configuration of the repeat, they can be classified as simple, simple with non-consensus (incomplete) repeats, compound, and complex STRs (Gill *et al.*, 1997). These markers typically have estimated mutation rates in the order of magnitude of 10^{-3} (Weber & Wong, 1993) and they are the most commonly used

markers in forensic and kinship investigations, given the simplicity of their analysis, their high heterozygosity and high discrimination power, when compared, for example, to the aforementioned SNPs (Amorim & Pereira, 2005). Autosomal STRs are the most used for kinship evaluations, though STRs in the X and Y-chromosomes can also be used to complement those found in the autosomes (Diegoli, 2015).

1.2.3. Evaluation of DNA evidence

1.2.3.1. Likelihood Ratio

After analysis of the genetic markers' (e.g. STRs) results, the quantification of the evidence is made and presented through a Likelihood Ratio (LR), which measures the strength of the evidence regarding the hypothesis being tested. If the variable E represents the genetic evidence and $\mathrm{H1}$ and $\mathrm{H2}$ represent two competing hypotheses *a priori* defined, which are mutually exclusive and exhaustive — assuming a standard paternity test, for example, $\mathrm{H1}$ is the hypothesis that the individuals are related as father and child and $\mathrm{H2}$ is the hypothesis that the individuals are unrelated – then $\mathrm{P(H1|E)}$ and $\mathrm{P(H2|E)}$ are the probabilities of the first and second hypotheses, respectively, according to the evidence. Therefore, according to the Bayes Theorem, we get:

$$\frac{P(H1|E)}{P(H2|E)} = \frac{P(H1)}{P(H2)} \times \frac{P(E|H1)}{P(E|H2)}$$

$\mathrm{P(H1)}$ and $\mathrm{P(H2)}$ are the probabilities *a priori* of each of the hypotheses, based on prior non-scientific data. However, generally, each of the hypotheses is considered to have the same probability *a priori*, which means that $\frac{P(H1)}{P(H2)} = 1$. Therefore, the final Likelihood Ratio shall be given by:

$$LR = \frac{P(E|H1)}{P(E|H2)}$$

where $\mathrm{P(E|H1)}$ is the probability of the observations assuming that the individuals are related as father and child, and $\mathrm{P(E|H2)}$ is the probability of such evidence assuming that they are unrelated. The numerical result (let's say *X*) means that the evidence is *X* times more likely assuming $\mathrm{H1}$ than assuming $\mathrm{H2}$. It is worth to note that this is not the same as stating that $\mathrm{H1}$ is *X* times more likely than $\mathrm{H2}$, as such an equivalence would constitute the transposed conditional fallacy, or prosecutor's fallacy (Balding & Donnelly, 1994).

When working with a battery of independently segregated markers, as will be the case on this work (focusing on independent autosomal STRs, an overall result is achieved by multiplication of the partial values obtained for each marker.

1.2.3.2. Software `Familias`

One of the most used software programs to perform this quantitative evaluation is `Familias`, which has been developed by Petter Mostad and Thore Egeland (Norwegian Computing Center) in cooperation with Bjørnar Olaisen, Margurethe Stenersen, and Bente Mevåg (Institute of Forensic Medicine, Oslo) (Egeland *et al.*, 2000). `Familias` has been validated for calculating likelihood ratios for parentage and kinship by Drábek, 2009 and it has undergone multiple updates and improvements since then. Our choice of this software is based on the facts that it is available for free, it allows for the use of different mutation models and it can be used either through its own user interface, or through the package `Familias` for the R programming language (Mostad *et al.*, 2016), allowing for calculations at very large scales – which is the case of our work.

1.2.3.3. Mendelian incompatibilities: mutations and silent alleles

Mutation can be defined as a genetic phenomenon characterized by an unexpected change in the genome of some cells of an individual, which can be transmitted to the offspring if occurring in the germinal line. This often results in a child not sharing any alleles with one of the parents in a given genetic marker, or having an allele that is different from all of their parents' alleles in the same marker, which is designated as a Mendelian incompatibility, since it does not follow the rules of codominant transmission established by Gregor Mendel in 1866 (Bateson, 1901). From this point onwards, mentions to mutations will refer to germinal mutations, which are those that are relevant to kinship analysis.

Mutations in STRs can have multiple causes, the most frequent being a phenomenon called *strand slippage* (Schlötterer & Tautz, 1992), during DNA replication, where the polymerase duplicates or skips a sequence repetition, producing a different variant with either more or fewer repetitions than the original allele (Ellegren, 2004).

Besides mutations, Mendelian incompatibilities might also be observed due to undetected silent alleles, which may lead to apparent opposite homozygosity between, for example, a father and his child. Such a case, which could be explained by the presence of a silent allele, is considered a second order incompatibility. When such consideration is not possible (e.g.: the two alleles from the child (heterozygous) are both

absent from the father, or the child has an allele which is absent in both the mother and the father), the incompatibilities can only be explained with the occurrence of mutations and, therefore, classify as first order incompatibilities (Pinto *et al.*, 2013). The occurrence of silent alleles has always been taken into account throughout this work.

In the presence of Mendelian incompatibilities, the likelihood ratios regarding a given kinship must thus account for mutations and also for the occurrence of silent alleles, which might lower the kinship indices (Amorim & Carneiro, 2008). However, Mendelian incompatibilities cannot be found in all kinships – for example, a pair of full-siblings or half-siblings may not share any Identity-by-Descent alleles on a given marker with 25% and 50% probability, respectively, which means that no possible genetic observation between them (when tested in duos, without another relative, such as the mother, to add genetic information) could lead to a Mendelian incompatibility.

1.3. Mutation Models

1.3.1. Mutation rate estimates

Mutation rate estimations for human autosomal STRs are generally obtained by genotyping a large group of pedigrees (trios) where parentage is undoubted or has previously been confirmed with a negligible degree of uncertainty. Mendelian incompatibilities between filial and parental alleles should then be identified and attributed to one of the paternal lineages. The frequency of such incompatibilities, given the total number of meiosis analyzed, is considered to correspond to an estimate of the general mutation rate for the marker in question (AABB, 2008).

However, considerations about the origin of mutations tend to be biased — for example, in a case where an incompatibility can be explained either by a 1-step mutation or a 3-step mutation, a prior preference for a model emphasizing single-step mutations would lead to the mutational event being ascribed to one of the parental lines, when, in reality, it might have happened in the other (Vicard & Dawid, 2004). This ambiguity is a problem in all modes of transmission except for the Y-chromosome, where, given its haploidy, there is no ambiguity as to which paternal allele has mutated into which filial allele (Pinto *et al*., 2014).

Not all forensic laboratories adopt the same practices when considering mutations: some routinely specify mutation models for all markers independently of the case data, as recommended in Egeland *et al.*, 2016 (p. 26), who states that it might be dubious to

change the mutation model only to fit specific observations, after a Mendelian incompatibility is found. However, some laboratories choose to only do so when in the presence of incompatibilities. This option can be justified by the fact that the apparent mutation rates that have been estimated for autosomal markers are generally underestimated (they are actually incompatibility rates, since hidden mutations are not considered).

Hidden mutations are mutational events that do not lead to Mendelian incompatibilities, due to one parental allele mutating into an allele that coincides with the alternative parental allele. Such mutations cannot be detected, as they will be (wrongly) considered as “normal”, non-mutated, allelic transmissions. Further analysis on this subject has been carried out by Slooten & Ricciardi (2013).

It is here worth to note that hidden mutations, despite not being considered in the estimation of mutation rates, are considered in the computations of the software we choose to develop the work (unless the user specifies a null mutation rate).

1.3.2. Mutation models

Mutation rates have been shown to differ significantly across different STRs, with factors such as the structure or length of the original allele (Brinkmann *et al*., 1998), or the difference in number of repeats of the original and mutated alleles (Weber & Wong, 1993). The Appendix 1 of the Annual Report Summary for Testing in 2008 by the American Association of Blood Banks (AABB) provides a list of estimated mutation rates for 17 commonly used STRs (under the biased framework previously referred), demonstrating large differences between paternal and maternal meiosis, as well as within each lineage. While paternal estimated mutation rates range from $7x10^{-5}$ to $3.7x10^{-3}$, maternal rates are generally lower, ranging from $4.3x10^{-5}$ to $1.3x10^{-3}$.

Therefore, different parameterized models exist, based on apparent mutation frequencies, and can be used to account for Mendelian incompatibilities found between two supposed relatives in kinship investigations (Egeland *et al.,* 2016; Simonsson & Mostad, 2016). In the pedigrees where no Mendelian incompatibilities can be observed, the possibility of mutations is still considered when using our chosen software and settings. Mutation matrices can thus be constructed using few parameters based on the different mutation models, and are generally represented by:

$$M=\begin{bmatrix} m_{11} & m_{12} & m_{13} & \cdots & m_{1n} \\ m_{21} & m_{22} & m_{23} & \cdots & m_{2n} \\ m_{31} & m_{32} & m_{33} & \cdots & m_{3n} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ m_{n1} & m_{n2} & m_{n3} & \cdots & m_{nn} \end{bmatrix}$$

where n is the number of possible alleles for the marker in question and m_{ij} represents the probability that allele i is transmitted as allele j (mutated) assuming that allele i was transmitted. Values along the diagonal (m_{ii}) are the probabilities of each allele being transmitted without mutating and should therefore be close to 1. If R represents the overall mutation rate, assuming that the probability is independent of which is the initial allele, then m_{ii} = 1-R. All values must be positive and each row must sum 1 (Egeland *et al.*, 2016, pp. 166-167).

1.3.2.1. The “Equal” Model

The Equal Mutation Model is the simplest and relies on the assumptions that every allele has the same probability to suffer a mutation, and also that the probabilities of mutation from a given allele to any other possible allele are the same. Although it does not seem to be biologically realistic in the case of STRs, it is used for its simplicity of computation (as some pedigrees could take large amounts of time to process with more complex mutation models), or when little information is known about which mutations are more or less likely than others in the markers in question, such as in the case of SNPs.

1.3.2.2. The “Proportional to Frequency” Model

According to this model based on allele frequencies, the probability of mutating to an allele is proportional to that allele’s frequency, irrespectively of the type or frequency of the original allele. In other words, it assumes that when a mutation takes place, the resulting allele is simply randomly generated from the population gene frequency distribution. It does not seem to be a biologically realistic model (Vicard & Dawid, 2004).

1.3.2.3. The “Stepwise” Model

Stemming from the rather extreme Single-Step Model, according to which STR mutations can only occur in single steps — that is, mutations can only result in the insertion or deletion a single repeat, with no possibility for multiple-step alterations (Ohta & Kimura, 1973; Valdes *et al.*, 1993) — the Stepwise model is based on the fact that one-step mutations seem to be the most commonly occurring in STRs (Ellegren, 2004), but it does not exclude the possibility of multiple-step mutations.

In this model, all "possible" (previously described) alleles are considered, and the probability of mutation from allele i to allele j decreases as a function of the difference in length between the original and mutated alleles. Another parameter (called *Mutation Range* in `Familias` and generally represented by r, such that $0<r<1$), must thus be taken into account — an addition or subtraction of $k+1$ repeat units is r times as probable as an addition or subtraction of k repeat units (Egeland *et al.*, 2016, p. 168), provided that the marker in question contains only alleles with complete repeat units.

However, not all alleles in STR markers contain only complete repeat units. Some are non-consensus alleles that fall between two complete units, such as the allele 9.3 in the locus TH01, which contains nine 4-nucleotide repetitions and an incomplete repetition with only 3 nucleotides, as described in Puers *et al.*, 1993. The Stepwise model considers these microvariants as equal to alleles with an integer number of repeat units and, therefore, considers the probability of mutation from a 9 to a 9.3, for example, to be the same as the probability of mutation from an 8 to a 9, which also does not seem to be realistic from a biological point of view.

1.3.2.4. The "Extended Stepwise" Model

Unlike the Stepwise model above — which considers these microvariants as equal to alleles with an integer number of repeat units — the Extended Stepwise model reflects the knowledge that mutations from a microvariant to an integer alleles (and vice versa) are far less likely than mutations between two integer alleles, or between two non-consensus alleles.

Therefore, the Extended Stepwise model shares every characteristic with the standard Stepwise model, with the exception that two different mutation rates need to be defined: $R1$, the integer-length mutation rate (mutations between two integer alleles or between two non-consensus alleles with integer-length difference); and $R2$, the fractional-length mutation rate (mutations between the two groups). The probability that an allele is transmitted without mutation is thus given by $1-R1-R2$ (Egeland *et al.*, 2016, p. 169).

Full mutation matrices for all the aforementioned models may be consulted in Egeland *et al*., 2016, pp. 166-172.

2. Aims

In this work, we intend to analyze and quantify the extent of the impact that the use of different mutation models and parameters has on the likelihoods of some commonly tested kinship problems: paternity, full-sibship and half-sibship. The analyses will be computed both per marker and at a global scale resorting to computer-simulated genetic family profiles of the different pedigrees assumed in the hypotheses. In the case of paternity tests, we also considered the case where, unknowingly, a close relative of the real father is tested as the putative one. We will also analyze the impact of consistently considering the possibility of mutation, or considering it only in the genetic profiles revealing Mendelian incompatibilities.

3. Material and methods

3.1. Genetic markers

Ideally, the set of markers to be used in the simulations and kinship analyses should be large enough to provide sufficient discriminating power, be well described and have extensive information available on their apparent mutation or incompatibility rates.

A set of 17 independent autosomal STRs (CSF1PO, D2S1338, D3S1358, D5S818, D7S820, D8S1179, D13S317, D16S539, D18S51, D19S433, D21S11, FGA, Penta D, Penta E, TH01, TPO, and VWA) was thus selected, corresponding to the markers included in the commercial kits *AmpF/STR Identifiler* and *Powerplex 16 System*. The database considered was the one of the Northern Portugal (Amorim *et al.* 2006; Melo *et al.*, 2014) and extensive information on their apparent mutation frequencies as gathered from the previously mentioned Annual Report Summary for Testing in 2008, by the American Association of Blood Banks. This report was arguably the most adequate source we were able to find for this purpose since more recent reports from the same organization do not present such detailed information.

Additionally, 10 fictitious STR markers have been created with specific distributions of allele frequencies, as follows:

Table 1 – Alleles and respective frequencies of the fictitious STRs to be analyzed.

	Frequency				
Allele	*Marker 1*	*Marker 2*	*Marker 3*	*Marker 4*	*Marker 5*
8	0.125	0.1	0.02	0.066667	0.066667
9	0.125	0.1	0.08	0.066667	0.066667
10	0.125	0.1	0.15	0.3	0.3
10.1	0	0	0	0	0
11	0.125	0.1	0.25	0.066667	0.066667
11.1	0	0	0	0	0
12	0.125	0.3	0.25	0.3	0.066667
12.1	0	0	0	0	0
13	0.125	0.1	0.15	0.066667	0.3
14	0.125	0.1	0.08	0.066667	0.066667
15	0.125	0.1	0.02	0.066667	0.066667
	Frequency				
Allele	*Marker 6*	*Marker 7*	*Marker 8*	*Marker 9*	*Marker 10*
8	0	0	0.015	0.061667	0.061667
9	0.125	0.1	0.075	0.061667	0.061667
10	0.125	0.1	0.145	0.3	0.3

10.1	0	0	0.01	0.01	0.01
11	0.125	0.1	0.25	0.061667	0.061667
11.1	0.125	0.1	0.01	0.01	0.01
12	0.125	0.3	0.25	0.3	0.061667
12.1	0.125	0.1	0.01	0.01	0.01
13	0.125	0.1	0.145	0.061667	0.3
14	0.125	0.1	0.075	0.061667	0.061667
15	0	0	0.015	0.061667	0.061667

3.2. Computations

3.2.1. Determination of incompatibility rates

In order to generate a realistic sample, real incompatibility rates had to be included in our code for generating the profiles. Using the aforementioned 2008 AABB Report as a source, determination of both male and female Mendelian incompatibility rates was performed by dividing the sum of the male/female reported incompatibilities for each marker by the overall number of respective meiosis analyzed. Separate incompatibility rates were calculated the same way for 1-, 2-, 3-, and 4-step incompatibilities, according to the data from the report, in order to fit the requirements of the Stepwise and Extended Stepwise mutation models.

Indeterminate incompatibilities – that is, those whose paternal or maternal origin is uncertain – were also included and attributed to the paternal/maternal lineages in the same proportion as they appeared in those respective lineages in the cases where no indetermination existed (AABB, 2008, p.11). All of these were considered to be 1-step incompatibilities, which is considered to be the most likely scenario by the scientific community, as previously mentioned in section 1.3.1. Thus, incompatibility rates were obtained for each of the 17 real STRs, as presented in Appendix 1.

It is worth to note that the considered report did not present detailed data for the Penta D and Penta E markers, aside from two general incompatibility rates for males and females, with no differentiation according to the number of mutational steps. These rates were thus considered to be exclusively referring to 1-step incompatibilities and multiple-step incompatibility rates for these markers were set to 0.

For the 10 fictitious markers, 1- to 4-step incompatibility rates were established by calculating the mean values of the 17 real STRs' incompatibility rates obtained, and applied equally to all ten markers.

3.2.2. Simulations

The generation of the simulated genetic profiles for the kinship problems to be addressed was carried out through algorithms computed in R, considering a table file with the allele frequencies for all markers involved. In order to simulate a realistic occurrence of silent alleles, an extra allele (called “99” for clarity and easy identification) was manually added to every marker in the allele frequency table, with a relative frequency of $5x10^{-3}$. All frequencies were then normalized so that their sum was equal to 1.

For the “seed” ancestral individuals of each pedigree, alleles were assigned according to the allele frequencies in the aforementioned table: for each marker, the allele frequencies were converted into cumulative frequencies — that is, after ordering all alleles by size, each allele should have a frequency equal to the sum of the original frequencies of the allele in question and all alleles above it, so that the cumulative frequency of the largest allele equals 1. Using randomly generated numbers between 0 and 1, random selection of all alleles according to the frequency distribution of the markers was made, whereby the shortest allele among those whose cumulative frequencies were greater than the respective randomly generated number was selected each time. This way, it was assured that the proportion of times each allele was assigned to ancestral individuals matched the population frequency of that specific allele.

The previously determined incompatibility rates were then incorporated in the script for the generation of offspring. It is important to highlight that the whole process is based on incompatibility rates and not mutation rates, so it would be inadequate to simply determine the outcomes of an allele transmission by defining the length of the filial allele (from parental-4 to parental+4 repeats) and applying the previously determined rates. Doing so would be incorrectly using the determined rates as mutation rates and since not every mutation would result in an incompatibility (hidden mutations would also be considered), the incompatibility rates would be incompatible with those obtained from the AABB Report.

A secondary script was thus created that would take, for each marker, a total of five variables: two vectors with the parents’ alleles, two vectors consisting of the male and female incompatibility rates for 1–4 steps, and a vector with the list of possible alleles for the respective locus. The script would then generate a matrix listing all possible children genotypes for the marker in question and their respective probabilities, based on the differences in STR lengths (0 to 4, when applicable) and the incompatibility rates provided. These genotypic probabilities were then converted into cumulative frequencies

and randomly generated numbers were once again used to select one of the possible genotypes for each child, per marker.

The R scripts were also adapted to consider the silent allele and perform computations in its presence, according with biological rules of genetic transmission. Whenever allele “99” had been selected as a first allele on a given locus for the “seed” individuals, we restricted the second allele selection to only the codominant alleles list (with no allele “99”), avoiding the occurrence of homozygous individuals for the silent allele, which we had no reliable way of analyzing through `Familias` or its R package (Patter *et al.*, 2016). When simulating meiosis – that is, when creating the offspring individuals – and where both parents had one “99” allele in a given marker, the resulting genotype 99–99 was automatically deleted from the possible genotype matrices (the remaining frequencies were normalized), again to avoid cases of homozygosity for the silent allele.

Lastly, after allele assignment to all individuals, every “99” allele found was replaced with the alternative allele in the same locus, that is, every individual possessing a silent allele was converted into an apparent homozygous for the alternative allele. This way, as required, the software `Familias` was given no information as to whether such individuals were homozygous, or heterozygous with a silent allele.

3.2.3. The Stepwise model problem

Unlike the user-interface of `Familias`, the R package did not allow direct use of the standard Stepwise mutation model, since it could not assimilate microvariants as full repeats – R would never interpret a mutation from 15 to 15.2 repeats as a full-step mutation and use the primary mutation rate for its consideration, as required by the standard Stepwise model. Instead, it would inevitably interpret it as a microvariant and use a secondary mutation rate, which corresponds to the Extended Stepwise mutation model. Indeed, in this particular topic, the use of `Familias` interface does not provide the same result of its R version. Thus, all profiles had to go through a transformation to exclude microvariants while maintaining all the relevant information for `Familias`. This was achieved by scanning through every profile and replacing every allele with its respective row number (after filling in any existing gaps between alleles differing in more than one repetition with no intermediate alleles) in the external allele frequency tables. A marker with alleles 12, 13, 13.2 and 14, for example, would be converted into 1, 2, 3 and 4.

This profile conversion process occurred automatically upon calculation of the Likelihood Ratios using the Stepwise mutation model, also providing `Familias` with the converted allele names. This way, the relative genotypes were preserved, but the software could not detect the “masked” microvariants, which could be treated as full repeats, thus enabling proper calculation of the likelihoods.

3.3. Kinship problems

The problems we chose to address were some of the most commonly questioned kinships, as follows:

3.3.1. Parent-Child vs Unrelated

Individuals were simulated as pictured in figures 1-5 (100,000 families each), where the blue-colored individuals are the ones whose kinship is questioned and the red-colored individuals (the mother of B in all cases) can be (or not) available for testing, depending on whether analyzing duos or trios.

a)

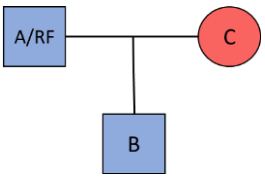

Figure 1 – Pedigree representing the case where the putative father A is the real father of B

b)

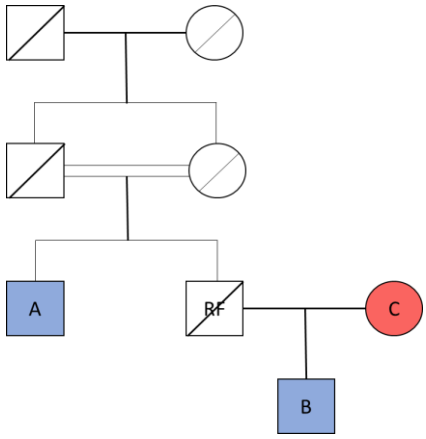

Figure 2 – Pedigree representing the case where the putative father A is a full brother of the real father (parents are related as full-siblings) of B

c)

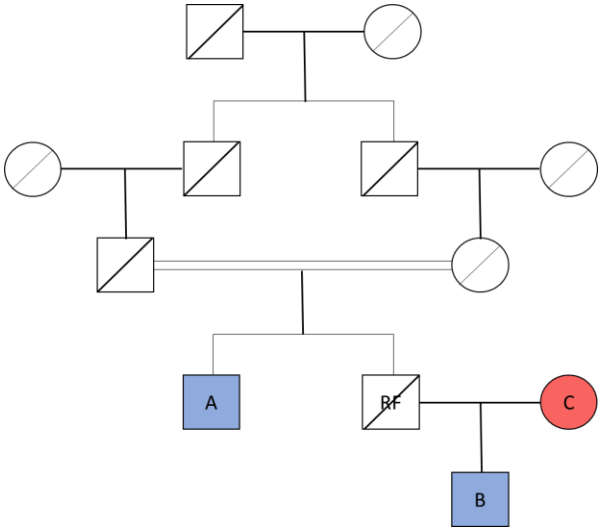

Figure 3 Pedigree representing the case where the putative father A is a full brother of the real father (parents are related as first cousins) of B

d)

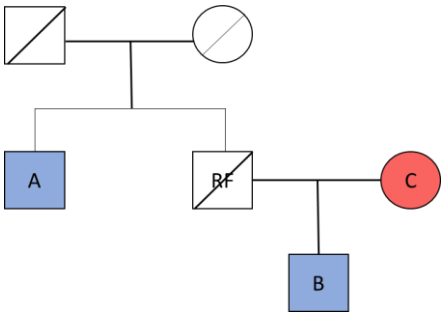

Figure 4 – Pedigree representing the case where the putative father A is a full brother of the real father (parents are unrelated) of B

e)

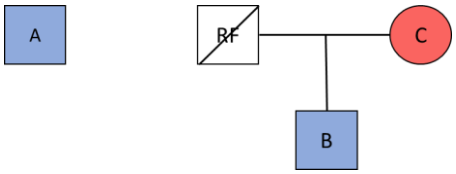

Figure 5 – Pedigree representing the case where the putative father A is unrelated to B.

3.3.2. Full-siblings vs Unrelated

Individuals were simulated as (100,000 families each):

3.3.2.1. A and B are related as full-siblings
3.3.2.2. A and B are unrelated

3.3.3. Half-siblings vs Unrelated

Individuals were simulated as (100,000 families each):

3.3.3.1. A and B are related as half-siblings
3.3.3.2. A and B are unrelated

3.3.4. Full-siblings vs Half-siblings

Individuals were simulated as (100,000 families each):

3.3.4.1. A and B are related as full-siblings

3.3.4.2. A and B are related as half-siblings

In all of the abovementioned cases, the genetic information of the mother of B was considered when analyzing trios, and absent when analyzing duos.

3.4. Mutation models

The following, already described (see section 1.3.2), mutation models and parameters were used for kinship evaluations:

3.4.1. Null (mutation rate = 0);

3.4.2. Equal (mutation rate=10^{-3});

3.4.3. Proportional to Frequency (mutation rate=10^{-3});

3.4.4. Stepwise (mutation rate=10^{-3}, range=0.1);

3.4.5. Extended Stepwise (mutation rate1=10^{-3}, mutation rate2 = 10^{-6}, range=0.1);

3.4.6. Extended Stepwise II (mutation rate1=$5x10^{-3}$, mutation rate2 = 10^{-6}, range=0.1).

3.5. Statistical analysis

3.5.1. LR Calculations

With multiple R scripts, Likelihood Ratios with the six different mutation models and parameters (from 3.4.1. to 3.4.6.) were obtained using the functions from the `Familias` R package, after reading the generated profiles and allele frequencies and defining the two alternative hypotheses at stake. Every case was analyzed both assuming duos (only the genetic information of the individuals A and B, whose kinship is questioned, was used in the analysis) and trios (the genetic profile of the mother of B was also considered). Partial (per marker) and total (for the complete set of 17 STRs) results were stored.

3.5.2. Mendelian incompatibilities

For each case (from 3.3.1. to 3.3.3.), the proportion of observed paternal and maternal Mendelian incompatibilities was analyzed, and comparisons were made regarding the number of incompatibilities found when analyzing the cases in duos (when applicable) and trios.

3.5.3. The impact of considering mutations when no Mendelian incompatibilities are found (i.e. Hidden mutations)

The null mutation model was used to measure the impact of consistently considering, or not, the possibility of mutations, namely when they do not lead to incompatibilities – the so-called hidden mutations. When considering no mutation (using the Null model), any incompatibility would lead to LR=0, or LR=NA (when in the presence of incompatibilities in relationships given as certain (in cases when trios are analyzed and there is an incompatibility mother/offspring), resulting in an attempted division by 0). Excluding all such cases, thus focusing only on cases where no Mendelian incompatibilities have been found, it was possible to compare, using tables of simple ratios, the results obtained when using the Null model (assuming no mutations) with the results obtained assuming the different mutation models (considering hidden mutations). In these tables, each ratio (r) was allocated to one of five main categories: *R<1/1.1*; *1/1.1<R<0.9999*; *R=1*; *1.0001<R<1.1*; *and R>1.1*. Note that the category *R=1* is actually defined by $R=1\pm\varepsilon$, with $\varepsilon=10^{-5}$, to account for minor differences caused by the rounding off of the resulting LRs.

3.5.4. The impact of considering different mutation models

Setting the Null and Extended Stepwise II models aside (the latter will only be compared to the Extended Stepwise model to analyze the impact of altering the parameters within the same model), the results obtained assuming each of the remaining models were also compared through a similar analysis to the one already performed for hidden mutations, with the same tables of ratios described in 3.5.3. The cases where incompatibilities were found were analyzed separately from those with no incompatibilities. The ratios when analyzing duos were also compared to those when analyzing trios.

3.5.5. The impact of the parameters in the Extended Stepwise Model

Assuming the Extended Stepwise mutation model as the most biologically realistic, this model was used to weigh the impact of altering the parameters. Specifically, the LRs were calculated using a mutation rate 1 (within the same microvariant group) equal to 10^{-3} (Extended Stepwise I), or equal to $5\text{x}10^{-3}$ (Extended Stepwise II). Ratios were computed to compare the results obtained with the different parameters, considering

cases where Mendelian incompatibilities had been found separately from those where no incompatibilities existed. As in 3.5.4., the differences between these models when considering duos were compared to the differences when analyzing trios.

4. Results and Discussion

4.1. Mendelian incompatibilities

4.1.1. Parent-Child vs. Unrelated

In the problem of paternity, since the sharing of IBD (Identity-by-descent) alleles is required between parents and offspring (unless mutation), Mendelian incompatibilities can be found when analyzing both duos and trios. In the case of duos, incompatibilities can be found between A and B whenever the two individuals do not share any allele on a given locus. In the case of trios, two types of incompatibility may occur: between A and B, whose relationship is in doubt (LR=0 when not considering mutations), and between B and his/her mother C, whose relationship is given as certain, therefore resulting in an attempted division by 0 in the LR calculation. A summary is presented in table 1 below:

Table 2 – The proportion of paternal and maternal incompatibilities found in each case.

	Duos	*Trios*	
Case	*Paternal (proportion)*	*Paternal (proportion)*	*Maternal(proportion)*
a.	0.0010	0.0015	0.0003
b.	0.0186	0.2453	0.0002
c.	0.2033	0.2816	0.0003
d.	0.2155	0.3008	0.0003
e.	0.4219	0.5894	0.0003

a. Putative father A is the real father of B

The analysis performed in duos revealed 1,736 incompatibilities between A and B, which corresponds to a proportion of ~10^{-3}, out of 17 (markers) * 100,000 (simulations). When analyzing trios, this number increased by a factor of ~1.55 (2,611 incompatibilities, proportion of 1.5×10^{-3}), while 515 (proportion of 3×10^{-4}) incompatibilities between B and the real mother C were observed.

b. Putative father A and the real father of B are full brothers (whose parents are related as full-siblings)

In duos, 315,581 incompatibilities (proportion of ~0.18) were found between A and B, which increased by a factor of ~1.32 when analyzing trios, with 417,072 incompatibilities (proportion of ~0.2453) observed. These values were roughly 182 and 160 times those of case a., respectively. Meanwhile, the number of maternal incompatibilities found was 389 (proportion of ~$2.3x10^{-4}$).

c. Putative father A and the real father of B are full brothers (whose parents are related as first cousins)

In this case, 345,634 incompatibilities (proportion of ~0.2033) occurred between A and B when in duos, while this value increased by a factor of ~1.39 times when trios were considered (478,796 incompatibilities, proportion of ~0.2816). These values represent ~1.10 times and ~1.15 times the values of case b, respectively. The number of maternal incompatibilities observed was 496 (proportion of ~$2.9x10^{-4}$).

d. Putative father A and the real father of B are full brothers (whose parents are unrelated)

In this case, 366,288 incompatibilities (proportion of ~0.2155) between A and B were found in duos, while 511,363 incompatibilities (proportion of ~0.3008), corresponding to an increase by a factor of ~1.4 in relation to duos, were found when analyzing trios. Once again, these values are greater than those in the previous cases, as they correspond to ~1.06 times and ~1.07 times, respectively, the values of case c. The number of maternal incompatibilities observed was ~505.

e. Putative father A is unrelated to the real father of B

Lastly, when individuals A and B were simulated as unrelated, 717,243 incompatibilities (proportion of ~0.4219) were found between A and B in duos, while 1,002,062 incompatibilities (proportion of ~0.5894) occurred in trios, representing an increase by a factor of ~1.42 from duos to trios, and an amount corresponding to 1.96 times the values of case d., in both duos and trios. The number of maternal incompatibilities remained practically stable, as 522 incompatibilities (proportion of $3x10^{-4}$) were found.

As expected, the number of paternal incompatibilities decreases with the increase in genetic relatedness of the putative father to the real father (and, consequently, to the child whose paternity needs to be tested) and it is greater when analyzing trios, since

the relationship of the child with the mother is unquestioned, which leads to the exclusion of certain paternal allele transmissions that are considered to occur when analyzing only duos – any ambiguous incompatibility will be preferably ascribed by the software to the parent whose relationship is questioned, which, in this case, is the paternal relationship. (e.g., consider a case where the child presents the alleles 14-15, while the supposed father and the mother have the alleles 14-16 and 13-14, respectively – when considering trios, the transmission of the allele 14 will be ascribed by the software to the maternal meiosis, leaving the supposed father sharing no alleles with the child. In the absence of the mother, the allele 14 would be considered to have come from the supposed father, while the allele 15 could have come from the mother, who had not been genotyped).

When comparing cases a. to e., the differences in the number of paternal incompatibilities found (in both duos and trios) are largest between case a. and all other cases, by two orders of magnitude, in relation to the comparisons between all the remaining cases. Considering only the cases where A is a full-brother of the real father of B (cases b., c. and d.), the genetic relatedness of their parents does not seem to have much impact on the number of incompatibilities found, with the maximum ratio being equal to ~1.23, between cases b. and d., when considering trios. The number of paternal incompatibilities approximately doubled when comparing these cases with case e., where A is unrelated to B.

The quantity of maternal incompatibilities, on the other hand, remained roughly the same, within the order of magnitude of 10^{-4} throughout all the cases, since the maternal relationship was always given as certain, so incompatibilities can occur only in the presence of maternal mutations.

4.1.2. Full-siblings vs. Unrelated

In this problem, Mendelian incompatibilities can only be found when analyzing trios, since there is a 25% probability that two full-brothers do not share IBD alleles in a given market (in other words, two full-siblings can be genetically as unrelated individuals with 25% probability). Thus, and assuming C as the undoubted mother of B, two types of incompatibilities can be observed in trios: incompatibilities involving individual A, whose relationship with the mother, C, is uncertain; and incompatibilities between B and the mother C, whose relationship is unquestioned.

Therefore, considering trios, when individuals were simulated as full-siblings, 529 Mendelian incompatibilities (proportion of $3x10^{-4}$) regarding individual A were found. This number, as expected, increased (~1353 times) when individuals were simulated as

unrelated, with 715,635 incompatibilities (proportion of ~0.4210) occurring. On the other hand, and similarly to the case of paternity, 507 and 522 (proportion of ~$3x10^{-4}$) incompatibilities were found between B and his/her mother C, in the cases where A and B were simulated as full-siblings and as unrelated, respectively, since their relationship was not questioned in both cases.

4.1.3. Half-siblings vs. Unrelated

Since a pair of half-siblings (A and B, in this case) does not share IBD alleles in a given marker with 50% probability, no Mendelian incompatibilities can occur between them whether duos or trios are being analyzed. Therefore, only incompatibilities between B and the undoubted mother C can occur when analyzing trios. In cases where A and B were simulated as half-siblings, 507 incompatibilities were found between B and C, while 522 incompatibilities were found when they were simulated as unrelated, both corresponding to proportions of ~$3x10^{-4}$, as in the previous problems (1.1.1 and 1.2.1).

4.1.4. Full-siblings vs. Half-siblings

As in the problem of Full-siblings vs Unrelated, in this case, Mendelian incompatibilities between A and B can only be found when considering trios, since two full-siblings have 25% probability of not sharing any IBD alleles on a given marker (50% in the case of half-siblings). Incompatibilities between B and the mother C can also be observed when analyzing trios.

Thus, excluding the aforementioned 507 incompatibilities (proportion of ~$3x10^{-4}$) found between B and the mother C in individuals simulated assuming full-sibship – and the same number when individuals were simulated assuming half-sibship – 529 incompatibilities (proportion of ~$3x10^{-4}$) were found in trios when the individuals were simulated as full-siblings, while this number increased by a factor of 1357.5 when they were simulated as half-siblings (718,115 incompatibilities found, proportion of ~0.4224, which is similar to that of the unrelated individuals in the problem of Full-siblings vs Unrelated).

4.2. The impact of considering mutations in cases with no incompatibilities (i.e. Hidden mutations)

As previously described, in order to evaluate the impact of consistently considering or disregarding the occurrence of hidden mutations in the 17 Au-STRs from the database of North Portugal, we compared the Likelihood Ratios obtained for all the cases where no incompatibilities were found when using the Null mutation model with the results obtained with all of the other models, through tables of simple ratios – that is, ratios were calculated using the LRs considering the Null model as the numerator, and each of the remaining models as the denominator. The results are summarized in Table 3 below, for all kinship problems. The average ratio per marker corresponds to the average of the mean ratios obtained for each marker, while the average ratio in 17 markers corresponds to the product of all mean ratios of each marker.

Note that cases b., c. and d. of the first kinship problem have not been considered in this analysis, since they would not provide any further information regarding the impact of considering hidden mutations, since each individual case must be either compatible or incompatible with the hypothesis of paternity, regardless of how they have been generated, so cases a. and e. should be sufficient to provide all necessary information.

Table 3 – Summary of the ratios between the LRs obtained with the Null model (in the numerator) and the remaining models (in the denominator) in cases with no incompatibilities.

Kinship Problem		*Main Hypothesis*	*Alternative Hypothesis*
Parent-Child vs Unrelated	*Average ratio per marker (r)*	1.0005 to 1.0012	0.9995 to 1.0005
	Average ratio in 17 markers	1.0088 to 1.0203	0.9919 to 1.0093
	Proportion of r<1/1.1 or r>1.1	0 to 0.0002	0 to 0.0003
Full-Siblings vs Unrelated	*Average ratio per marker (r)*	1 to 1.0007	0.9970 to 0.9978
	Average ratio in 17 markers	0.9995 to 1.0137	0.9502 to 0.9647
	Proportion of r<1/1.1 or r>1.1	0 to 0.0036	0 to 0.0071
Half-siblings vs Unrelated	*Average ratio per marker (r)*	1 to 1.0001	0.9986 to 0.9992
	Average ratio in 17 markers	0.9996 to 1.0023	0.9756 to 0.9863
	Proportion of r<1/1.1 or r>1.1	0 to 0.0019	0 to 0.0034
Full-siblings vs Half-siblings	*Average ratio per marker (r)*	0. 9994 to 1.0008	0.9980 to 0.9989
	Average ratio in 17 markers	0.9904 to 1.0126	0.9651 to 0.9808
	Proportion of r<1/1.1 or r>1.1	0 to 0.0025	0 to 0.0034

Parent-Child vs. Unrelated

When the pedigrees at stake were Parent-Child and Unrelated, the assumption of absence of mutations led to higher likelihood ratios in most of the cases, for most

mutation models and markers and for families generated under the different assumptions. Indeed, even for the cases where the individuals were simulated as Unrelated, the LRs were mostly greater (and thus favoring paternity) if assuming the absence of mutation than otherwise.

It should however be remarked that when the set of fictitious markers is considered, if the higher LRs (in the absence of mutation) occur for all models, markers and individuals in duos, the same is not observed when trios are considered.

Overall, and despite the occurrence of some extreme cases, the impact of consistently considering or not hidden mutations is expected to be smooth. Indeed, the proportion of cases where the LR, per marker, differed in less than 10% equated 99.9908%, and after analyzing the set of 17 Au-STRs, the expected average value of the ratio of the obtained LRs assuming or not the possibility of hidden mutations varied between ~0.9919 (for a duo of unrelated individuals and the Proportional Mutation Model) and ~1.0203 (for a trio of Parent-Child and the Equal Mutation Model). Particularly, when the results per marker obtained assuming the Extended model were compared with those assuming the Null model, in 99.9906% of cases the likelihood ratios differed in less than 10%, and the final LR is expected to differ in less than 2%.

We had a poster presentation at the 27th Congress of the International Society of Forensic Genetics (2017, Seoul, Republic of Korea), where we discussed the cases where the individuals are simulated assuming the main hypothesis of the different kinship problems (Parent-Child, in this case), considering the 17 real Au-STRs analyzed as a set, and the mutation models here presented. This poster resulted in a conference proceeding (Machado *et al.,* in press), which is also attached in Appendix 6.

As shown in the mentioned work, after analyzing the 17 Au-STRs as a set in individuals related as Parent-Child (duos and trios), the ratio between the total LR considering no mutation and the one considering different models varied from ~1.0088 (for duos and the Proportional mutation model) to ~1.0203 (for trios and the Equal mutation model).

Nevertheless, despite their low frequency, there are cases where the impact was substantial. Figure 6 below shows an example of such a case, found in marker TH01, where the ratio between the LRs obtained with the Null and Extended Stepwise mutation models (considered as numerator and denominator, respectively), is ~0.5982.

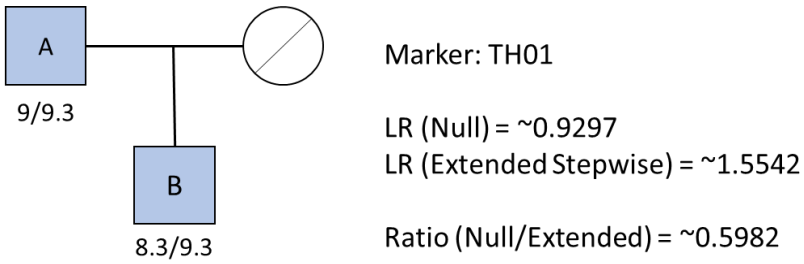

Figure 6 – Case-example showing the genotypes of a Parent-Child duo for marker TH01 and respective LRs, calculated with the Null and Extended Stepwise mutation models considering paternity and unrelatedness as the main and alternative hypotheses, respectively.

4.2.1. Full-siblings vs. Unrelated

In the case where the hypotheses are full-sibship and unrelatedness, the impact of considering (or not) hidden mutations seems to be slightly higher than for the previous case, likely due to the higher number of meiosis involved.

In this kinship problem, the analysis per marker leading to LRs differing in less than 10% equated ~ 99.8312%. After analyzing 17 Au-STRs, the expected average value varied between ~0.9502 (for a trio “unrelated” and the Proportional Model) and ~1.0137 (for a trio of Full-siblings and the Equal model).

In this case, it seems clear that the impact is greater when the individuals were simulated as unrelated and when trios are considered. Particularly, when the Extended Mutation Model is considered, a difference inferior to 10% is expected in 99.9028% of the analyses (per marker), and the final LR after analyzing 17 Au-STRs is expected to differ in less than 5%.

After analyzing the 17 Au-STRs and individuals related as full-siblings (duos and trios) the ratio between the final LR considering no mutation and the one considering different mutation models varied from ~0.9995 (for duos and the Proportional mutation model) to ~1.0136 (for trios and the Equal mutation model) (Machado *et al.,* in press).

As before, some sporadic cases showed significant differences, as has happened in the example below, for the marker D21S11:

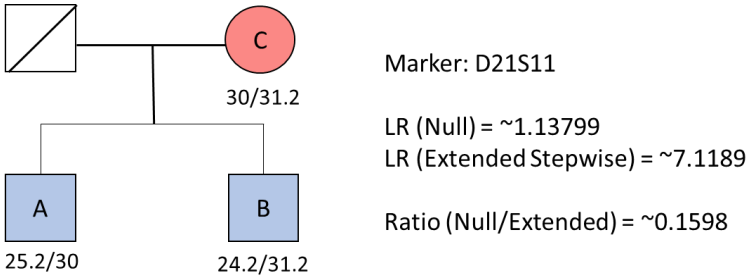

Figure 7 – Case-example showing the genotypes of a trio of individuals simulated assuming the hypothesis of Full-sibship for marker D21S11 and respective LRs, calculated with the Null and Extended Stepwise mutation models considering full-sibship and unrelatedness as the main and alternative hypotheses, respectively.

Figure 5 above shows an example of the genotypes of two full-siblings and the mother in marker D21S11 and the respective LRs calculated considering the Null and Extended Stepwise mutation models. As we can see, the ratio between the LRs using these models equals ~0.1598, which, even though it represents an outlier, is a considerable difference.

4.2.2. Half-siblings vs. Unrelated

The impact when considering the kinship problem involving the hypotheses of half-sibship and unrelatedness is intermediate to the previous two, which is justified by the intermediate number of meiosis involved. Also in this case the impact is stronger when the individuals were simulated as unrelated and trios were analyzed. The proportion of cases reaching differences under 10% equated 99.9039% of the analyzed allelic transmissions. The average difference in the final result is expected to vary between ~1.0023 and ~0.9756.

Considering the Extended model, a difference lesser than 10% is expected in 99.9506% of cases, and the final LR is expected to differ in less than 3%.

The final LR after considering the analysis of the 17 independent markers as a set and individuals simulated as half-siblings (duos and trios) revealed ratios varying between ~0.9996 (for trios and the Proportional mutation model) to ~1.0023 (for trios and the Equal mutation model) (Machado *et al.,* in press).

4.2.3. Full-siblings vs. Half-siblings

In the case where the hypotheses of full-sibship and half-sibship are compared the results were similar: 99.9109% of the comparisons revealed differences lesser than

10%, and the final result after analyzing 17 STRs is expected to vary between ~0.9651 (for trios, half-siblings and Proportional model) and 1.0135 (for trios, full-siblings and Equal Model).

Assuming the Extended Mutation Model as the alternative model, a difference lesser than 10% is expected in 99.9504% of the cases (analyses per marker), and the final LR is expected to differ in less than 3%.

Assuming individuals simulated as Full-siblings (duos and trios) and, as before, a battery of 17 STRs, we obtained ratios between LR not considering mutations and otherwise varying between ~0.9904 (for duos and the Proportional mutation model) and ~1.0135 (for trios and the Equal mutation model) (Machado *et al.,* in press).

4.3. The impact of considering different mutation models

Similar analyses to those of section 1.2 were performed for comparing the remaining four mutation models between them, both for the 17 Au-STRS from the database of North Portugal and the 10 markers with fictitious allele frequencies. The results for cases with Mendelian incompatibilities and cases without them are presented in separate, as well as the results obtained when analyzing duos or trios.

4.3.1. For the 17 Au-STRs from the database of North Portugal

Parent-Child vs Unrelated

The results obtained for the 17 real Au-STRs in compatible and incompatible cases of this kinship problem are presented in Tables A3 to A6, Appendix 2.

As expected, the influence of the use of different mutation models in cases where no Mendelian incompatibilities occur (Tables A3 and A4, Appendix 2) is small, with the frequency of cases where the ratio per marker is lower than 1/1.1 or greater than 1.1 (i.e. LRs differing in more than 10%) never exceeding ~0.0002 when analyzing individuals simulated as Parent-Child, or ~0.0004 when analyzing unrelated individuals in duos. For the Unrelated trios, this proportion was null for all models. For example, the average ratio per marker in Parent-Child duos, considering all models, ranges from ~0.9999 to ~1.0001, while the median ratio ranges from ~0.9998 to ~1.0002. Considering the 17 markers (through the product of the average ratios per maker), the average impact of altering the mutation model for the same cases is expected to range from ~0.9987 to ~1.0015, while the median impact should range from ~0.9967 to ~1.0033. Similar values are also observed in Parent-Child trios and in duos and trios of unrelated individuals.

The Proportional model seems to result in overall higher likelihood ratios, as the ratios between the LRs with this model and the others seem to consistently produce higher results, with the average and median ratios being always greater than 1.

For all cases where the real father of B is a full-brother of the putative father A (that is, cases b., c. and d. of this problem) the ratios are extremely similar, both when analyzing duos or trios, although the average ratios per marker seem to be slightly lower than those of case a. and slightly higher than those of case e, but in this case we must be aware that much less cases (compatibilities) can be observed and consequently analyzed, so these slight differences can be due to a smaller sample.

However, when isolating the cases with Mendelian incompatibilities (Tables A5 and A6, Appendix 2), the variation was, as expected, greater. For example, the average ratios per marker using the Extended Stepwise model as the numerator range from ~2.9255 to ~19.2089 in Parent-Child duos, as opposed to the cases with no Mendelian incompatibilities, where the same ratios ranged from ~1 to ~1.0001.

As usual, some extreme sporadic cases occurred. Take Figure 8 below as a case-example of such a result in Parent-Child duos, in the comparison between the LRs obtained with the Extended Stepwise model (in the numerator) and the Proportional model (in the denominator), where the difference in the LRs leads to a ratio of ~1046.6667:

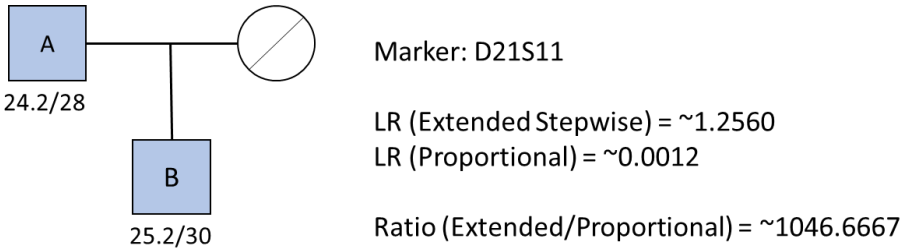

Figure 8 – Case-example showing the genotypes of a Parent-Child duo for marker D21S11 and respective LRs, calculated with the Extended Stepwise and Proportional to Frequency mutation models considering paternity and unrelatedness as the main and alternative hypotheses, respectively. Note that the LR considering the Extended Stepwise model favors the first hypothesis, paternity (albeit weekly), while the LR with the Proportional mutation model favors the alternative hypothesis, unrelatedness.

As expected, the results also seem to point towards much greater differences between the average and the median ratios per marker when analyzing unrelated individuals, due to the much greater variation in the results throughout the 17 (markers) * 100,000 (simulated profiles) = 1,700,000 allelic transmissions analyzed, than when considering individuals that have been generated as Parent-Child.

When analyzing **Parent-Child individuals in duos**, the proportion of cases where the ratio per marker shows differences between LRs greater than 10% is never lower than ~0.9136 when considering the Equal or Proportional models as the numerators, while this minimum frequency drops to ~0.2713 when comparing the Stepwise and Extended Stepwise models. The latter is due to the mutation models only differing when considering markers with microvariant alleles, which are not recognized as such by the Stepwise model that simply ranks the alleles by size, considering only their relative position. The maximum frequency of such cases (i.e. LRs differing in more than 10%) is similar for all models (~0.9407 for the Proportional model, when compared to the Equal model, and ~0.9781 for the remaining models).

Considering the respective trios, however, this proportion seems to be lower, ranging from ~0.8884 to ~0.8938 for the Equal model (when compared to the Stepwise and Proportional models, respectively) and from ~0.8938 to ~0.9050 for the Proportional model (when compared to the Equal and Stepwise models, respectively). For the Stepwise and Extended Stepwise models, these frequencies range from ~0.2246 when comparing the LRs with each of these models to one another, to ~0.9050 and ~0.8948, respectively, when both are compared to the Proportional model. The average ratios per marker when the Extended Stepwise model is compared to the Proportional model (as the numerator and denominator, respectively), range from ~2.9070 to ~14.1721 in Parent-Child individuals, in trios.

A further extreme case-example is provided in Figure 9, again observed in marker D21S11:

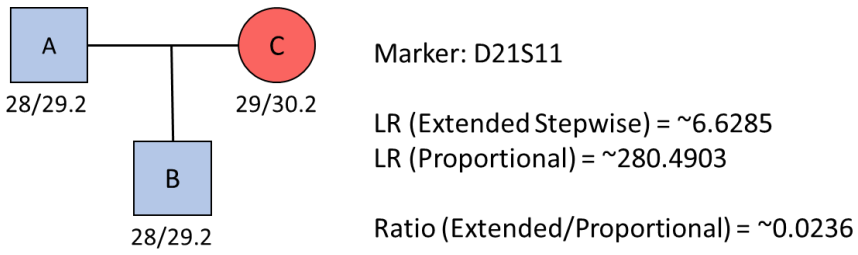

Figure 9 – Case-example showing the genotypes of a trio of individuals simulated assuming the hypothesis of paternity for marker D21S11 and respective LRs, calculated with the Extended Stepwise and Proportional to Frequency mutation models considering paternity and unrelatedness as the main and alternative hypotheses, respectively. Note that in this case, a maternal incompatibility was found, while both alleles of B are compatible with those of individual A.

The proportion of cases where LRs differ in more than 10% appear to be similar **within cases b. to e.** (where the putative father is not the real father of the child) and

they do not seem to consistently increase or decrease when analyzing trios. While there is no apparent significant difference **between duos and trios** of **case a.**, regarding the average ratios per marker, all other cases (**b. to e.**) show major increases in the variation average ratios per marker, by several orders of magnitude, when analyzing trios, in comparison with duos. The exception is the comparisons using the LRs obtained with the Stepwise model (in the numerator), which only slightly increase from duos to trios. For example, considering **case b**., the average ratios per marker with the LRs considering the Extended Stepwise model (in the numerator) range from ~1.2355 to ~5065.5 in duos, and a major increase in the variation these average ratios occurs when considering trios, ranging from ~1.2193 to ~$2.3x10^7$. In contrast, the average ratios with the LRs obtained with the Stepwise model (in the numerator) show a much smaller difference between duos and trios – they vary from ~1.2279 to ~31.9154 in duos, and from ~1.2975 to ~47.0158.

As expected, in the cases where the real father and putative father are full-brothers, case b. produces the lowest average ratios (closer to those of case a.), since the genetic similarity between them is the greatest. However, rather surprisingly, case c. presents consistently higher ratios than those of case d., which were expected to be higher due to the lower genetic similarity of the real and putative fathers in case d.

According to Machado *et al.* (in press), after analysis of the 17 markers as a set in individuals simulated as Parent-Child (duos and trios), the final LR revealed ratios varying from ~0.9824 (when comparing the LRs obtained with the Equal/Stepwise mutation models, in trios) to ~1.3386 (when comparing the LRs obtained with the Extended Stepwise/Proportional mutation models, in trios).

Full-siblings vs Unrelated

According to Table A7 in Appendix 2, the average and mean ratios per marker obtained for cases with no Mendelian incompatibilities are similar to those observed for the previous kinship problem (Parent-Child vs Unrelated).

In **Full-siblings individuals**, the average ratios per marker range from ~1 to ~1.0003, while the median ratios per marker range from ~0.9983 to ~1.0017, which translate to average impacts of ~0.9992 to ~1.005 when considering the 17 STRs in question. No significant differences are observed between mutation models or between duos and trios. Similar results were obtained for the unrelated individuals, with the average ratios per marker varying from ~0.9999 to ~1.0009 and the median ratios per marker from ~0.0.997 to ~1.003. However, the proportion of cases where the difference

in the LRs was greater than 10% is generally higher than in the previous problem (approximately by one order of magnitude), ranging from ~0.0008 (when comparing the Proportional and Extended Stepwise models) to ~0.0035 (when comparing the Equal and Proportional models), in duos of Full-siblings. These percentages approximately double when considering unrelated individuals, ranging from ~0.0014 to ~0.0066 observed in the same models' comparisons. Slight decreases occur when considering trios, such that these proportions range from ~0.0006 to ~0.0025 for Full-siblings and from ~0.0011 to ~0.0050 for unrelated individuals.

The analysis of the cases of Full-siblings with incompatibilities only (due to the consideration of the genetic profile of the undoubted mother of one of the two putative full-siblings), whose results are presented in Table A8, Appendix 2, revealed much greater variations, with the average ratios per marker for the Extended Stepwise model, for example, ranging from ~2.2646 to ~13.1598 (when compared to the Equal and Proportional models, respectively), while the average ratios per marker for the Proportional model range from ~0.8786 to ~2.1186 (when compared to the Extended Stepwise and Stepwise models, respectively).

Once again, some cases with extreme differences were found, such as the case portrayed in Figure 10, regarding the comparison of the LRs with the Proportional (in the numerator) and Stepwise (in the denominator) models, respectively, for marker Penta E:

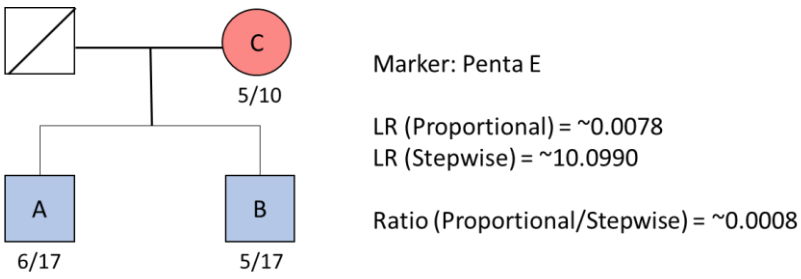

Figure 10 – Case-example showing the genotypes of a trio of individuals simulated assuming the hypothesis of Full-sibship for marker Penta E and respective LRs, calculated with the Proportional and Stepwise mutation models considering full-sibship and unrelatedness as the main and alternative hypotheses, respectively. Note that the LR considering the Proportional model favors the alternative hypothesis, unrelatedness, while the LR with the Stepwise mutation model favors the main hypothesis, full-sibship.

When considering the whole set of 17 markers (through the product of the average ratios obtained for each marker), the average impact of the latter should range from ~0.0743 to ~319.5788, while this impact would range from ~7516 to 4.3×10^{12} when considering the former. The comparisons between either the Stepwise or Extended Stepwise and the other two models result in much greater variations than when comparing these two models between them (especially since they produce exactly the

same results in the absence of microvariant alleles), or between the Equal and Proportional models.

When analyzing the unrelated individuals, the ratios were expectedly more variable – considering the same examples, the average ratios per marker for the Extended model range from ~1.097 to ~10887.9 (when compared to the Proportional and Stepwise models, respectively), and from ~2.3031 to $5.17x10^7$ for the Proportional model (when compared to the Equal and Stepwise models, respectively). When considering the set of 17 markers, however, the Stepwise model seems to produce much more variable average ratios in Full-siblings (ranging from ~0.209 to ~10^{11}, when compared to the Extended Stepwise and Proportional models, respectively), than in unrelated individuals, where they range from ~9.312 to ~$2.38x10^7$ (when compared to the same models).

Therefore, as in the problem of paternity, the difference between the median ratios per marker and the average ratios per marker is much more pronounced when considering unrelated individuals than when analyzing individuals simulated as Full-siblings.

For full-sibling individuals, the proportion of cases where the difference in the LRs was greater than 10% varies from ~0.6506 to ~0.6988 when considering the Equal model (in comparisons with the Extended and Proportional models, respectively) and, similarly, from ~0.6988 to ~0.7191 for the Proportional model (when compared to the Proportional and Stepwise models, respectively). As in the problem of paternity, the minimum proportion of such cases when considering the Stepwise or Extended Stepwise model in the numerator occurs when comparing these models to one another (~0.2056) while the maximum proportions of such cases in for the same comparisons are ~0.7191 and ~0.7172, respectively, when both are compared to the Proportional model.

Since no incompatibilities can occur in duos of full-siblings, as explained in section 4.1, no comparisons between duos and trios are applicable.

After analysis of the 17 markers as a set in individuals simulated as Full-siblings (duos and trios), the final LR revealed ratios varying from ~0.9909 (when comparing the LRs obtained with the Equal/Null mutation models, in trios) to ~1.0797 (when comparing the LRs obtained with the Extended Stepwise/Proportional mutation models, in trios) (Machado *et al.*, in press). However, the minimum ratio observed disregarding those involving the Null mutation model – which we do not intend to consider in this section, was ~0.999 (when comparing the LRs obtained with the Stepwise/Extended Stepwise mutation models, in trios).

Half-siblings vs Unrelated

The results for cases with no Mendelian incompatibilities for the kinship problem of Half-siblings vs Unrelated are shown in Table A9, Appendix 2. The average and mean ratios per marker are similar to those from the previous kinship problems. For half-siblings, the average ratios per marker range from ~1 to ~1.0001 in duos and from ~1 to ~1.0003 in trios. Considering the full set of 17 markers, the average ratios are expected to range from ~0.9999 to ~1.0012 in duos and from ~0.9996 to ~1.0027 in trios. For unrelated individuals, the average ratios per marker range from ~0.9999 to ~1.0002 in duos and from ~0.9999 to ~1.0003 in trios. Considering the full set of 17 markers, the average ratios range from ~0.9987 to ~1.0037 in duos and from ~0.9984 to ~1.0059 in trios. The Proportional mutation model seems, once again, to result in generally higher likelihood ratios, as the median ratios (both per marker and considering the set of 17 markers) using the LRs obtained with the Proportional mutation model in the numerator are consistently higher than 1. In contrast, the median ratios using the LRs obtained with the Equal model as the numerator are consistently inferior to 1.

The proportion of cases where the difference in the LRs was greater than 10% is equivalent for all models, ranging from ~0.0004 to ~0.0014 in duos and from ~0.0004 to ~0.0018 in trios of half-siblings. As expected, these proportions are higher when analyzing unrelated individuals, ranging from ~0.0006 to ~0.0024 in duos and from ~0.0006 to ~0.0033 in trios.

Since a pair of Half-siblings may not share any IBD alleles with 50% probability, the results when analyzing cases with Mendelian incompatibilities in this kinship problem (presented in Table A10) correspond only to incompatibilities found between individual B and his/her mother C. They are, therefore, much less variable than the results presented in the previous kinship problems, since they are not directly connected to the kinship being questioned. In fact, the average ratios per marker for half-siblings vary only from ~0.9887 (for Proportional/Extended Stepwise) to ~1.1921 (for Extended Stepwise/Equal).

Figure 11 shows a case-example where one the largest differences was found in Half-siblings trios (between the LRs obtained with the Extended Stepwise and Equal models, as the numerator and denominator, respectively, for marker D21S11):

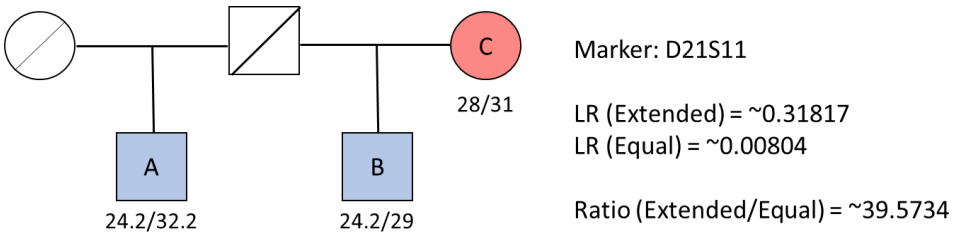

Figure 11 – Case-example showing the genotypes of a trio simulated assuming the hypothesis of Half-sibship for marker Penta E and respective LRs, calculated with the Proportional and Stepwise mutation models considering full-sibship and unrelatedness as the main and alternative hypotheses, respectively.

After analysis of the 17 markers as a set in individuals simulated as Half-siblings (duos and trios), the final LR revealed ratios varying from ~0.9996 (when comparing the LRs obtained with the Stepwise/Extended Stepwise mutation models, in trios) to ~1.044 (when comparing the LRs obtained with the Extended Stepwise/Equal mutation models, in trios) (Machado *et al.*, in press).

Full-siblings vs Half-siblings

In the cases where no Mendelian incompatibilities occur (Table A11, Appendix 2), when analyzing full-siblings, the average ratios per marker range from ~1 to ~1.0001 in both duos and trios, considering all markers. The variation is greater (albeit small) when analyzing half-siblings, since the average ratio per marker ranges from ~0.9992 to ~1.0007. Likewise, the expected average ratio considering the 17 markers ranges from ~1 to ~1.0024 for full-siblings, and from ~0.9873 to ~1.017 for half-siblings.

In full-sibling duos, the proportion of cases where the difference in the LRs was greater than 10% varies from ~0.0005 (when comparing the Extended Stepwise and Proportional models) to ~0.0024 (when comparing the Equal and Proportional models). A decrease is observed when analyzing trios, where this frequency ranges from ~0.0004 (when comparing the Extended Stepwise and Proportional models) to ~0.0014 (when comparing the Equal and Stepwise models). When analyzing half-siblings, the frequency of such cases ranges from ~0.0007 to ~0.0033 in duos (when comparing the Proportional/Extended Stepwise and Equal/Proportional models, respectively). In trios, the frequency drops to a minimum of ~0.0005 and a maximum of ~0.0022 in trios (when comparing the LRs obtained with the Proportional/Extended Stepwise and Equal/Stepwise mutation models, respectively). None of the models seems to produce significantly higher or lower results than the others.

In the cases with Mendelian incompatibilities only (Table A12), the average ratios per marker range from ~0.9132 to ~11.6465 (when comparing the Proportional/Extended Stepwise models, and the opposite). Therefore, when considering the set of 17 markers, the expected average ratio ranges from ~0.1557 to ~$1.9x10^{12}$. Much greater variation in the average ratios per marker is found in half-siblings, where the ratios using the Equal model as the numerator, for example, range from ~8.6406 to ~$4.87x10^{61}$.

Figure 12 shows an extreme example of two full-siblings analyzed in trios (using the genetic information of the mother C) tested for this kinship problem, with full-sibship as the main hypothesis, and **half-sibship as the alternative**, for marker D18S51 and comparing the LRs obtained with the Equal and Stepwise mutation models:

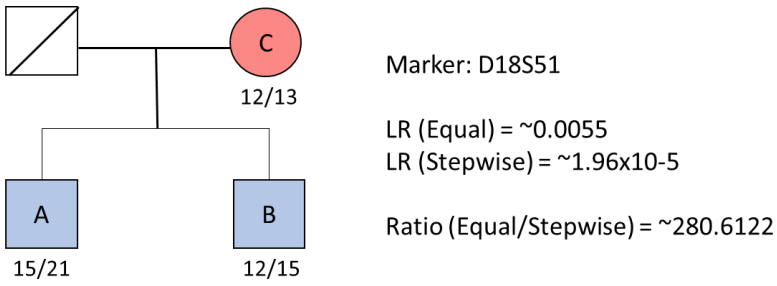

Figure 12 – Case-example showing the genotypes of a trio of individuals simulated assuming the hypothesis of Full-sibship for marker D18S51 and respective LRs, calculated with the Equal and Stepwise mutation models considering full-sibship and half-sibship as the main and alternative hypotheses, respectively.

For the Equal and Proportional models, in full-siblings, the proportion of cases where the difference in the LRs was greater than 10% ranges from ~0.5193 (when these models are compared to one another) to ~0.5598 and ~0.5405 respectively, when both are compared to the Stepwise model. For the Stepwise and Extended Stepwise models, however, the minimum proportion of such cases is expectedly lower (~0.1882) when compared to one another, and the maximums are ~0.5598 and ~0.5569, respectively, when both are compared to the Equal model.

In half-siblings, however, these proportions range from ~0.9599 to ~0.9787 for the Equal model (when compared to the Proportional and Stepwise models, respectively) and from ~0.9276 to ~0.9599 for the Proportional model (when compared to the Extended Stepwise and Equal models, respectively). When comparing the Stepwise and Extended Stepwise models to one another, the proportion of such cases is ~0.3341, while each of them reach the maximum proportions of ~0.9787 and ~0.9746, respectively, when compared to the Equal model.

After analysis of the 17 markers as a set in individuals simulated as Full-siblings (duos and trios), the final LR revealed ratios varying from ~0.9988 (when comparing the

LRs obtained with the Stepwise/Extended Stepwise mutation models, in trios) to ~1.0747 (when comparing the LRs obtained with the Extended Stepwise/Proportional mutation models, in trios) (Machado *et al.*, in press).

4.3.2. For the 10 markers with fictitious allele frequencies:

Due to size constraints and the different purpose of the analysis of the fictitious alleles (they are intended to enlighten about which types of markers, in terms of allele frequency distribution, are more prone to be influenced by the use of different mutation models), the results obtained for these markers are presented in Appendix 3 (Tables A13 to A22), with no specification and differentiation between the models, as previously presented for the 17 real STRs, but instead with differentiation between each of the 10 markers to allow for comparison between them.

We can see that in the problem of paternity and the two problems of full-sibship, in the presence of incompatibilities only, alleles 8, 9 and 10 seem to result in much more variation and magnitude of the average ratios than the other markers when analyzing individuals generated as the alternative hypotheses or intermediate cases in the paternity problem (that is, as half-siblings in the problem of Full-siblings vs Half-siblings, and unrelated individuals for the problem of Full-siblings vs Unrelated, and cases b. to e. of Parent-Child vs Unrelated). For example, while the average ratios in marker 4 in unrelated duos of the paternity problem range from ~0.9934 to ~58.5, the variation in marker 8 is from ~0.7402 to ~4172.58. In Full-siblings vs Half-siblings, as another example, the average ratios vary from ~0.995 to ~327.7 in marker 1, while in marker 10 this variation is from ~0.8798 to ~77416.

Such a discrepancy seems to be correlated with the fact that the three last markers have a significantly larger number of alleles (11, while the remaining seven markers have only 8). However, this discrepancy is not observed in the results regarding individuals generated as the first hypothesis in question, or in any of the cases in the Half-siblings vs Unrelated problem, which could be explained by the fact that half-siblings may not share IBD alleles with 50% probability, therefore the kinship indices (and thus the variation thereof) are lower.

As we can observe for all kinship problems, the minimum proportion of cases in which the difference between the LRs was greater than 10% in markers 1 to 6 is null. In markers 1 to 5, the reason is the fact that they do not have any microvariant alleles, which means that the likelihood ratios obtained when considering either the Stepwise or the Extended Stepwise mutation models must be exactly the same, resulting in all ratios

equal to one. For marker 6, however, the reason is that all its alleles are equifrequent, which means that when considering the Proportional to Frequency model, all alleles are equivalent, leading to ratios equal to one when comparing the LRs obtained with this model and the Equal model. Marker 1 combines both of these situations, since it has 8 equifrequent alleles with no microvariants.

In both problems of full-sibship (and in cases with incompatibilities only) marker 3 presents the lowest maximum proportion of cases where the difference in the LRs was greater than 10% of all markers, in full-siblings individuals – when Unrelated is the alternative hypothesis, the maximum proportion of such cases in marker 3 is ~0.4474, while the lowest maximum of other markers is ~0.5652, observed in marker 5. Likewise, when Half-siblings is the alternative hypothesis, ~0.3158 is the maximum percentage of such cases in marker 3, while the lowest maximum percentage of the remaining markers occurs in marker 1, at ~0.4878.

4.4. The impact of the parameters in the Extended Stepwise model

A similar analysis to that of the previous section was performed aiming to compare the results obtained considering the same mutation model – the Extended Stepwise – but assuming a different integer-length mutation rate. Thus, in the numerator of the comparative ratios was considered the Extended Stepwise II (mutation rate 1 = $5x10^{-3}$; mutation rate 2 = $1x10^{-6}$; mutation range = 0.1) , and the Extended Stepwise I (mutation rate 1 = $1x10^{-3}$; mutation rate 2 = $1x10^{-6}$; mutation range = 0.1), was considered in the denominator, in order to get an insight on the impact of increasing the integer-length mutation rate by a factor of 5. The results of these analyses are presented in Appendix 4.

4.4.1. For the 17 Au-STRs from the database of North Portugal

Parent-Child vs Unrelated

In the problem of paternity, in cases with no incompatibilities (Tables A23 and A24), we can see that the impact of altering the mutation model in duos is highest case a., where the average ratio per marker equals ~0.9978, and lowest in case b., where the

average ratio per marker equals ~0.9992, being intermediate for cases c. (average ratio per marker ~0.9991), d. (~0.9991) and e. (~1.0009), which, despite being greater than one, reflects an equivalent impact to those of cases c. and d. In trios, the average ratios per marker are consistently lower than 1, at ~0.9959, ~0.9975, 0.9972, ~0.9972 and ~0.9999 for cases a. to e., respectively. This means that, when considering trios, cases a. to d. show larger impacts when compared to the analysis in duos, while case e. shows a smaller impact, with an average ratio per marker closer to 1, becoming the case where the impact is lower.

The proportion of cases where the difference is greater than 10% is similar in both duos and trios (although slightly higher in trios). In the intermediate cases, the proportion is approximately to 10 times greater than that of case a. (~0.0060 to ~0.0077, in comparison with ~0.0007 in case a.), while the same increase is of ~20 times for case e.

In the presence of incompatibilities only (Tables A25 and A26), the average ratios per marker are consistently close to 5 in duos (ranging from ~4.8742 to ~4.9992, in cases b. and a., respectively), which directly relates to the increase in the integer-length mutation rate in the Extended Stepwise Model II (considered in the numerator) which is 5 times higher than the mutation rate considered in Extended Stepwise Model I (considered in the denominator). When analyzing trios, the average ratios per marker are roughly maintained in cases b. to e., while it drops to ~4.478 in case a. The proportion of cases where the difference exceeds 10% decreases in all cases, from duos to trios, albeit decreasing more significantly in case a. – in duos, the proportion equals 1, while in trios it drops to ~0.8356. In cases b. to e., the decrease is significantly smoother, with the maximum being from ~0.9685 (duos) to ~0.9396 (trios), in case b.

Figure 13 shows an example of a case (Parent-Child trios) where the impact of the increase in the mutation rate was highest:

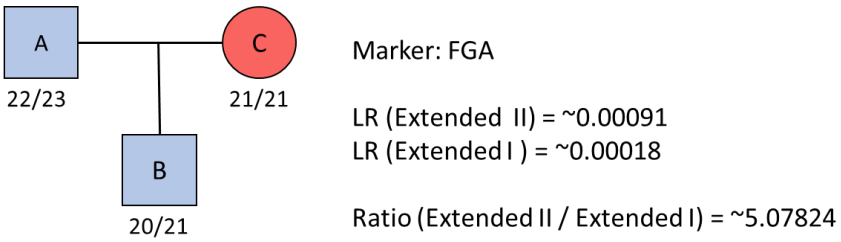

Figure 13 – Case-example showing the genotypes of a trio of individuals simulated assuming the hypothesis of paternity for marker FGA and respective LRs, calculated with the Extended Stepwise II and Extended Stepwise I mutation models considering paternity and unrelatedness as the main and alternative hypotheses, respectively.

Full-siblings vs Unrelated

In this kinship problem, in the absence of incompatibilities (Table A27, Appendix 4), the average ratios are similar to those of the previous problem, decreasing slightly when trios are considered, both when the individuals were simulated assuming the main or the alternative hypothesis. In full-sibling individuals, the increase in the mutation rate when cases with no incompatibilities are considered seems to lead to lower likelihood ratios, as the average ratios per marker are lower than 1 (~0.9999 in duos, ~0.9977 in trios), while the opposite occurs with unrelated individuals, with average ratios per marker of ~1.0111 (duos) and ~1.0107 (trios).

In cases with incompatibilities, however, the increase in the mutation rate seems to lead to a clear increase in the likelihood ratio, as the average ratios per marker are ~3.0410 and ~4.9235 for full-siblings and unrelated individuals, respectively (in trios, since no incompatibilities can occur in duos).

An example of a case (Full-siblings, trio) where the impact of increasing the integer-length mutation rate was highest is provided in Figure 14 below:

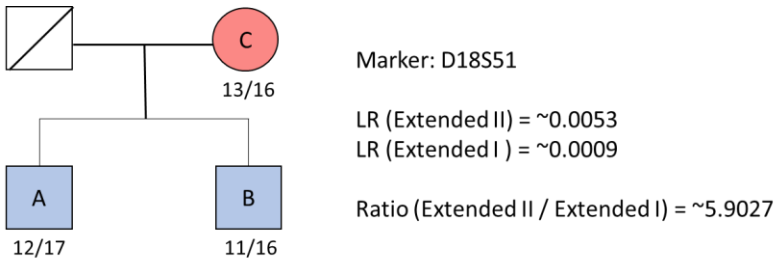

Figure 14 – Case-example showing the genotypes of a trio of individuals simulated assuming the hypothesis of full-sibship for marker D18S51 and respective LRs, calculated with the Extended Stepwise II and Extended Stepwise I mutation models considering full-sibship and unrelatedness as the main and alternative hypotheses, respectively.

The proportion of cases where the difference exceeds 10% in compatible cases is roughly maintained between duos and trios of full-sibling individuals (~0.0058 and ~0.0057, respectively), while it approximately triplicates (from ~0.0117 to ~0.0333) in unrelated individuals. In cases with incompatibilities (Table A28), close to half of the ratios (~0.5116) in full-siblings individuals correspond to differences over 10%, while ~0.9751 do so in unrelated individuals.

Half-siblings vs Unrelated

Out of all kinship problems analyzed, this problem shows the smaller impact from the fivefold increase in the integer-length mutation rate. In the absence of incompatibilities (Table A29, Appendix 4), the average ratios per marker in half-sibling individuals are ~1 in both duos and trios (the expected average ratios after the product of the 17 markers are ~1.0006 and ~0.9997, respectively). For unrelated individuals, the differences are only slightly larger, with average ratios per marker of ~1.0035 in duos and ~1.0056 in trios.

The proportion of cases where the impact reaches 10% approximately doubles for both cases, from duos to trios – in half-sibling individuals, from ~0.0015 to ~0.0029, and in unrelated individuals, from ~0.0024 to ~0.0050.

When analyzing cases with incompatibilities only (Table A30), the difference is expectedly minimal, since incompatibilities can only be found between B and the mother C, although it shows that the mutation rate increase leads to lower LRs in Half-siblings (average ratio per marker of ~0.9998, median ratio per marker of ~0.9967), while the opposite is observed for unrelated individuals (average ratio per marker of ~1.0083, median ratio per marker of ~1.0029). The proportion of cases with at least 10% difference is similar in both situations (~0.0059 in Half-siblings, ~0.0057 in Unrelated).

Full-siblings vs Half-siblings

In compatible cases only (Table A31, Appendix 4), when analyzing duos, the average ratios per marker are greater when the individuals simulated assuming the hypothesis of half-sibship (~1.0058) than when individuals simulated assuming full-sibship are considered (~1.0020) and, for both cases, the increase in mutation rate in the mutation model seems to lead to higher LRs. However, when trios were considered, the average ratios seem to decrease for full-sibling individuals (to values lesser than 1 – the average ratio per marker in Full-siblings trios is ~0.9973), but increase for half-sibling individuals.

The proportion of cases where the difference is greater than 10% is similar **between duos and trios** of Full-siblings (~0.0034 and ~0.0033, respectively), but increases ~6.48 times (from ~0.0044 in duos to ~0.0285 in trios) in individuals generated as Half-siblings.

When considering cases with incompatibilities only (trios, since no incompatibilities are found in duos) (Table A32), the average ratio per marker in Full-siblings is ~3.0022, with the proportion of cases where the difference is greater than 10% being of approximately half of the total (~0.5116), while the average ratio per marker is closer to 5 (~4.8988) in Half-sibling individuals, with the proportion of cases with greater than 10% difference being ~0.9747.

An example of a case where the impact was highest, in individuals generated assuming the hypothesis of full-sibship (and analyzed in trios) was found in marker Penta E, as pictured below:

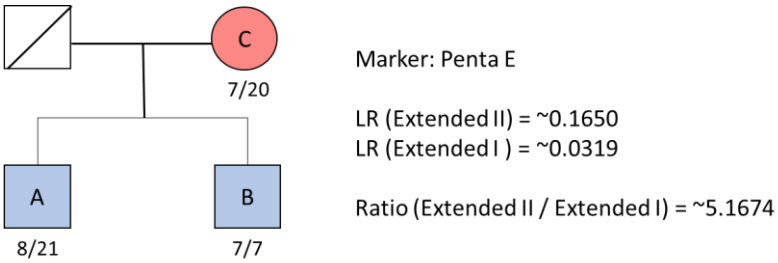

Figure 15 – Case-example showing the genotypes of a trio of individuals simulated assuming the hypothesis of full-sibship for marker Penta E and respective LRs, calculated with the Extended Stepwise II and Extended Stepwise I mutation models considering full-sibship and half-sibship as the main and alternative hypotheses, respectively.

4.4.2. For the 10 markers with fictitious allele frequencies

Parent-Child vs Unrelated

In cases with no incompatibilities, for both duos and trios (Tables A33 and A34 of Appendix 5), all cases, from a. to e., present overall similar results for all markers. It seems that the increase in the integer-length mutation rate in the Extended Stepwise Model II leads in most of the cases to lower LRs, as the average ratios are consistently lower than 1. The exceptions are markers 3 and 8, **in case e. only**, since both show ratios of ~1.0007 in duos and ~1.0001 in trios. There could be a correlation between this observations and the allele frequency configurations of these markers – out of all 10 fictitious markers, 3 and 8 are those who have 6 alleles with bell-shaped frequencies (along with two centered, consecutive, and equifrequent modal alleles in marker 3, and two equifrequent modal integer alleles differing in one repeat, surrounded by two non-integer low equifrequent alleles in marker 8, with another one separating the modal alleles from one another).

The proportion of cases where the difference in LRs is greater than 10% is roughly similar for most markers, in **both duos and trios**, in the cases where the putative father is either the real father or a full-brother of him – this proportion ranges from ~0.0002 to ~0.0006 in case a. a from ~0.0006 to ~0.0025 in cases b., c., and d., which only slightly vary. The exceptions are, again, markers 3 and 8, along with marker 1 (all equifrequent alleles, with no microvariants). For these markers, the proportion of cases where the difference in the LRs is greater than 10% is null.

When the individuals were simulated as unrelated, however, the differences in these proportions are more accentuated, both between markers and between duos and trios (showing a clear increase when trios are analyzed, with the exception of the three aforementioned markers). Marker 7 seems to have the significantly highest proportion of cases with greater than 10% difference in the LRs, with ~0.0051 in duos and ~0.0074 in trios (for reference, the second marker with highest proportions is marker 4, with ~0.0033 in duos and ~0.0044 in trios. Conversely, marker 2 shows the lowest proportions of such cases, at ~0.0014 in duos and ~0.0021 in trios.

However, no conclusions could be pointed out from these observations, at least considering allele distributions, since both of these markers have somewhat similar allele frequency configurations, with one centered modal allele and seven equifrequent alleles (although marker 7 has two non-integer alleles surrounding the modal allele).

In the cases with incompatibilities only, **in duos** (Table A35, Appendix 5), all markers with no microvariants (1 to 5) show the same results for all cases (a. to e.) in regards to the average ratio (5.0000), median ratio (5.0000) and the proportion of cases where the difference exceeds 10% (which equals 1). The remaining markers have slightly lower average ratios and proportions (with the exception of case a., where the proportion of cases with more than 10% difference remains equal to 1), with marker 6, which has 8 equifrequent alleles with two non-integers differing in one repeat, presenting clearly lower average ratios and proportions in cases b. to e.. For example, for case b., while the average ratios of other markers range from ~4.3658 to 5, the average ratio in marker 6 is ~3.4246. The same is observed regarding the proportion of cases where the difference is greater than 10%, with other markers ranging from ~0.8630 to 1 in case b., while marker 6 shows a proportion of ~0.6087.

When trios are considered (Table A36), there is slightly more variability between markers and cases. In case a., there is no evident difference in the average ratios between the ten markers, ranging from ~4.3604 (marker 10) to ~4.5924 (marker 5). However, in cases b. to e., markers 1 to 5 consistently show ratios slightly greater than 5, while markers 6 to 10 showing ratios somewhere between 4 and 5, similar to those of

all markers in case a. As in the analysis of duos, marker 6 presents significantly lower average ratios (from ~3.1290 to ~3.3583) and proportions of cases with more than 10% difference in LRs (from ~0.4815 to ~0.5475) than the remaining markers, for cases b. to e.

Full-siblings vs Unrelated

In this problem, in the absence of incompatibilities (Table A37, Appendix 5), the average ratios per marker are roughly similar for all markers, in both duos and trios for both hypotheses in question, with the exception of marker 2, which shows greater average rations than the other markers. For example, in duos of full-sibling individuals, the average ratio in marker 2 is ~1.0023, while the maximum average ratio of other markers is 1.0002 (in marker 3). The same occurs in full-sibling trios and in both duos and trios of unrelated individuals. It is worth to note that all 10 markers showed a decrease in the average ratios of full-siblings individuals, to values lower than 1, when trios were considered. The same is not observed in unrelated individuals, where a general slight increase in the average ratios occurs.

Regarding the proportion of cases where the difference in the LRs is greater than 10%, markers 3 and 8, once again, present the highest values – in the same example of full-sibling duos, this proportions are ~0.0055 for marker 3 and ~0.0062 for marker 8, while the maximum proportion of the remaining markers is ~0.0014, in marker 10. Again, as described in section 3.3.2, a larger number of alleles seems to be correlated with an increase in these proportions, as happens in markers 8, 9 and 10, for all cases.

When only incompatibilities are considered (Table A38), the results for the individuals simulated assuming half-sibship show the average ratios are roughly similar for all marker, ranging only from ~2.0457, in marker 3, to ~3.5366, in marker 8. Regarding the proportion of cases where the difference in LRs exceeds 10%, there is more evident variability – marker 3 is the marker with the clear lowest proportion ~0.2362 (for reference, the second lowest is found in marker 9, with ~0.3409), while marker 8 presents the highest proportion of such cases: ~0.6327. No clear patterns were found to allow (either in the average ratios or the proportion of cases where the difference is greater than 10%) for conclusions to be taken regarding the relationship between the configuration of the allele frequencies of the markers, and the effect of increasing the integer-length mutation rate in the mutation model considered.

Half-siblings vs Unrelated

In cases with no Mendelian incompatibilities (Table A39, Appendix 5), all of the average ratios, for all markers are extremely close to 1. Indeed, in the cases simulated assuming the hypothesis of half-sibship, the average ratios vary only from ~1.000 (markers 6 and 9, in duos; markers 6, 7, 9 and 10 in trios) to ~1.0011 (marker 2, in both duos and trios). In unrelated individuals, the average ratios range from ~1.0034 (markers 3 and 8, in duos) to ~1.0078 (marker 2, in trios). In fact, marker 2 present higher ratios (and, since the values are greater than one, greater impacts) than the rest of the models – in unrelated individuals, for example, the average ratios in marker 3 are ~1.0054 in duos and ~1.0078 in trios, while the second highest average ratios are ~1.0038 in duos (markers 1 and 6), and ~1.0065 in trios (marker 9).

Marker 2 has one centered modal allele with seven other equifrequent alleles, thus it could be suggested that such a configuration results in higher impacts, at least in cases with no incompatibilities of the problem of Half-siblings vs Unrelated.

In fact, the same is observed for the unrelated individuals tested for half-sibship, in cases with mendelian incompatibilities only (Table A40), although, as previously mentioned, these incompatibilities pertain only to the relationship between one of the supposed half-siblings and his/her mother – the average ratio in marker 2 is ~1.0101, while the second highest ratio is equal to ~1.0086, in marker 10.

However, such is not the case in the case when the individuals are, in fact, simulated assuming the hypothesis of half-sibship, where the highest impact is found in marker 6, with an average ratio of ~0.9971.

Regarding the proportion of cases where the difference in the LRs is greater than 10%, it is null for all markers of both hypotheses, in incompatible cases only. In cases with no Mendelian incompatibilities, only markers 8, 9 and 10 show such proportions greater than 0 in duos of both hypotheses, with ~0.0007, ~0.0006 and ~0.0006, respectively, for half-sibling individuals, and ~0.0015, ~0.0012 and ~0.0011 for unrelated individuals. In trios, only markers 1 and 6 have null frequencies of such cases, with the proportions in the remaining markers ranging from ~0.0001 (marker 4) to ~0.0014 (marker 8) in half-sibling individuals, and from ~0.0001 (marker 2) to ~0.0010 (marker 3) in unrelated individuals.

As before, no clear patterns allow for conclusions to be taken regarding the relationship between the allele frequency configurations of the markers and the impact of increasing the mutation rate in the mutation model.

Full-siblings vs Half-siblings

In this problem, for cases with no Mendelian incompatibilities only (Table A41, Appendix 5) and individuals simulated assuming the hypothesis of full-sibship, the average ratios in duos are greater than one for all markers, which indicates that, on average, the increase in the integer-length mutation rate in the mutation model leads to higher LRs in all markers. The opposite happens when analyzing trios of the same cases, as the average ratios are lower than 1 for all markers. Such as in the previous kinship problem, an increase in the impact is found on marker 2, in duos, as the average ratio is ~1.0040, while the average ratios in all other markers range from ~1.0022 to ~1.0025. However, the same is not observed in trios, where marker 2 shows an average ratio of ~0.9970, while the average ratios in the other markers range from ~1.0068 to ~1.0074.

In the presence of Mendelian incompatibilities only (Table A42), for the individuals simulated assuming the hypothesis of full-sibship, the average ratios range from ~2.0492 (for marker 3) to ~3.5248 (in marker 8).

Regarding the proportion of cases where the difference in the LRs is greater than 10%, these same two markers (3 and 8) also show the lowest and highest proportions (~0.2632 and ~0.6327, respectively). Again, both of these markers have two modal equifrequent alleles and six alleles with bell-shaped frequencies (although marker 8 has 3 non-integer alleles, separating the modal alleles from the rest of the alleles and from one another). In the cases where no incompatibilities are observed, only markers 3, 8, 9 and 10 show proportions greater than zero (~0.0020, ~0.0041, ~0.0006 and ~0.0007, respectively) in full-siblings duos, while they range from ~0.0001 (marker 1) to ~0.0027 (marker 9) throughout all markers, in the respective trio.

Due to an unfortunate and late-detected problem with the output text files containing the LRs relative to the fictitious markers in individuals simulated assuming half-sibship for this kinship problem and analysis (they were accidentally overwritten), such results are therefore not here presented or discussed.

5. Conclusions

In regards to the impact of consistently considering mutation in kinship analyses even in cases where no incompatibilities are found, in comparison with its use only in the case of Mendelian incompatibilities (i.e. the impact of considering the occurrence of hidden mutations), it is expected to be very low, whichever mutation model is considered. Given our results, the impact seems to depend on the kinship in question, on the allele frequencies of the analyzed markers and on the genotyped individuals (i.e. whether duos or trios are considered).

The same applies for the comparisons between the likelihood ratios obtained with each one of the four mutation models considered (Equal, Proportional, Stepwise and Extended Stepwise), in cases where no Mendelian incompatibilities are observed. In the case where only incompatibilities are considered, however, the results seem to be much more variable – especially when individuals simulated assuming the alternative hypothesis in a given kinship problem are tested, given that the incompatibilities found are generally of greater magnitudes – but not to an extent that could robustly point towards different hypotheses depending on the mutation model considered, with the exception of some extreme cases, which are outliers, found in all kinship problems.

No clear distinction could be made regarding which type of markers is more prone to larger differences due to the mutation model, although it could be suggested that markers with a greater number of alleles show greater variability, at least when individuals are simulated assuming the alternative or hypotheses (namely Half-siblings in Full-siblings vs Half-siblings, and Unrelated in Full-siblings vs Unrelated and Parent-Child vs Unrelated), as well as the intermediate cases (e., c. and d.) in the paternity problem.

Concerning the increase in the integer-length mutation rate specified in the Extended Stepwise mutation model, it shows little to no impact in cases with no Mendelian incompatibilities (although the increase in the mutation rate, as expected, seems to result in an increase in the likelihood ratios calculated). In cases with Mendelian incompatibilities only, the maximum average impact seems to be roughly the increase in the mutation rate (i.e. 5 times greater).

Future work could be developed with fictitious markers (with more variability, especially regarding the number of alleles, which seems to have an unexpected impact) to evaluate which kinds are more prone to suffer differences due to the use

of different mutation models. Furthermore, as mentioned in (Machado *et al.*, in press), a broader approach should be taken considering the paternity cases where the individuals tested as the putative father is, in fact, a close relative of him, as well as the cases where individuals are simulated assuming the alternative hypothesis, in all of the kinship problems.

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Appendices

Appendix 1

Table A1 – Estimated maternal incompatibility rates for the 17 real Au-STRs

Marker	*1-step*	*2-step*	*3-step*	*4-step*
CSF1PO	0.000254825	0	0	0
D2S1338	0.000177078	5.44855E-05	0	1.36214E-05
D3S1358	0.000204922	6.02711E-06	0	0
D5S818	0.000299652	0	0	0
D7S820	7.26141E-05	0	0	0
D8S1179	0.000321584	5.95525E-06	0	0
D13S317	0.000425653	1.01346E-05	0	0
D16S539	0.000481093	0	0	0
D18S51	0.000665215	4.23319E-05	0	0
D19S433	0.000583226	1.29606E-05	0	0
D21S11	0.00128916	5.96833E-06	0	0
FGA	0.000509431	6.13772E-06	0	6.13772E-06
PD	0.000253	0	0	0
PE	0.000253	0	0	0
TH01	4.31186E-05	0	0	0
TPO	8.1367E-05	0	0	0
VWA	0.000445606	1.80651E-05	0	0

Table A2 – Estimated paternal incompatibility rates for the 17 real Au-STRs

Marker	*1-step*	*2-step*	*3-step*	*4-step*
CSF1PO	0.002024768	0	0	0
D2S1338	0.001512139	1.40013E-05	0	0
D3S1358	0.001673754	1.13091E-05	0	5.65457E-06
D5S818	0.001732689	9.16767E-06	0	0
D7S820	0.001341491	0	0	0
D8S1179	0.002007785	2.79636E-05	0	0
D13S317	0.001806972	9.08026E-06	0	0
D16S539	0.001121051	5.66187E-06	0	0
D18S51	0.002446019	7.22961E-05	1.20494E-05	0
D19S433	0.000718716	2.66191E-05	0	0
D21S11	0.001691779	1.69744E-05	0	0
FGA	0.003637103	6.97208E-05	5.81007E-06	0
PD	0.000259	0	0	0
PE	0.00026	0	0	0
TH01	5.84426E-05	1.16885E-05	0	0
TPO	0.000130114	0	0	0
VWA	0.003229942	2.79891E-05	0	0

Appendix 2

Summarized tables of ratios regarding the impact of considering different mutation models, for the 17 real autosomal STRs:

Table A3 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **duos**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		a	b	c	d	e
Equal	*Average ratio per marker (r)*	0.9999 to 1	0.9996 to 0.9998	0.9997 to 0.9999	0.9997 to 0.9999	0.9994 to 0.9997
	Average ratio in 17 markers	0.9987 to 0.9995	0.9934 to 0.9971	0.9944 to 0.9978	0.9945 to 0.9979	0.9892 to 0.9956
	Median ratio per marker	0.9998 to 1	0.9998 to 1	0.9998 to 1	0.9997 to 0.9999	0.9997 to 0.9999
	Proportion of r<1/1.1 or r>1.1	0.0002 to 0.0002	0.0002 to 0.0002	0.0002 to 0.0003	0.0002 to 0.0003	0.0003 to 0.0004
Proportional	*Average ratio per marker (r)*	1 to 1.0001	1.0002 to 1.0004	1.0001 to 1.0003	1.0001 to 1.0003	1.0003 to 1.0007
	Average ratio in 17 markers	1.0005 to 1.0015	1.0031 to 1.0069	1.0025 to 1.0059	1.0025 to 1.0059	1.0047 to 1.0113
	Median ratio per marker	1.0001 to 1.0002	1.0001 to 1.0002	1.0001 to 1.0002	1.0001 to 1.0003	1.0002 to 1.0003
	Proportion of r<1/1.1 or r>1.1	0.0001 to 0.0002	0 to 0.0002	0.0001 to 0.0002	0.0001 to 0.0002	0.0002 to 0.0003
Stepwise	*Average ratio per marker (r)*	1 to 1	0.9998 to 1.0002	0.9998 to 1.0002	0.9998 to 1.0001	0.9996 to 1.0003
	Average ratio in 17 markers	0.9993 to 1.0007	0.9965 to 1.0032	0.9968 to 1.0026	0.9967 to 1.0025	0.9939 to 1.0049
	Median ratio per marker	0.9999 to 1	0.9999 to 1	0.9998 to 1	0.9998 to 1.0001	0.9998 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0.0001 to 0.0002	0.0001 to 0.0002	0.0001 to 0.0003	0.0001 to 0.0003	0.0002 to 0.0004
Extended Stepwise	*Average ratio per marker (r)*	1 to 1.0001	0.9998 to 1.0002	0.9999 to 1.0002	0.9999 to 1.0002	0.9997 to 1.0004
	Average ratio in 17 markers	0.9996 to 1.001	0.9971 to 1.0039	0.9977 to 1.0035	0.9977 to 1.0034	0.9957 to 1.0068
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1	0.9999 to 1.0001	0.9999 to 1.0001	0.9998 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0.0001 to 0.0002	0 to 0.0002	0.0001 to 0.0003	0.0001 to 0.0002	0.0002 to 0.0004

Table A4 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **trios**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		a	b	c	d	e
Equal	*Average ratio per marker (r)*	0.9998 to 0.9999	0.9995 to 0.9998	0.9995 to 0.9998	0.9995 to 0.9998	0.9991 to 0.9996
	Average ratio in 17 markers	0.996 to 0.9985	0.9909 to 0.9963	0.9916 to 0.9966	0.9918 to 0.9967	0.985 to 0.9936
	Median ratio per marker	0.9999 to 1	1 to 1	0.9999 to 1	0.9999 to 1	0.9998 to 1
	Proportion of r<1/1.1 or r>1.1	0.0002 to 0.0002	0.0001 to 0.0003	0.0002 to 0.0002	0.0001 to 0.0002	0 to 0
Proportional	*Average ratio per marker (r)*	1.0001 to 1.0002	1.0002 to 1.0006	1.0002 to 1.0005	1.0002 to 1.0005	1.0004 to 1.0009
	Average ratio in 17 markers	1.0018 to 1.0041	1.004 to 1.0096	1.0038 to 1.0087	1.0037 to 1.0085	1.0065 to 1.0155
	Median ratio per marker	1 to 1.0001	1 to 1	1 to 1.0001	1.0001 to 1.0001	1.0001 to 1.0002
	Proportion of r<1/1.1 or r>1.1	0.0001 to 0.0002	0.0001 to 0.0003	0.0001 to 0.0002	0.0001 to 0.0001	0 to 0
Stepwise	*Average ratio per marker (r)*	0.9999 to 1.0001	0.9997 to 1.0002	0.9997 to 1.0002	0.9997 to 1.0002	0.9995 to 1.0004
	Average ratio in 17 markers	0.9977 to 1.0017	0.9947 to 1.0041	0.9951 to 1.0037	0.9952 to 1.0036	0.9914 to 1.0066
	Median ratio per marker	1 to 1	1 to 1	0.9999 to 1	0.9999 to 1	0.9999 to 1
	Proportion of r<1/1.1 or r>1.1	0.0001 to 0.0002	0.0002 to 0.0003	0.0001 to 0.0002	0.0001 to 0.0002	0 to 0
Extended Stepwise	*Average ratio per marker (r)*	0.9999 to 1.0001	0.9998 to 1.0003	0.9998 to 1.0003	0.9998 to 1.0003	0.9996 to 1.0005
	Average ratio in 17 markers	0.9983 to 1.0024	0.9962 to 1.0056	0.9964 to 1.005	0.9965 to 1.0049	0.9938 to 1.0091
	Median ratio per marker	1 to 1	1 to 1	1 to 1	0.9999 to 1	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0.0001 to 0.0002	0.0001 to 0.0002	0.0001 to 0.0002	0.0001 to 0.0002	0 to 0

Table A5 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **duos**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		a	b	c	d	e
Equal	*Average ratio per marker (r)*	0.6863 to 5.4531	1.1112 to 1.24×10^{8}	1.1816 to 7.34×10^{8}	1.1651 to 4.99×10^{8}	1.1747 to 7.8×10^{8}
	Average ratio in 17 markers	0.0004 to 9.9×10^{7}	3.7583 to 3.9×10^{52}	16.0326 to 6.77×10^{61}	12.77 to 5.85×10^{59}	14.5129 to 1.5×10^{62}
	Median ratio per marker	0.3776 to 3.6931	0.4582 to 2.8836	0.4689 to 1.9234	0.4658 to 1.7101	0.4685 to 1.7103
	Proportion of r<1/1.1 or r>1.1	0.9407 to 0.9781	0.9577 to 0.9779	0.9583 to 0.9725	0.9583 to 0.9713	0.9584 to 0.9714
Proportional	*Average ratio per marker (r)*	0.7388 to 4.176	2.2582 to 3.88×10^{7}	2.2927 to 1.9×10^{9}	2.3054 to 3.19×10^{8}	2.3037 to 1.23×10^{9}
	Average ratio in 17 markers	0.0001 to 50.4903	6.6×10^{5} to 1.8×10^{54}	8.2×10^{5} to 3×10^{59}	9.1×10^{5} to 1.4×10^{56}	8.0×10^{5} to 3×10^{56}
	Median ratio per marker	0.5855 to 1.5465	1.6455 to 7.7147	1.5746 to 3.6989	1.5593 to 3.5123	1.5361 to 3.4976
	Proportion of r<1/1.1 or r>1.1	0.9136 to 0.9407	0.9124 to 0.9577	0.9132 to 0.9583	0.9111 to 0.9583	0.9122 to 0.9584
Stepwise	*Average ratio per marker (r)*	0.8751 to 16.3804	1.2279 to 31.9154	1.1321 to 23.4312	1.1144 to 21.5672	1.0912 to 21.4139
	Average ratio in 17 markers	0.0579 to 3.14×10^{13}	12.2953 to 1.6×10^{7}	7.7267 to 2.5×10^{7}	6.1104 to 1.7×10^{7}	4.1877 to 1.5×10^{7}
	Median ratio per marker	0.8324 to 12.8766	0.4884 to 1.119	0.5309 to 1.1641	0.5389 to 1.2055	0.5438 to 1.1964
	Proportion of r<1/1.1 or r>1.1	0.2713 to 0.9781	0.3208 to 0.9779	0.333 to 0.9725	0.3326 to 0.9713	0.3337 to 0.9714
Extended Stepwise	*Average ratio per marker (r)*	2.9255 to 19.2089	1.2355 to 5065.2	1.1146 to 68068.7	1.0996 to 28583.5	1.0687 to 10745.2
	Average ratio in 17 markers	10^{5} to 10^{15}	21.4772 to 6.5×10^{13}	5.9082 to 3.46×10^{17}	4.7735 to 187×10^{18}	2.9573 to 4.5×10^{18}
	Median ratio per marker	2.6356 to 13.1709	0.6501 to 3.6137	0.67 to 2.6772	0.6724 to 2.6143	0.6788 to 2.6143
	Proportion of r<1/1.1 or r>1.1	0.2713 to 0.9781	0.3208 to 0.9742	0.333 to 0.9692	0.3326 to 0.9682	0.3337 to 0.9682

Table A6 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **trios**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		**a**	**b**	**c**	**d**	**e**
Equal	*Average ratio per marker (r)*	0.5634 to 5.2457	1.1579 to $2.6x10^{10}$	1.241 to $1.6x10^{22}$	1.2059 to $714x10^{19}$	1.2123 to $1.45x10^{24}$
	Average ratio in 17 markers	0 to $9.4x10^{9}$	6.539 to $1.2x10^{75}$	35.0889 to $2x10^{93}$	22.286 to $3..3x10^{88}$	24.08 to $7.15x10^{92}$
	Median ratio per marker	0.438 to 0.9998	0.4482 to 4.832	0.426 to 4.3201	0.4244 to 4.0177	0.4267 to 4.2162
	Proportion of r<1/1.1 or r>1.1	0.8884 to 0.8938	0.9311 to 0.9849	0.9338 to 0.9844	0.9336 to 0.9844	0.9331 to 0.9849
Proportional	*Average ratio per marker (r)*	0.7125 to 4.571	2.4971 to $1.7x10^{9}$	2.5063 to $8.9x10^{19}$	2.5143 to $4x10^{17}$	2.5049 to $7.8x10^{21}$
	Average ratio in 17 markers	0.0028 to 2012.27	$3.7x10^{6}$ to $5x10^{72}$	$3.8x10^{6}$ to $2.6x10^{83}$	$4x10^{6}$ to 5x10 75	$3.8x10^{6}$ to $3.9x10^{81}$
	Median ratio per marker	0.5879 to 1.3548	2.4315 to 14.6275	2.615 to 12.0023	2.4944 to 11.1452	2.6064 to 11.0975
	Proportion of r<1/1.1 or r>1.1	0.8938 to 0.905	0.9311 to 0.9402	0.9296 to 0.9348	0.9261 to 0.9336	0.9265 to 0.9331
Stepwise	*Average ratio per marker (r)*	0.8682 to 11.5872	1.2975 to 47.0158	1.1758 to 35.9511	1.148 to 34.5951	1.1198 to 34.7099
	Average ratio in 17 markers	0.0433 to $3x10^{15}$	29.1286 to $1.8x10^{8}$	14.423 to $1.8x10^{8}$	9.6982 to $1.1x10^{8}$	6.0389 to $1.7x10^{8}$
	Median ratio per marker	0.8844 to 1.8977	0.3871 to 0.9063	0.4295 to 1.1693	0.4474 to 1.1782	0.4463 to 1.1707
	Proportion of r<1/1.1 or r>1.1	0.2246 to 0.905	0.3202 to 0.9849	0.3203 to 0.9844	0.3169 to 0.9844	0.3192 to 0.9849
Extended Stepwise	*Average ratio per marker (r)*	2.907 to 14.1721	1.2193 to $2.4x10^{7}$	1.189 to $4.25x10^{19}$	1.1476 to $1.9x10^{17}$	1.1043 to $3.7x10^{21}$
	Average ratio in 17 markers	$2.2x10^{5}$ to $9.4x10^{16}$	13.4914 to $7.2.10^{25}$	16.9332 to 10^{41}	9.5352 to $3x10^{36}$	4.797 to $1.2x10^{43}$
	Median ratio per marker	1.8625 to 2.6676	0.4837 to 8.4207	0.542 to 8.1083	0.5694 to 8.0654	0.5586 to 8.0647
	Proportion of r<1/1.1 or r>1.1	0.2246 to 0.8948	0.3202 to 0.9822	0.3203 to 0.9814	0.3169 to 0.9816	0.3192 to 0.9821

Table A7 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **duos and trios**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		**Full-siblings (duos)**	**Unrelated (duos)**	**Full-siblings (trios)**	**Unrelated (trios)**
Equal	*Average ratio per marker (r)*	1.0001 to 1.0002	1.0005 to 1.0008	1 to 1.0001	0.9996 to 1.0001
	Average ratio in 17 markers	1.0009 to 1.0027	1.0089 to 1.0129	0.9992 to 1.0013	0.9936 to 1.0012
	Median ratio per marker	0.9983 to 0.9999	0.997 to 0.9995	0.9994 to 0.9999	0.9976 to 1
	Proportion of r<1/1.1 or r>1.1	0.0032 to 0.0035	0.006 to 0.0066	0.0023 to 0.0025	0.0045 to 0.005
Proportional	*Average ratio per marker (r)*	1.0001 to 1.0003	0.9999 to 1.0001	1.0001 to 1.0003	1.0003 to 1.0009
	Average ratio in 17 markers	1.0009 to 1.0047	0.9979 to 1.0016	1.0011 to 1.0051	1.0051 to 1.0158
	Median ratio per marker	1.0005 to 1.0017	1.0012 to 1.003	1.0003 to 1.0006	1.001 to 1.0024
	Proportion of r<1/1.1 or r>1.1	0.0008 to 0.0035	0.0014 to 0.0066	0.0006 to 0.0025	0.0011 to 0.005
Stepwise	*Average ratio per marker (r)*	1.0001 to 1.0002	1 to 1.0004	1 to 1.0002	0.9998 to 1.0005
	Average ratio in 17 markers	1.0009 to 1.0031	0.9999 to 1.0071	1.0001 to 1.0031	0.9965 to 1.0081
	Median ratio per marker	0.999 to 1.0001	0.998 to 1.0005	0.9996 to 1.0001	0.9983 to 1
	Proportion of r<1/1.1 or r>1.1	0.0009 to 0.0033	0.0017 to 0.0063	0.0007 to 0.0024	0.0012 to 0.0047
Extended Stepwise	*Average ratio per marker (r)*	1.0001 to 1.0003	1 to 1.0003	1 to 1.0003	0.9999 to 1.0007
	Average ratio in 17 markers	1.001 to 1.0044	1.0008 to 1.005	1.0004 to 1.0045	0.998 to 1.0118
	Median ratio per marker	0.9995 to 1.0004	0.9988 to 1.0011	0.9997 to 1.0001	0.999 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0.0008 to 0.0032	0.0014 to 0.006	0.0006 to 0.0023	0.0011 to 0.0045

Table A8 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **trios**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		Full-siblings (trios)	Unrelated (trios)
Equal	*Average ratio per marker (r)*	1.3172 to 4.3371	1.2572 to 1.16×10^{8}
	Median ratio per marker	0.6336 to 0.9891	0.4729 to 2.0376
	Proportion of r<1/1.1 or r>1.1	0.6506 to 0.6988	0.9601 to 0.9748
Proportional	*Average ratio per marker (r)*	0.8786 to 2.1186	2.3031 to 5.17×10^{7}
	Median ratio per marker	0.7842 to 1.0604	1.6502 to 4.1569
	Proportion of r<1/1.1 or r>1.1	0.6988 to 0.7191	0.92 to 0.9601
Stepwise	*Average ratio per marker (r)*	0.9216 to 12.0141	1.1452 to 21.4089
	Median ratio per marker	0.9532 to 1.3821	0.5188 to 1.1777
	Proportion of r<1/1.1 or r>1.1	0.2056 to 0.7191	0.3349 to 0.9748
Extended Stepwise	*Average ratio per marker (r)*	2.2646 to 13.1598	1.097 to 10887.864
	Median ratio per marker	1.0762 to 1.8308	0.6517 to 2.7271
	Proportion of r<1/1.1 or r>1.1	0.2056 to 0.7172	0.3349 to 0.9706

Table A9 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Half-siblings vs Unrelated** problem, in **duos and trios**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		**Half-siblings (duos)**	**Unrelated (duos)**	**Half-siblings (trios)**	**Unrelated (trios)**
Equal	*Average ratio per marker (r)*	1 to 1	1.0002 to 1.0002	1 to 1.0001	1.0002 to 1.0003
	Average ratio in 17 markers	1 to 1.0008	1.0027 to 1.0037	0.9996 to 1.0009	1.004 to 1.0059
	Median ratio per marker	0.9992 to 0.9998	0.999 to 0.9997	0.9994 to 0.9999	0.9986 to 0.9999
	Proportion of r<1/1.1 or r>1.1	0.0014 to 0.0014	0.0023 to 0.0024	0.0017 to 0.0018	0.0031 to 0.0033
Proportional	*Average ratio per marker (r)*	1 to 1.0001	0.9999 to 1	1 to 1.0002	0.9999 to 1
	Average ratio in 17 markers	1.0001 to 1.0012	0.9987 to 1.0004	1.0003 to 1.0027	0.9984 to 1.0007
	Median ratio per marker	1.0003 to 1.0008	1.0004 to 1.001	1.0003 to 1.0006	1.0004 to 1.0014
	Proportion of r<1/1.1 or r>1.1	0.0004 to 0.0014	0.0006 to 0.0024	0.0004 to 0.0018	0.0006 to 0.0033
Stepwise	*Average ratio per marker (r)*	1 to 1	1 to 1.0001	1 to 1.0001	1 to 1.0002
	Average ratio in 17 markers	0.9999 to 1.0007	0.9994 to 1.0018	0.9997 to 1.0015	0.9993 to 1.0028
	Median ratio per marker	0.9995 to 1.0002	0.9994 to 1.0003	0.9996 to 1.0001	0.9991 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0.0006 to 0.0014	0.0009 to 0.0023	0.0006 to 0.0018	0.0009 to 0.0032
Extended Stepwise	*Average ratio per marker (r)*	1 to 1.0001	1 to 1.0001	1 to 1.0002	1 to 1.0001
	Average ratio in 17 markers	1.0004 to 1.0013	0.9994 to 1.0012	1.0007 to 1.0027	1 to 1.0024
	Median ratio per marker	0.9997 to 1.0004	0.9996 to 1.0005	0.9997 to 1.0002	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0.0004 to 0.0014	0.0006 to 0.0023	0.0004 to 0.0017	0.0006 to 0.0031

Table A10 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Half-siblings vs Unrelated** problem, in **trios**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		**Half-siblings (trios)**	**Unrelated (trios)**
Equal	*Average ratio per marker (r)*	1.0065 to 1.0702	1.0659 to 1.0775
	Average ratio in 17 markers	0.9838 to 3.0431	2.8569 to 3.4078
	Median ratio per marker	0.9877 to 1.0264	0.9987 to 1.0221
	Proportion of r<1/1.1 or r>1.1	0.3294 to 0.426	0.1954 to 0.2759
Proportional	*Average ratio per marker (r)*	0.9887 to 1.0383	0.9623 to 1.0349
	Average ratio in 17 markers	0.6446 to 1.6942	0.5043 to 1.6102
	Median ratio per marker	0.9394 to 0.9798	0.9809 to 0.9841
	Proportion of r<1/1.1 or r>1.1	0.426 to 0.5286	0.2759 to 0.3352
Stepwise	*Average ratio per marker (r)*	0.9931 to 1.1805	0.9975 to 1.0631
	Average ratio in 17 markers	0.8859 to 13.6125	0.9572 to 2.7018
	Median ratio per marker	0.9966 to 1.0786	1.0005 to 1.0264
	Proportion of r<1/1.1 or r>1.1	0.1164 to 0.5286	0.0575 to 0.3352
Extended Stepwise	*Average ratio per marker (r)*	1.0389 to 1.1921	1.0122 to 1.0671
	Average ratio in 17 markers	1.8413 to 15.7977	1.217 to 2.8814
	Median ratio per marker	1.0038 to 1.0837	0.9995 to 1.0272
	Proportion of r<1/1.1 or r>1.1	0.1164 to 0.5148	0.0575 to 0.3295

Table A11 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Full-siblings vs Half-siblings** problem, in **duos and trios**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		**Full-siblings (duos)**	**Half-siblings (duos)**	**Full-siblings (trios)**	**Half-siblings (trios)**
Equal	*Average ratio per marker (r)*	1.0001 to 1.0001	1.0001 to 1.0002	1 to 1	0.9992 to 0.9998
	Average ratio in 17 markers	1.0012 to 1.0021	1.002 to 1.0034	0.9992 to 1.0001	0.9873 to 0.9958
	Median ratio per marker	0.9989 to 1	0.9981 to 1	0.9999 to 1	0.9997 to 1
	Proportion of r<1/1.1 or r>1.1	0.0022 to 0.0024	0.003 to 0.0033	0.0013 to 0.0014	0.002 to 0.0022
Proportional	*Average ratio per marker (r)*	1 to 1.0001	1 to 1.0001	1 to 1.0001	1.0004 to 1.001
	Average ratio in 17 markers	1 to 1.0015	0.9993 to 1.0014	1.0005 to 1.0024	1.0062 to 1.017
	Median ratio per marker	1.0003 to 1.0011	1.0007 to 1.0019	1 to 1.0001	1.0001 to 1.0003
	Proportion of r<1/1.1 or r>1.1	0.0005 to 0.0024	0.0007 to 0.0033	0.0004 to 0.0013	0.0005 to 0.0021
Stepwise	*Average ratio per marker (r)*	1 to 1.0001	1 to 1.0001	1 to 1.0001	0.9996 to 1.0005
	Average ratio in 17 markers	1.0003 to 1.001	1 to 1.0015	1 to 1.0017	0.9932 to 1.0082
	Median ratio per marker	0.9993 to 1	0.9987 to 1	1 to 1	0.9998 to 1
	Proportion of r<1/1.1 or r>1.1	0.0007 to 0.0023	0.0009 to 0.003	0.0005 to 0.0014	0.0006 to 0.0022
Extended Stepwise	*Average ratio per marker (r)*	1.0001 to 1.0001	1.0001 to 1.0001	1 to 1.0001	0.9997 to 1.0007
	Average ratio in 17 markers	1.0009 to 1.0016	1.0012 to 1.0023	1.0001 to 1.0021	0.9955 to 1.0114
	Median ratio per marker	0.9997 to 1.0002	0.9993 to 1.0003	1 to 1	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0.0005 to 0.0022	0.0007 to 0.003	0.0004 to 0.0013	0.0005 to 0.002

Table A12 – Summary of the ratios between the LRs obtained with the different mutation models, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Full-siblings vs Half-siblings** problem, in **trios**. In each row, the mutation model in the first column was considered in the numerator, with the remaining models being in the denominators.

Mutation model (numerator)		**Full-siblings (trios)**	**Half-siblings (trios)**
Equal	*Average ratio per marker (r)*	1.3327 to 3.7094	1.138 to $7.5x10^{8}$
	Average ratio in 17 markers	0.2784 to $1.56x10^{6}$	8.6406 to $4.87x10^{61}$
	Median ratio per marker	0.7986 to 0.9703	0.4361 to 2.2014
	Proportion of r<1/1.1 or r>1.1	0.5193 to 0.5598	0.9599 to 0.9787
Proportional	*Average ratio per marker (r)*	0.9132 to 2.1307	2.432 to $1.2x10^{9}$
	Average ratio in 17 markers	0.1557 to 412.4864	$2.2x10^{6}$ to $3.9x10^{55}$
	Median ratio per marker	0.9164 to 1.0701	1.9637 to 5.3203
	Proportion of r<1/1.1 or r>1.1	0.5193 to 0.5405	0.9276 to 0.9599
Stepwise	*Average ratio per marker (r)*	0.916 to 10.2828	1.0978 to 21.7097
	Average ratio in 17 markers	0.1799 to $3.6x10^{10}$	4.6505 to $3.1x10^{7}$
	Median ratio per marker	0.967 to 1.1792	0.4654 to 1.2066
	Proportion of r<1/1.1 or r>1.1	0.1882 to 0.5598	0.3341 to 0.9787
Extended Stepwise	*Average ratio per marker (r)*	2.1204 to 11.6465	1.0709 to 92774.6344
	Average ratio in 17 markers	6784.6 to $1.9x10^{12}$	3.0665 to $5x10^{18}$
	Median ratio per marker	1.045 to 1.4041	0.5971 to 2.8047
	Proportion of r<1/1.1 or r>1.1	0.1882 to 0.5569	0.3341 to 0.9746

Appendix 3

Summarized tables of ratios regarding the impact of considering different mutation models, for the 10 markers with fictitious allele frequencies:

Table A13 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **duos**. All ratios between all models are considered for each marker.

Marker		a	b	c	d	e
1	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	1 to 1	0.9999 to 1.0001	1 to 1	1 to 1	1 to 1
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
2	Average ratio per marker (r)	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
3	Average ratio per marker (r)	1 to 1	0.9998 to 1.0002	0.9998 to 1.0002	0.9999 to 1.0002	0.9997 to 1.0003
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9998 to 1.0002
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
4	Average ratio per marker (r)	1 to 1	0.9996 to 1.0004	0.9997 to 1.0003	0.9997 to 1.0003	0.9993 to 1.0007
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
5	Average ratio per marker (r)	1 to 1	0.9996 to 1.0004	0.9996 to 1.0004	0.9997 to 1.0003	0.9992 to 1.0008
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9995 to 1.0005
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
6	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1	1 to 1

	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
7	Average ratio per marker (r)	1 to 1	0.9999 to 1.0001	0.9999 to 1.0001	1 to 1	0.9999 to 1.0001
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
8	Average ratio per marker (r)	0.9999 to 1.0001	0.9996 to 1.0004	0.9997 to 1.0003	0.9997 to 1.0003	0.9994 to 1.0006
	Median ratio per marker	0.9997 to 1.0003	0.9997 to 1.0003	0.9997 to 1.0003	0.9997 to 1.0003	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
9	Average ratio per marker (r)	0.9999 to 1.0001	0.9995 to 1.0005	0.9996 to 1.0004	0.9996 to 1.0004	0.9991 to 1.0009
	Median ratio per marker	0.9999 to 1.0001	0.9997 to 1.0003	0.9995 to 1.0005	0.9995 to 1.0005	0.9995 to 1.0005
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
10	Average ratio per marker (r)	0.9999 to 1.0001	0.9995 to 1.0005	0.9996 to 1.0004	0.9996 to 1.0004	0.9992 to 1.0008
	Median ratio per marker	0.9999 to 1.0001	0.9997 to 1.0003	0.9996 to 1.0004	0.9995 to 1.0005	0.9995 to 1.0005
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0

Table A14 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **trios**. All ratios between all models are considered for each marker.

Marker		**a**	**b**	**c**	**d**	**e**
1	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	1 to 1	1 to 1	1 to 1	1 to 1	1 to 1
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
2	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
3	Average ratio per marker (r)	0.9999 to 1.0001	0.9997 to 1.0003	0.9998 to 1.0002	0.9999 to 1.0001	0.9995 to 1.0005
	Median ratio per marker	1 to 1	1 to 1	1 to 1	1 to 1	0.9999 to 1.0001

	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
4	Average ratio per marker (r)	0.9998 to 1.0002	0.9995 to 1.0005	0.9995 to 1.0005	0.9998 to 1.0002	0.999 to 1.0011
	Median ratio per marker	0.9998 to 1.0002	0.9999 to 1.0001	0.9998 to 1.0002	0.9998 to 1.0002	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
5	Average ratio per marker (r)	0.9998 to 1.0002	0.9994 to 1.0006	0.9995 to 1.0005	0.9998 to 1.0002	0.9988 to 1.0012
	Median ratio per marker	0.9998 to 1.0002	0.9999 to 1.0001	0.9998 to 1.0002	0.9998 to 1.0002	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
6	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	1 to 1	1 to 1	1 to 1	1 to 1	1 to 1
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
7	Average ratio per marker (r)	1 to 1	0.9999 to 1.0001	0.9999 to 1.0001	1 to 1	0.9998 to 1.0002
	Median ratio per marker	1 to 1	1 to 1	1 to 1	1 to 1	0.9998 to 1.0002
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
8	Average ratio per marker (r)	0.9997 to 1.0003	0.9995 to 1.0005	0.9996 to 1.0004	0.9997 to 1.0003	0.9992 to 1.0009
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9998 to 1.0002
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
9	Average ratio per marker (r)	0.9997 to 1.0003	0.9993 to 1.0007	0.9994 to 1.0006	0.9997 to 1.0003	0.9987 to 1.0013
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0
10	Average ratio per marker (r)	0.9997 to 1.0003	0.9994 to 1.0006	0.9994 to 1.0006	0.9997 to 1.0003	0.9987 to 1.0013
	Median ratio per marker	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9999 to 1.0001	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0	0 to 0

Table A15 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **duos**. All ratios between all models are considered for each marker.

Marker		a	b	c	d	e
1	Average ratio per marker (r)	0.6984 to 1.6777	0.995 to 386.6008	0.995 to 274.8774	0.995 to 262.7402	0.995 to 269.7246
	Median ratio per marker	0.6182 to 1.6175	0.8781 to 1.1388	0.9037 to 1.1066	0.9041 to 1.1061	0.9037 to 1.1066
	Proportion of r<1/1.1 or r>1.1	0 to 0.873	0 to 0.9254	0 to 0.8848	0 to 0.8753	0 to 0.8752
2	Average ratio per marker (r)	0.9106 to 1.7138	0.9526 to 296.3508	0.9588 to 288.0465	0.9605 to 265.7433	0.9603 to 263.5246
	Median ratio per marker	0.5259 to 1.9014	0.8375 to 1.194	0.8375 to 1.194	0.8375 to 1.194	0.8375 to 1.194
	Proportion of r<1/1.1 or r>1.1	0 to 1	0 to 1	0 to 1	0 to 1	0 to 1
3	Average ratio per marker (r)	0.8443 to 1.8916	1 to 36.5049	1 to 18.1249	1 to 13.4261	1 to 15.3036
	Median ratio per marker	0.6031 to 1.6581	0.7737 to 1.2926	0.7737 to 1.2926	0.7737 to 1.2926	0.7737 to 1.2926
	Proportion of r<1/1.1 or r>1.1	0 to 0.9921	0 to 0.9561	0 to 0.954	0 to 0.9558	0 to 0.9552
4	Average ratio per marker (r)	0.7222 to 2.1226	1 to 137.8512	1 to 81.4549	1 to 72.0581	0.9934 to 58.5032
	Median ratio per marker	0.5363 to 1.8647	0.5447 to 1.836	0.5962 to 1.6773	0.5983 to 1.6714	0.5983 to 1.6714
	Proportion of r<1/1.1 or r>1.1	0 to 1	0 to 1	0 to 1	0 to 1	0 to 1
5	Average ratio per marker (r)	0.6114 to 2.2763	1 to 171.5042	0.9942 to 108.2354	0.988 to 95.8469	0.9934 to 89.0471
	Median ratio per marker	0.3734 to 2.6778	0.5887 to 1.6987	0.593 to 1.6864	0.593 to 1.6864	0.5983 to 1.6714
	Proportion of r<1/1.1 or r>1.1	0 to 1	0 to 1	0 to 1	0 to 1	0 to 1
6	Average ratio per marker (r)	0.6992 to 23.3408	0.99 to 348.2299	0.995 to 294.2469	0.9861 to 296.0458	0.9945 to 278.6698
	Median ratio per marker	0.4591 to 2.1782	0.1667 to 5.9985	0.8302 to 1.2045	0.8302 to 1.2045	0.8302 to 1.2045
	Proportion of r<1/1.1 or r>1.1	0 to 0.9225	0 to 0.9668	0 to 0.9472	0 to 0.9426	0 to 0.943
7	Average ratio per marker (r)	0.7417 to 4.1914	1.0143 to 195.4828	1.0037 to 125.8518	1.0019 to 126.9848	0.9978 to 136.5506
	Median ratio per marker	0.5282 to 1.8931	0.4294 to 2.3289	0.662 to 1.5106	0.6963 to 1.4361	0.6963 to 1.4361
	Proportion of r<1/1.1 or r>1.1	0.694 to 1	0.7893 to 1	0.7881 to 1	0.7856 to 1	0.7838 to 1
8	Average ratio per marker (r)	0.8519 to 5.2702	0.7561 to 13402.0864	0.7442 to 4013.0628	0.7351 to 4019.0531	0.7402 to 4172.5803
	Median ratio per marker	0.4082 to 2.45	0.086 to 11.6334	0.0998 to 10.0154	0.0999 to 10.0112	0.0999 to 10.0112
	Proportion of r<1/1.1 or r>1.1	0.7685 to 0.9907	0.8759 to 0.9946	0.8842 to 0.9923	0.8932 to 0.992	0.8937 to 0.9918

9	Average ratio per marker (r)	0.606 to 4.5965	0.8049 to 71647.2043	0.8061 to 33064.9829	0.803 to 26485.1286	0.7958 to 27610.475
	Median ratio per marker	0.3413 to 2.9302	0.1 to 10.005	0.1 to 10	0.133 to 7.5178	0.1324 to 7.551
	Proportion of r<1/1.1 or r>1.1	0.6372 to 1	0.7861 to 1	0.7927 to 1	0.7858 to 1	0.7882 to 1
10	Average ratio per marker (r)	0.5361 to 3.9349	0.9145 to 106210.3928	0.9214 to 64415.2449	0.9124 to 53487.1129	0.9049 to 56569.1572
	Median ratio per marker	0.3434 to 2.912	0.2284 to 4.3784	0.2643 to 3.7835	0.2643 to 3.783	0.2643 to 3.783
	Proportion of r<1/1.1 or r>1.1	0.4615 to 1	0.6725 to 1	0.6824 to 1	0.6793 to 1	0.6846 to 1

Table A16 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **trios**. All ratios between all models are considered for each marker.

Marker		**a**	**b**	**c**	**d**	**e**
1	Average ratio per marker (r)	0.5968 to 2.1111	0.995 to 2754.6854	0.9935 to 1422.2084	0.995 to 1254.7255	0.995 to 1254.7255
	Median ratio per marker	0.5997 to 1.6675	0.3149 to 3.1761	0.3231 to 3.0955	0.3313 to 3.0184	0.3313 to 3.0184
	Proportion of r<1/1.1 or r>1.1	0 to 0.9231	0 to 0.9771	0 to 0.9738	0 to 0.9707	0 to 0.9707
2	Average ratio per marker (r)	0.7298 to 2.1578	1 to 2815.7774	1 to 1515.8152	0.9941 to 1215.2795	0.9941 to 1215.2795
	Median ratio per marker	0.5051 to 1.9797	0.3164 to 3.1603	0.3247 to 3.0802	0.3312 to 3.0189	0.3312 to 3.0189
	Proportion of r<1/1.1 or r>1.1	0 to 0.9378	0 to 0.9993	0 to 0.9996	0 to 0.9999	0 to 0.9999
3	Average ratio per marker (r)	0.6135 to 2.3413	1 to 209.6045	1 to 87.8354	1 to 74.8187	1 to 74.8187
	Median ratio per marker	0.5769 to 1.7335	0.6339 to 1.5775	0.6283 to 1.5916	0.6283 to 1.5916	0.6283 to 1.5916
	Proportion of r<1/1.1 or r>1.1	0 to 0.9437	0 to 0.9896	0 to 0.9896	0 to 0.9889	0 to 0.9889
4	Average ratio per marker (r)	0.6828 to 3.031	0.9694 to 1173.7053	0.9751 to 472.2844	0.956 to 405.5798	0.956 to 405.5798
	Median ratio per marker	0.356 to 2.809	0.2681 to 3.7303	0.3121 to 3.2043	0.3178 to 3.1468	0.3178 to 3.1468
	Proportion of r<1/1.1 or r>1.1	0 to 0.974	0 to 0.9996	0 to 0.9996	0 to 0.9999	0 to 0.9999
5	Average ratio per marker (r)	0.5031 to 3.1103	0.947 to 1115.2974	0.9454 to 525.7158	0.941 to 383.816	0.941 to 383.816
	Median ratio per marker	0.3566 to 2.8042	0.3166 to 3.1587	0.3308 to 3.0229	0.3308 to 3.0227	0.3308 to 3.0227
	Proportion of r<1/1.1 or r>1.1	0 to 0.9554	0 to 0.9998	0 to 0.9996	0 to 1	0 to 1

6	Average ratio per marker (r)	0.4101 to 56.573	0.9847 to 2796.2306	0.995 to 1509.3751	0.9922 to 1282.5698	0.9922 to 1282.5698
	Median ratio per marker	0.1469 to 7.2817	0.0017 to 573.9607	0.0167 to 59.8692	0.032 to 31.2939	0.032 to 31.2939
	Proportion of r<1/1.1 or r>1.1	0 to 0.9526	0 to 0.9935	0 to 0.9903	0 to 0.9899	0 to 0.9899
7	Average ratio per marker (r)	0.6083 to 5.6152	1.0186 to 1866.7298	1.0006 to 1011.5282	0.9987 to 753.4341	0.9987 to 753.4341
	Median ratio per marker	0.5013 to 1.9948	0.1912 to 5.2304	0.2087 to 4.7909	0.2089 to 4.7872	0.2089 to 4.7872
	Proportion of r<1/1.1 or r>1.1	0.5708 to 0.967	0.8064 to 0.9997	0.7846 to 0.9997	0.7753 to 0.9999	0.7753 to 0.9999
8	Average ratio per marker (r)	0.4631 to 5.489	0.6483 to 94829.3133	0.6493 to 23597.087	0.6407 to 23299.631	0.6407 to 23299.631
	Median ratio per marker	0.404 to 2.4751	0.0816 to 12.2515	0.0928 to 10.7735	0.0928 to 10.7735	0.0928 to 10.7735
	Proportion of r<1/1.1 or r>1.1	0.5968 to 0.957	0.8085 to 0.9998	0.8068 to 0.9998	0.8074 to 0.9999	0.8074 to 0.9999
9	Average ratio per marker (r)	0.4387 to 5.4243	0.6945 to 568532.6547	0.6955 to 224365.8518	0.6935 to 174345.5654	0.6935 to 174345.5654
	Median ratio per marker	0.3332 to 3.0019	0.0595 to 16.8111	0.0604 to 16.5658	0.0604 to 16.5634	0.0604 to 16.5634
	Proportion of r<1/1.1 or r>1.1	0.5158 to 0.9737	0.7921 to 0.9998	0.7765 to 1	0.7729 to 1	0.7729 to 1
10	Average ratio per marker (r)	0.4498 to 4.8859	0.8454 to 543352.3474	0.8491 to 254478.8679	0.8347 to 230473.3729	0.8347 to 230473.3729
	Median ratio per marker	0.3405 to 2.9369	0.1 to 9.9996	0.1002 to 9.9781	0.1099 to 9.1016	0.1099 to 9.1016
	Proportion of r<1/1.1 or r>1.1	0.3906 to 0.974	0.6775 to 0.9999	0.6449 to 0.9999	0.64 to 1	0.64 to 1

Table A17 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **duos and trios**. All ratios between all models are considered for each marker.

Marker		Full-siblings (duos)	Unrelated (duos)	Full-siblings (trios)	Unrelated (trios)
1	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	0.9998 to 1.0002	0.9991 to 1.0009	0.9998 to 1.0002	0.9985 to 1.0015
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
2	Average ratio per marker (r)	0.9994 to 1.0006	0.9991 to 1.0009	0.9997 to 1.0004	0.9994 to 1.0006
	Median ratio per marker	0.9996 to 1.0004	0.9987 to 1.0013	0.9997 to 1.0003	0.9985 to 1.0015
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
3	Average ratio per marker (r)	1 to 1	0.9996 to 1.0004	1 to 1.0001	0.9997 to 1.0003
	Median ratio per marker	0.9994 to 1.0006	0.999 to 1.001	0.9998 to 1.0002	0.9994 to 1.0006
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
4	Average ratio per marker (r)	1 to 1	0.9996 to 1.0004	1 to 1	0.9995 to 1.0006
	Median ratio per marker	0.999 to 1.001	0.999 to 1.001	0.9995 to 1.0005	0.9985 to 1.0015
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
5	Average ratio per marker (r)	1 to 1	0.9996 to 1.0004	0.9999 to 1.0001	0.9994 to 1.0007
	Median ratio per marker	0.9994 to 1.0006	0.9989 to 1.0011	0.9995 to 1.0005	0.999 to 1.001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
6	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	0.9995 to 1.0005	0.9985 to 1.0015	0.9997 to 1.0003	0.9981 to 1.0019
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
7	Average ratio per marker (r)	1 to 1	0.9999 to 1.0001	1 to 1	1 to 1.0001
	Median ratio per marker	0.9994 to 1.0006	0.9986 to 1.0014	0.9996 to 1.0004	0.9983 to 1.0017
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
8	Average ratio per marker (r)	1 to 1.0001	0.9993 to 1.0009	0.9999 to 1.0002	0.9998 to 1.0005
	Median ratio per marker	0.9978 to 1.0022	0.9958 to 1.0043	0.9994 to 1.0006	0.9962 to 1.0038
	Proportion of r<1/1.1 or r>1.1	0 to 0.0004	0 to 0.0003	0 to 0.0024	0 to 0.0058
9	Average ratio per marker (r)	1 to 1.0001	0.9994 to 1.0007	0.9999 to 1.0002	0.9995 to 1.0008
	Median ratio per marker	0.9984 to 1.0016	0.9959 to 1.0041	0.9993 to 1.0007	0.9966 to 1.0034
	Proportion of r<1/1.1 or r>1.1	0 to 0.0003	0 to 0.0004	0 to 0.0021	0 to 0.0054
10	Average ratio per marker (r)	0.9999 to 1.0001	0.9995 to 1.0007	0.9999 to 1.0002	0.9994 to 1.0008
	Median ratio per marker	0.9988 to 1.0012	0.9968 to 1.0032	0.9993 to 1.0007	0.9973 to 1.0027
	Proportion of r<1/1.1 or r>1.1	0 to 0.0004	0 to 0.0004	0 to 0.0017	0 to 0.0039

Table A18 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **trios**. All ratios between all models are considered for each marker.

Marker		Full-siblings (trios)	Unrelated (trios)
1	Average ratio per marker (r)	0.7037 to 1.6217	0.9916 to 315.3244
	Median ratio per marker	0.6164 to 1.6222	0.8776 to 1.1395
	Proportion of r<1/1.1 or r>1.1	0 to 0.6829	0 to 0.9029
2	Average ratio per marker (r)	0.7241 to 1.8188	0.9726 to 274.981
	Median ratio per marker	0.5699 to 1.7545	0.8373 to 1.1943
	Proportion of r<1/1.1 or r>1.1	0 to 0.7059	0 to 0.9731
3	Average ratio per marker (r)	0.8295 to 1.5768	1 to 17.2846
	Median ratio per marker	0.9966 to 1.0034	0.7725 to 1.2944
	Proportion of r<1/1.1 or r>1.1	0 to 0.4474	0 to 0.9731
4	Average ratio per marker (r)	0.6428 to 2.3499	0.995 to 76.8993
	Median ratio per marker	0.6109 to 1.6371	0.5389 to 1.8557
	Proportion of r<1/1.1 or r>1.1	0 to 0.7857	0 to 0.9959
5	Average ratio per marker (r)	0.9145 to 1.9893	0.9952 to 120.0442
	Median ratio per marker	0.8561 to 1.2002	0.5793 to 1.7262
	Proportion of r<1/1.1 or r>1.1	0 to 0.5652	0 to 0.9946
6	Average ratio per marker (r)	0.6835 to 15.2718	0.995 to 293.2293
	Median ratio per marker	0.6 to 1.6668	0.3442 to 2.9053
	Proportion of r<1/1.1 or r>1.1	0 to 0.7049	0 to 0.9572
7	Average ratio per marker (r)	0.9934 to 1.9937	0.9992 to 157.1275
	Median ratio per marker	0.5732 to 1.7445	0.6289 to 1.5901
	Proportion of r<1/1.1 or r>1.1	0.4722 to 0.6944	0.7823 to 0.9647
8	Average ratio per marker (r)	0.901 to 4.3084	0.7358 to 5941.8932
	Median ratio per marker	0.7492 to 1.3348	0.0996 to 10.0353
	Proportion of r<1/1.1 or r>1.1	0.5306 to 0.7959	0.8893 to 0.9941
9	Average ratio per marker (r)	0.6268 to 2.6877	0.796 to 31685.8645
	Median ratio per marker	0.6246 to 1.6011	0.1313 to 7.6158
	Proportion of r<1/1.1 or r>1.1	0.3409 to 0.7045	0.7902 to 0.9982
10	Average ratio per marker (r)	0.8346 to 2.0256	0.9051 to 64922.7633
	Median ratio per marker	0.6541 to 1.5332	0.2387 to 4.1894
	Proportion of r<1/1.1 or r>1.1	0.2692 to 0.7308	0.687 to 0.998

Table A19 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Half-siblings vs Unrelated** problem, in **duos and trios**. All ratios between all models are considered for each marker.

Marker		Half-siblings (duos)	Unrelated (duos)	Half-siblings (trios)	Unrelated (trios)
1	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	1 to 1	1 to 1	0.9999 to 1.0001	0.9998 to 1.0002
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
2	Average ratio per marker (r)	0.9997 to 1.0003	0.9996 to 1.0004	0.9997 to 1.0003	0.9996 to 1.0004
	Median ratio per marker	0.9997 to 1.0003	0.9996 to 1.0004	0.9998 to 1.0002	0.9997 to 1.0003
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
3	Average ratio per marker (r)	1 to 1	0.9999 to 1.0001	1 to 1	0.9998 to 1.0002
	Median ratio per marker	0.9997 to 1.0003	0.9995 to 1.0005	0.9997 to 1.0003	0.9995 to 1.0005
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
4	Average ratio per marker (r)	1 to 1	0.9999 to 1.0001	1 to 1	0.9998 to 1.0002
	Median ratio per marker	0.9997 to 1.0003	0.9997 to 1.0003	0.9995 to 1.0005	0.9992 to 1.0008
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
5	Average ratio per marker (r)	1 to 1	0.9999 to 1.0001	1 to 1	0.9998 to 1.0002
	Median ratio per marker	0.9997 to 1.0003	0.9997 to 1.0003	0.9995 to 1.0005	0.9994 to 1.0006
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
6	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	0.9998 to 1.0002	0.9998 to 1.0002	0.9998 to 1.0002	0.9992 to 1.0008
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
7	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	0.9999 to 1.0001
	Median ratio per marker	0.9999 to 1.0001	0.9997 to 1.0003	0.9999 to 1.0001	0.9995 to 1.0005
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
8	Average ratio per marker (r)	1 to 1	0.9998 to 1.0003	1 to 1	0.9997 to 1.0004
	Median ratio per marker	0.999 to 1.001	0.9989 to 1.0011	0.9992 to 1.0008	0.9986 to 1.0014
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0.0006	0 to 0.0011
9	Average ratio per marker (r)	1 to 1	0.9999 to 1.0002	1 to 1.0001	0.9997 to 1.0004
	Median ratio per marker	0.999 to 1.001	0.9987 to 1.0013	0.999 to 1.001	0.9987 to 1.0013
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0.0004	0 to 0.0008
10	Average ratio per marker (r)	1 to 1	0.9999 to 1.0002	1 to 1.0001	0.9997 to 1.0003
	Median ratio per marker	0.9994 to 1.0006	0.9988 to 1.0012	0.9992 to 1.0008	0.9988 to 1.0012
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0.0003	0 to 0.0006

Table A20 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Half-siblings vs Unrelated** problem, in **trios**. All ratios between all models are considered for each marker.

Marker		Half-siblings (trios)	Unrelated (trios)
1	Average ratio per marker (r)	0.9785 to 1.1345	1 to 1.1783
	Median ratio per marker	1 to 1	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0.3704	0 to 0.3571
2	Average ratio per marker (r)	0.975 to 1.2364	0.9345 to 1.2405
	Median ratio per marker	0.906 to 1.1148	0.9964 to 1.0036
	Proportion of r<1/1.1 or r>1.1	0 to 0.8	0 to 0.3889
3	Average ratio per marker (r)	0.7946 to 2.1533	0.9503 to 1.1878
	Median ratio per marker	0.9991 to 1.0009	0.9994 to 1.0006
	Proportion of r<1/1.1 or r>1.1	0 to 0.5238	0 to 0.3333
4	Average ratio per marker (r)	0.9278 to 1.1656	0.9624 to 1.1752
	Median ratio per marker	0.9996 to 1.0004	0.9959 to 1.0042
	Proportion of r<1/1.1 or r>1.1	0 to 0.3889	0 to 0.5
5	Average ratio per marker (r)	0.9591 to 1.2055	0.908 to 1.4126
	Median ratio per marker	0.8922 to 1.135	0.9976 to 1.0024
	Proportion of r<1/1.1 or r>1.1	0 to 0.6429	0 to 0.4091
6	Average ratio per marker (r)	0.8548 to 1.7877	0.8656 to 1.4276
	Median ratio per marker	0.9988 to 1.0012	0.9972 to 1.0028
	Proportion of r<1/1.1 or r>1.1	0 to 0.4783	0 to 0.3333
7	Average ratio per marker (r)	0.8861 to 1.3371	0.9533 to 1.2562
	Median ratio per marker	0.9928 to 1.0073	0.9991 to 1.0009
	Proportion of r<1/1.1 or r>1.1	0.1429 to 0.5238	0.2308 to 0.4615
8	Average ratio per marker (r)	0.9295 to 1.4125	0.9898 to 1.0375
	Median ratio per marker	0.9984 to 1.0016	0.998 to 1.002
	Proportion of r<1/1.1 or r>1.1	0.0952 to 0.5238	0 to 0.1818
9	Average ratio per marker (r)	0.9455 to 1.2525	0.9503 to 1.349
	Median ratio per marker	0.7723 to 1.2949	0.999 to 1.001
	Proportion of r<1/1.1 or r>1.1	0.1364 to 0.6364	0.1333 to 0.4667
10	Average ratio per marker (r)	0.8405 to 1.2643	0.9019 to 2.0958
	Median ratio per marker	0.9956 to 1.0044	0.9974 to 1.0026
	Proportion of r<1/1.1 or r>1.1	0.1852 to 0.4815	0.1071 to 0.3214

Table A21 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Full-siblings vs Half-siblings** problem, in **duos and trios**. All ratios between all models are considered for each marker.

Marker		Full-siblings (duos)	Half-siblings (duos)	Full-siblings (trios)	Half-siblings (trios)
1	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	0.9996 to 1.0004	0.9988 to 1.0012	1 to 1	1 to 1
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
2	Average ratio per marker (r)	0.9997 to 1.0004	0.9995 to 1.0005	0.9999 to 1.0001	0.9998 to 1.0002
	Median ratio per marker	0.9996 to 1.0004	0.9989 to 1.0011	0.9999 to 1.0001	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
3	Average ratio per marker (r)	1 to 1	0.9999 to 1.0001	1 to 1	0.9996 to 1.0004
	Median ratio per marker	0.9998 to 1.0002	0.9995 to 1.0005	0.9999 to 1.0001	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
4	Average ratio per marker (r)	1 to 1	0.9998 to 1.0002	1 to 1.0001	0.9992 to 1.0009
	Median ratio per marker	0.9995 to 1.0005	0.9992 to 1.0008	0.9999 to 1.0001	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
5	Average ratio per marker (r)	1 to 1	0.9998 to 1.0002	1 to 1.0001	0.999 to 1.001
	Median ratio per marker	0.9995 to 1.0005	0.9991 to 1.0009	0.9999 to 1.0001	0.9996 to 1.0004
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
6	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1
	Median ratio per marker	0.999 to 1.001	0.9984 to 1.0016	0.9999 to 1.0001	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
7	Average ratio per marker (r)	1 to 1	1 to 1	1 to 1	1 to 1.0001
	Median ratio per marker	0.9995 to 1.0005	0.9987 to 1.0013	1 to 1	0.9999 to 1.0001
	Proportion of r<1/1.1 or r>1.1	0 to 0	0 to 0	0 to 0	0 to 0
8	Average ratio per marker (r)	0.9999 to 1.0001	0.9997 to 1.0004	0.9999 to 1.0001	0.9993 to 1.0008
	Median ratio per marker	0.9986 to 1.0014	0.9973 to 1.0028	0.9999 to 1.0001	0.9997 to 1.0003
	Proportion of r<1/1.1 or r>1.1	0 to 0.0002	0 to 0.0002	0 to 0.0011	0 to 0.0047
9	Average ratio per marker (r)	1 to 1.0001	0.9998 to 1.0003	0.9999 to 1.0001	0.999 to 1.0011
	Median ratio per marker	0.9992 to 1.0008	0.9975 to 1.0025	0.9999 to 1.0001	0.9995 to 1.0005
	Proportion of r<1/1.1 or r>1.1	0 to 0.0001	0 to 0.0001	0 to 0.0009	0 to 0.0042
10	Average ratio per marker (r)	1 to 1.0001	0.9998 to 1.0002	0.9999 to 1.0001	0.9991 to 1.0011
	Median ratio per marker	0.9994 to 1.0006	0.9978 to 1.0022	0.9999 to 1.0001	0.9995 to 1.0005
	Proportion of r<1/1.1 or r>1.1	0 to 0.0001	0 to 0.0002	0 to 0.0007	0 to 0.003

Table A22 – Summary of the ratios between the LRs obtained with the different mutation models, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Full-siblings vs Half-siblings** problem, in **trios**. All ratios between all models are considered for each marker.

Marker		Full-siblings (trios)	Half-siblings (trios)
1	Average ratio per marker (r)	0.7664 to 1.5078	0.995 to 327.1711
	Median ratio per marker	0.9264 to 1.0795	0.8413 to 1.1887
	Proportion of r<1/1.1 or r>1.1	0 to 0.4878	0 to 0.9519
2	Average ratio per marker (r)	0.7923 to 1.6907	0.9977 to 323.3316
	Median ratio per marker	0.9342 to 1.0705	0.6285 to 1.5912
	Proportion of r<1/1.1 or r>1.1	0 to 0.549	0 to 0.9603
3	Average ratio per marker (r)	0.8843 to 1.4954	1 to 18.08
	Median ratio per marker	0.9988 to 1.0012	0.6944 to 1.4401
	Proportion of r<1/1.1 or r>1.1	0 to 0.3158	0 to 0.9866
4	Average ratio per marker (r)	0.7039 to 2.2371	0.9806 to 87.5962
	Median ratio per marker	0.6995 to 1.4336	0.438 to 2.283
	Proportion of r<1/1.1 or r>1.1	0 to 0.6786	0 to 0.9963
5	Average ratio per marker (r)	0.9584 to 1.8929	0.9698 to 122.2923
	Median ratio per marker	0.9604 to 1.0429	0.4376 to 2.2853
	Proportion of r<1/1.1 or r>1.1	0 to 0.5217	0 to 0.9936
6	Average ratio per marker (r)	0.7237 to 14.8718	0.994 to 293.5305
	Median ratio per marker	0.9266 to 1.0792	0.3143 to 3.1814
	Proportion of r<1/1.1 or r>1.1	0 to 0.5902	0 to 0.9793
7	Average ratio per marker (r)	1.0033 to 1.9659	0.9996 to 178.0701
	Median ratio per marker	0.8919 to 1.1239	0.3721 to 2.6878
	Proportion of r<1/1.1 or r>1.1	0.4444 to 0.6111	0.7789 to 0.977
8	Average ratio per marker (r)	0.8745 to 4.2309	0.7033 to 5357.1217
	Median ratio per marker	0.9185 to 1.0887	0.0999 to 10.0087
	Proportion of r<1/1.1 or r>1.1	0.4898 to 0.7143	0.8681 to 0.995
9	Average ratio per marker (r)	0.7279 to 2.6877	0.756 to 42580.1983
	Median ratio per marker	0.8975 to 1.1143	0.1092 to 9.1535
	Proportion of r<1/1.1 or r>1.1	0.2727 to 0.5682	0.7891 to 0.9973
10	Average ratio per marker (r)	0.8173 to 1.9132	0.8798 to 77416.5972
	Median ratio per marker	0.9559 to 1.0462	0.2137 to 4.6787
	Proportion of r<1/1.1 or r>1.1	0.2308 to 0.5	0.6749 to 0.9961

Appendix 4

Summarized tables of ratios regarding the impact of increasing the integer-length mutation rate (5 times) in the Extended Stepwise model, for the 17 real autosomal STRs:

Table A23 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **duos and trios**.

	Parent-Child (duos)	Unrelated (duos)	Parent-Child (trios)	Unrelated (trios)
Average ratio per marker (r)	0.9978	1.0009	0.9959	0.9999
Average ratio in 17 markers	0.9636	1.0146	0.9321	0.9980
Median ratio per marker (r)	0.9971	0.9975	0.9960	0.9965
Proportion of r<1/1.1 or r>1.1	0.0007	0.0138	0.0007	0.0185

Table A24 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **trios**.

	a	b	c	d	e
Average ratio per marker (r)	0.9959	0.9975	0.9972	0.9972	0.9999
Average ratio in 17 markers	0.9321	0.9577	0.9542	0.9539	0.9980
Median ratio per marker (r)	0.9960	0.9960	0.9961	0.9961	0.9965
Proportion of r<1/1.1 or r>1.1	0.0007	0.0077	0.0065	0.0064	0.0185

Table A25 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **duos and trios**.

	Parent-Child (duos)	Unrelated (duos)	Parent-Child (trios)	Unrelated (trios)
Average ratio per marker (r)	4.9992	4.8979	4.0478	4.8730
Median ratio per marker (r)	5.0000	4.9996	4.4982	4.9986
Proportion of r<1/1.1 or r>1.1	1.0000	0.9751	0.8356	0.9507

Table A26 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **trios**.

	a	b	c	d	e
Average ratio per marker (r)	4.0478	4.8851	4.8733	4.8740	4.8730
Median ratio per marker (r)	4.4982	4.9983	4.9985	4.9986	4.9986
Proportion of r<1/1.1 or r>1.1	0.8356	0.9396	0.9490	0.9510	0.9507

Table A27 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **duos and trios**.

	Full-siblings (duos)	Unrelated (duos)	Full-siblings (trios)	Unrelated (trios)
Average ratio per marker (r)	0.9999	1.0111	0.9977	1.0107
Average ratio in 17 markers	0.9984	1.2066	0.9620	1.1991
Median ratio per marker (r)	0.9938	1.0048	0.9905	1.0006
Proportion of r<1/1.1 or r>1.1	0.0058	0.0117	0.0057	0.0333

Table A28 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **trios**.

	Full-siblings (trios)	Unrelated (trios)
Average ratio per marker (r)	3.0410	4.9235
Average ratio in 17 markers	$1.37X10^{8}$	$5.75X10^{11}$
Median ratio per marker (r)	3.3148	5.0007
Proportion of r<1/1.1 or r>1.1	0.5116	0.9751

Table A29 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Half-siblings vs Unrelated** problem, in **duos and trios**.

	Half-siblings (duos)	Unrelated (duos)	Half-siblings (trios)	Unrelated (trios)
Average ratio per marker (r)	1.0000	1.0035	1.0000	1.0056
Average ratio in 17 markers	1.0006	1.0604	0.9997	1.0992
Median ratio per marker (r)	0.9968	0.9994	0.9956	0.9999
Proportion of r<1/1.1 or r>1.1	0.0015	0.0024	0.0029	0.0050

Table A30 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **trios**.

	Half-siblings (trios)	Unrelated (trios)
Average ratio per marker (r)	0.9998	1.0083
Average ratio in 17 markers	0.9970	1.1499
Median ratio per marker (r)	0.9967	1.0029
Proportion of r<1/1.1 or r>1.1	0.0059	0.0057

Table A31 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **no incompatibilities**, of the **Full-siblings vs Half-siblings** problem, in **duos and trios**.

	Full-siblings (duos)	Half-siblings (duos)	Full-siblings (trios)	Half-siblings (trios)
Average ratio per marker (r)	1.0020	1.0058	0.9973	1.0069
Average ratio in 17 markers	1.0350	1.1026	0.9556	1.1239
Median ratio per marker (r)	0.9980	1.0018	0.9960	0.9975
Proportion of r<1/1.1 or r>1.1	0.0034	0.0044	0.0033	0.0285

Table A32 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 17 real Au-STRs considered and for cases with **only incompatibilities**, of the **Full-siblings vs Half-siblings** problem, in **trios**.

	Full-siblings (trios)	Half-siblings (trios)
Average ratio per marker (r)	3.0022	4.8988
Average ratio in 17 markers	$1.05x10^{8}$	$5.28X10^{11}$
Median ratio per marker (r)	3.2675	4.9990
Proportion of r<1/1.1 or r>1.1	0.5116	0.9747

Appendix 5

Summarized tables of ratios regarding the impact of increasing the integer-length mutation rate (5 times) in the Extended Stepwise model, for the 10 markers with fictitious allele frequencies:

Table A33 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **duos and trios**

Marker		Parent-Child (duos)	Unrelated (duos)	Parent-Child (trios)	Unrelated (trios)
1	Average ratio per marker (r)	0.9974	0.9982	0.9960	0.9972
	Median ratio per marker	0.9978	0.9978	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0000
2	Average ratio per marker (r)	0.9975	0.9983	0.9959	0.9971
	Median ratio per marker	0.9966	0.9978	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0002	0.0014	0.0002	0.0021
3	Average ratio per marker (r)	0.9978	1.0007	0.9961	1.0001
	Median ratio per marker	0.9978	0.9979	0.9961	0.9964
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0000
4	Average ratio per marker (r)	0.9978	0.9995	0.9955	0.9975
	Median ratio per marker	0.9962	0.9968	0.9960	0.9962
	Proportion of r<1/1.1 or r>1.1	0.0006	0.0033	0.0006	0.0044
5	Average ratio per marker (r)	0.9978	0.9992	0.9954	0.9971
	Median ratio per marker	0.9964	0.9968	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0032	0.0004	0.0043
6	Average ratio per marker (r)	0.9974	0.9982	0.9960	0.9972
	Median ratio per marker	0.9962	0.9964	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0003	0.0028	0.0003	0.0042
7	Average ratio per marker (r)	0.9976	0.9991	0.9958	0.9977
	Median ratio per marker	0.9964	0.9966	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0051	0.0004	0.0074
8	Average ratio per marker (r)	0.9978	1.0007	0.9961	1.0001
	Median ratio per marker	0.9978	0.9978	0.9960	0.9964
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0000
9	Average ratio per marker (r)	0.9977	0.9995	0.9954	0.9974
	Median ratio per marker	0.9962	0.9964	0.9960	0.9962
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0032	0.0004	0.0041
10	Average ratio per marker (r)	0.9977	0.9992	0.9954	0.9970
	Median ratio per marker	0.9963	0.9969	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0032	0.0004	0.0041

Table A34 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **trios**.

Marker		a	b	c	d	e
1	Average ratio per marker (r)	0.9960	0.9964	0.9963	0.9962	0.9972
	Median ratio per marker	0.9960	0.9960	0.9960	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0000	0.0000
2	Average ratio per marker (r)	0.9959	0.9963	0.9961	0.9961	0.9971
	Median ratio per marker	0.9960	0.9960	0.9960	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0002	0.0014	0.0006	0.0006	0.0021
3	Average ratio per marker (r)	0.9961	0.9977	0.9973	0.9973	1.0001
	Median ratio per marker	0.9961	0.9960	0.9961	0.9961	0.9964
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0000	0.0000
4	Average ratio per marker (r)	0.9955	0.9962	0.9961	0.9961	0.9975
	Median ratio per marker	0.9960	0.9960	0.9960	0.9961	0.9962
	Proportion of r<1/1.1 or r>1.1	0.0006	0.0020	0.0018	0.0018	0.0044
5	Average ratio per marker (r)	0.9954	0.9960	0.9959	0.9959	0.9971
	Median ratio per marker	0.9960	0.9960	0.9960	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0022	0.0018	0.0016	0.0043
6	Average ratio per marker (r)	0.9960	0.9964	0.9962	0.9962	0.9972
	Median ratio per marker	0.9960	0.9960	0.9960	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0003	0.0024	0.0015	0.0010	0.0042
7	Average ratio per marker (r)	0.9958	0.9965	0.9963	0.9963	0.9977
	Median ratio per marker	0.9960	0.9960	0.9960	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0025	0.0018	0.0021	0.0074
8	Average ratio per marker (r)	0.9961	0.9975	0.9973	0.9972	1.0001
	Median ratio per marker	0.9960	0.9960	0.9961	0.9961	0.9964
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0000	0.0000
9	Average ratio per marker (r)	0.9954	0.9961	0.9960	0.9960	0.9974
	Median ratio per marker	0.9960	0.9960	0.9960	0.9960	0.9962
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0021	0.0015	0.0014	0.0041
10	Average ratio per marker (r)	0.9954	0.9959	0.9959	0.9959	0.9970
	Median ratio per marker	0.9960	0.9960	0.9960	0.9960	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0021	0.0017	0.0016	0.0041

Table A35 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **duos and trios**.

Marker		Parent-Child (duos)	Unrelated (duos)	Parent-Child (trios)	Unrelated (trios)
1	Average ratio per marker (r)	5.0000	5.0000	4.4423	5.1536
	Median ratio per marker	5.0000	5.0000	4.9990	5.0000
	Proportion of r<1/1.1 or r>1.1	1.0000	1.0000	0.8615	0.9999
2	Average ratio per marker (r)	5.0000	5.0000	4.3746	5.1552
	Median ratio per marker	5.0000	5.0000	4.9992	5.0000
	Proportion of r<1/1.1 or r>1.1	1.0000	1.0000	0.8446	0.9999
3	Average ratio per marker (r)	5.0000	5.0000	4.4685	5.0329
	Median ratio per marker	5.0000	5.0000	4.9979	5.0000
	Proportion of r<1/1.1 or r>1.1	1.0000	1.0000	0.8685	0.9998
4	Average ratio per marker (r)	5.0000	5.0000	4.4413	5.0542
	Median ratio per marker	5.0000	5.0000	4.9909	5.0000
	Proportion of r<1/1.1 or r>1.1	1.0000	1.0000	0.8646	0.9998
5	Average ratio per marker (r)	5.0000	5.0000	4.5924	5.0758
	Median ratio per marker	5.0000	5.0000	4.9959	5.0000
	Proportion of r<1/1.1 or r>1.1	1.0000	1.0000	0.9018	0.9998
6	Average ratio per marker (r)	4.9976	3.6822	4.4904	3.3317
	Median ratio per marker	4.9986	4.9951	4.9986	4.9584
	Proportion of r<1/1.1 or r>1.1	1.0000	0.6735	0.8737	0.5409
7	Average ratio per marker (r)	4.9978	4.5695	4.5583	4.2325
	Median ratio per marker	4.9990	4.9972	4.9968	4.9926
	Proportion of r<1/1.1 or r>1.1	1.0000	0.9078	0.8915	0.8078
8	Average ratio per marker (r)	4.9936	4.9390	4.4782	4.8315
	Median ratio per marker	5.0000	5.0000	4.9984	4.9998
	Proportion of r<1/1.1 or r>1.1	1.0000	0.9953	0.8710	0.9541
9	Average ratio per marker (r)	4.9967	4.8973	4.5183	4.8233
	Median ratio per marker	5.0000	5.0000	4.9902	4.9999
	Proportion of r<1/1.1 or r>1.1	1.0000	0.9928	0.8842	0.9503
10	Average ratio per marker (r)	4.9994	4.8610	4.3604	4.8359
	Median ratio per marker	5.0000	5.0000	4.9909	4.9999
	Proportion of r<1/1.1 or r>1.1	1.0000	0.9909	0.8438	0.9517

Table A36 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Parent-Child vs Unrelated** problem, in **trios**.

Marker		a	b	c	d	e
1	Average ratio per marker (r)	4.4423	5.2678	5.1771	5.1570	5.1536
	Median ratio per marker	4.9990	5.0000	5.0000	5.0000	5.0000
	Proportion of r<1/1.1 or r>1.1	0.8615	0.9993	0.9996	0.9996	0.9999
2	Average ratio per marker (r)	4.3746	5.2671	5.1824	5.1516	5.1552
	Median ratio per marker	4.9992	5.0000	5.0000	5.0000	5.0000
	Proportion of r<1/1.1 or r>1.1	0.8446	0.9991	0.9994	0.9994	0.9999
3	Average ratio per marker (r)	4.4685	5.0702	5.0366	5.0279	5.0329
	Median ratio per marker	4.9979	5.0000	5.0000	5.0000	5.0000
	Proportion of r<1/1.1 or r>1.1	0.8685	0.9994	0.9995	0.9993	0.9998
4	Average ratio per marker (r)	4.4413	5.1114	5.0552	5.0454	5.0542
	Median ratio per marker	4.9909	5.0000	5.0000	5.0000	5.0000
	Proportion of r<1/1.1 or r>1.1	0.8646	0.9993	0.9995	0.9993	0.9998
5	Average ratio per marker (r)	4.5924	5.1707	5.0912	5.0801	5.0758
	Median ratio per marker	4.9959	5.0000	5.0000	5.0000	5.0000
	Proportion of r<1/1.1 or r>1.1	0.9018	0.9994	0.9994	0.9995	0.9998
6	Average ratio per marker (r)	4.4904	3.1290	3.2860	3.3583	3.3317
	Median ratio per marker	4.9986	1.0060	4.9273	4.9712	4.9584
	Proportion of r<1/1.1 or r>1.1	0.8737	0.4815	0.5296	0.5475	0.5409
7	Average ratio per marker (r)	4.5583	4.0625	4.1961	4.2369	4.2325
	Median ratio per marker	4.9968	4.9914	4.9923	4.9926	4.9926
	Proportion of r<1/1.1 or r>1.1	0.8915	0.7537	0.7960	0.8071	0.8078
8	Average ratio per marker (r)	4.4782	4.8148	4.8271	4.8333	4.8315
	Median ratio per marker	4.9984	4.9997	4.9997	4.9998	4.9998
	Proportion of r<1/1.1 or r>1.1	0.8710	0.9406	0.9505	0.9538	0.9541
9	Average ratio per marker (r)	4.5183	4.8361	4.8269	4.8247	4.8233
	Median ratio per marker	4.9902	4.9998	4.9999	4.9999	4.9999
	Proportion of r<1/1.1 or r>1.1	0.8842	0.9398	0.9499	0.9513	0.9503
10	Average ratio per marker (r)	4.3604	4.8641	4.8386	4.8354	4.8359
	Median ratio per marker	4.9909	4.9999	4.9999	4.9999	4.9999
	Proportion of r<1/1.1 or r>1.1	0.8438	0.9381	0.9495	0.9500	0.9517

Table A37 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **duos and trios**.

Marker		Full-siblings (duos)	Unrelated (duos)	Full-siblings (trios)	Unrelated (trios)
1	Average ratio per marker (r)	1.0001	1.0114	0.9975	1.0065
	Median ratio per marker	0.9955	1.0051	0.9908	0.9996
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0001	0.0029
2	Average ratio per marker (r)	1.0023	1.0154	0.9987	1.0090
	Median ratio per marker	0.9965	1.0095	0.9909	1.0013
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0007	0.0043
3	Average ratio per marker (r)	1.0002	1.0034	0.9979	1.0056
	Median ratio per marker	0.9972	1.0005	0.9910	1.0023
	Proportion of r<1/1.1 or r>1.1	0.0055	0.0000	0.0043	0.0010
4	Average ratio per marker (r)	1.0000	1.0037	0.9978	1.0063
	Median ratio per marker	0.9890	1.0004	0.9897	0.9994
	Proportion of r<1/1.1 or r>1.1	0.0002	0.0000	0.0026	0.0002
5	Average ratio per marker (r)	1.0001	1.0037	0.9977	1.0064
	Median ratio per marker	0.9899	1.0006	0.9900	1.0004
	Proportion of r<1/1.1 or r>1.1	0.0004	0.0000	0.0020	0.0003
6	Average ratio per marker (r)	1.0001	1.0038	0.9975	1.0059
	Median ratio per marker	0.9944	1.0000	0.9908	1.0000
	Proportion of r<1/1.1 or r>1.1	0.0006	0.0000	0.0004	0.0000
7	Average ratio per marker (r)	1.0001	1.0037	0.9977	1.0060
	Median ratio per marker	0.9933	0.9997	0.9906	1.0001
	Proportion of r<1/1.1 or r>1.1	0.0001	0.0000	0.0016	0.0003
8	Average ratio per marker (r)	1.0001	1.0034	0.9978	1.0056
	Median ratio per marker	0.9969	1.0001	0.9909	1.0021
	Proportion of r<1/1.1 or r>1.1	0.0062	0.0015	0.0037	0.0027
9	Average ratio per marker (r)	1.0000	1.0039	0.9978	1.0064
	Median ratio per marker	0.9884	1.0000	0.9895	0.9990
	Proportion of r<1/1.1 or r>1.1	0.0011	0.0012	0.0030	0.0012
10	Average ratio per marker (r)	1.0002	1.0039	0.9978	1.0065
	Median ratio per marker	0.9892	1.0010	0.9897	0.9999
	Proportion of r<1/1.1 or r>1.1	0.0014	0.0011	0.0029	0.0011

Table A38 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Full-siblings vs Unrelated** problem, in **trios**.

Marker		Full-siblings (trios)	Unrelated (trios)
1	Average ratio per marker (r)	3.0380	5.0284
	Median ratio per marker	4.9586	5.0090
	Proportion of r<1/1.1 or r>1.1	0.5122	0.9999
2	Average ratio per marker (r)	3.1993	5.0375
	Median ratio per marker	4.9601	5.0116
	Proportion of r<1/1.1 or r>1.1	0.5490	0.9998
3	Average ratio per marker (r)	2.0457	1.0042
	Median ratio per marker	1.0061	1.0022
	Proportion of r<1/1.1 or r>1.1	0.2632	0.0000
4	Average ratio per marker (r)	3.3509	1.0024
	Median ratio per marker	4.9381	0.9972
	Proportion of r<1/1.1 or r>1.1	0.5893	0.0000
5	Average ratio per marker (r)	2.5642	1.0026
	Median ratio per marker	1.0077	0.9986
	Proportion of r<1/1.1 or r>1.1	0.3913	0.0000
6	Average ratio per marker (r)	3.1621	1.0064
	Median ratio per marker	4.9541	1.0011
	Proportion of r<1/1.1 or r>1.1	0.5410	0.0000
7	Average ratio per marker (r)	3.2094	1.0035
	Median ratio per marker	4.9474	0.9991
	Proportion of r<1/1.1 or r>1.1	0.5556	0.0000
8	Average ratio per marker (r)	3.5366	0.9988
	Median ratio per marker	4.9640	1.0002
	Proportion of r<1/1.1 or r>1.1	0.6327	0.0000
9	Average ratio per marker (r)	2.3694	1.0043
	Median ratio per marker	0.9961	0.9995
	Proportion of r<1/1.1 or r>1.1	0.3409	0.0000
10	Average ratio per marker (r)	2.5335	1.0086
	Median ratio per marker	1.0060	1.0014
	Proportion of r<1/1.1 or r>1.1	0.3846	0.0000

Table A39 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Half-siblings vs Unrelated** problem, in **duos and trios**.

Marker		Half-siblings (duos)	Unrelated (duos)	Half-siblings (trios)	Unrelated (trios)
1	Average ratio per marker (r)	1.0001	1.0038	1.0001	1.0059
	Median ratio per marker	0.9976	1.0007	0.9964	1.0017
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0000
2	Average ratio per marker (r)	1.0011	1.0054	1.0011	1.0078
	Median ratio per marker	0.9980	1.0018	0.9961	1.0031
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0001
3	Average ratio per marker (r)	1.0001	1.0034	1.0001	1.0056
	Median ratio per marker	0.9977	1.0005	0.9964	1.0023
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0006	0.0010
4	Average ratio per marker (r)	1.0001	1.0037	1.0001	1.0063
	Median ratio per marker	0.9965	1.0004	0.9943	0.9994
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0001	0.0002
5	Average ratio per marker (r)	1.0001	1.0037	1.0001	1.0064
	Median ratio per marker	0.9969	1.0006	0.9944	1.0004
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0002	0.0003
6	Average ratio per marker (r)	1.0000	1.0038	1.0000	1.0059
	Median ratio per marker	0.9982	1.0000	0.9951	1.0000
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0000	0.0000
7	Average ratio per marker (r)	1.0001	1.0037	1.0000	1.0060
	Median ratio per marker	0.9976	0.9997	0.9950	1.0001
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000	0.0001	0.0003
8	Average ratio per marker (r)	1.0001	1.0034	1.0001	1.0056
	Median ratio per marker	0.9977	1.0001	0.9963	1.0021
	Proportion of r<1/1.1 or r>1.1	0.0007	0.0015	0.0014	0.0027
9	Average ratio per marker (r)	1.0000	1.0039	1.0000	1.0064
	Median ratio per marker	0.9961	1.0000	0.9941	0.9990
	Proportion of r<1/1.1 or r>1.1	0.0006	0.0012	0.0007	0.0012
10	Average ratio per marker (r)	1.0001	1.0039	1.0000	1.0065
	Median ratio per marker	0.9965	1.0010	0.9943	0.9999
	Proportion of r<1/1.1 or r>1.1	0.0006	0.0011	0.0006	0.0011

Table A40 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **only incompatibilities**, of the **Half-siblings vs Unrelated** problem, in **trios**.

Marker		Half-siblings (trios)	Unrelated (trios)
1	Average ratio per marker (r)	1.0000	1.0051
	Median ratio per marker	0.9955	1.0023
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
2	Average ratio per marker (r)	0.9985	1.0101
	Median ratio per marker	0.9962	1.0065
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
3	Average ratio per marker (r)	0.9976	1.0042
	Median ratio per marker	0.9958	1.0022
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
4	Average ratio per marker (r)	1.0012	1.0024
	Median ratio per marker	0.9982	0.9972
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
5	Average ratio per marker (r)	1.0009	1.0026
	Median ratio per marker	0.9948	0.9986
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
6	Average ratio per marker (r)	0.9971	1.0064
	Median ratio per marker	0.9939	1.0011
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
7	Average ratio per marker (r)	1.0012	1.0035
	Median ratio per marker	0.9968	0.9991
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
8	Average ratio per marker (r)	1.0010	0.9988
	Median ratio per marker	0.9970	1.0002
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
9	Average ratio per marker (r)	0.9981	1.0043
	Median ratio per marker	0.9942	0.9995
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000
10	Average ratio per marker (r)	1.0010	1.0086
	Median ratio per marker	0.9956	1.0014
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0000

Table A41 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Full-siblings vs Half-siblings** problem, in **duos and trios**. Only individuals simulated assuming full-sibship could be analyzed.

Marker		Full-siblings (duos)	Full-siblings (trios)
1	Average ratio per marker (r)	1.0024	0.9968
	Median ratio per marker	0.9995	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0001
2	Average ratio per marker (r)	1.0040	0.9970
	Median ratio per marker	1.0006	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0007
3	Average ratio per marker (r)	1.0022	0.9973
	Median ratio per marker	1.0004	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0020	0.0018
4	Average ratio per marker (r)	1.0023	0.9973
	Median ratio per marker	0.9952	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0020
5	Average ratio per marker (r)	1.0024	0.9973
	Median ratio per marker	0.9951	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0013
6	Average ratio per marker (r)	1.0024	0.9969
	Median ratio per marker	0.9984	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0003
7	Average ratio per marker (r)	1.0024	0.9971
	Median ratio per marker	0.9977	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0000	0.0010
8	Average ratio per marker (r)	1.0022	0.9973
	Median ratio per marker	1.0004	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0041	0.0026
9	Average ratio per marker (r)	1.0024	0.9973
	Median ratio per marker	0.9951	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0006	0.0027
10	Average ratio per marker (r)	1.0025	0.9974
	Median ratio per marker	0.9951	0.9960
	Proportion of r<1/1.1 or r>1.1	0.0007	0.0018

Table A42 – Summary of the ratios between the LRs obtained with the different mutation rates (5:1) specified in the Extended Stepwise model, for the 10 fictitious markers considered and for cases with **no incompatibilities**, of the **Full-siblings vs Half-siblings** problem, in **trios**. Only individuals simulated assuming full-sibship could be analyzed.

Marker		Full-siblings (trios)
1	Average ratio per marker (r)	3.0418
	Median ratio per marker	4.9328
	Proportion of r<1/1.1 or r>1.1	0.5122
2	Average ratio per marker (r)	3.1930
	Median ratio per marker	4.9779
	Proportion of r<1/1.1 or r>1.1	0.5490
3	Average ratio per marker (r)	2.0492
	Median ratio per marker	0.9970
	Proportion of r<1/1.1 or r>1.1	0.2632
4	Average ratio per marker (r)	3.3531
	Median ratio per marker	4.9719
	Proportion of r<1/1.1 or r>1.1	0.5893
5	Average ratio per marker (r)	2.5674
	Median ratio per marker	0.9978
	Proportion of r<1/1.1 or r>1.1	0.3913
6	Average ratio per marker (r)	3.1609
	Median ratio per marker	4.9636
	Proportion of r<1/1.1 or r>1.1	0.5410
7	Average ratio per marker (r)	3.2214
	Median ratio per marker	4.9805
	Proportion of r<1/1.1 or r>1.1	0.5556
8	Average ratio per marker (r)	3.5248
	Median ratio per marker	4.9855
	Proportion of r<1/1.1 or r>1.1	0.6327
9	Average ratio per marker (r)	2.3558
	Median ratio per marker	0.9961
	Proportion of r<1/1.1 or r>1.1	0.3409
10	Average ratio per marker (r)	2.5303
	Median ratio per marker	0.9977
	Proportion of r<1/1.1 or r>1.1	0.3846

Appendix 6

Conference proceedings resulting from the poster presentation at the 27th Conference of the International Society of Forensic Genetics.

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The influence of the different mutation models in kinship evaluation

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ABSTRACT

Different mutation models have been developed considering the genotypic observations of parent(s)/offspring duos or trios, even though, for autosomal transmission, only Mendelian incompatibilities, not mutations, are able to be identified. The most commonly considered mutation models are the so-called "Equal", "Proportional", "Stepwise" and "Extended Stepwise", all implemented in the software Familias.

In this work we simulated 100,000 profiles (duos and trios) of parent-child, full-siblings, and half-siblings, assuming a specific database for 17 autosomal STRs and probabilities of incompatibility inferred from the American Association of Blood Banks (AABB) report, 2008. Using the R version of the software Familias, we calculated the likelihood ratios where the probability of the genotypic configuration of the individuals assuming each of the pedigrees was compared with the probability of the same observations assuming unrelatedness. In the case of full-siblings, the comparison assuming half-sibship as the alternative pedigree was also considered. The results show that for profiles generated assuming the above mentioned pedigrees, except for unrelated, the use of different mutation models with parameters inferred from the proportion of observed mendelian incompatibilities does not result in major differences, which also indicates that the consideration of hidden mutations does not have a major influence in the final result.

Future work should be developed to measure the impact for cases where a close relative of the father, such as a brother, is analyzed as the putative father in a standard paternity test.

1. Introduction

Mendelian incompatibilities in autosomal loci might be observed due to germinal mutations or silent alleles. Even though only incompatibilities, not mutations, can be identified for autosomal transmissions, different parameterized mutation models have been developed, namely to conciliate the genotypic profiles of the individuals with the hypothesis under assumption in kinship investigations [1,2]. The most commonly considered are the "Equal", "Proportional to Frequency", "Stepwise" and "Extended Stepwise" models, which are all implemented in the software Familias [3]. In this work, we analyze the impact that the use of different mutation models has on the kinship indices, considering pedigrees simulated under the assumption of the main hypothesis of kinship.

2. Material and methods

Resorting to the R programming language, we generated 100,000 pedigrees of each considered kinships: parent-child, full- and half-siblings, for both duos and trios (undoubted mother available for testing), assuming a set of 17 independent autosomal STRs (AmpF/STR Identifiler and Powerplex 16 System) and a database from the North of Portugal [4]. The occurrence of silent alleles was taken into account, with frequency equal to 5×10^{-3}. Incompatibility rates per marker, presented in the AABB Annual Report Summary for Testing (2008) [5], were considered. Likelihood ratios (LRs) were obtained using the R version of Familias, where the probability of the genotypic observations assuming each of the pedigrees was compared with the probability of the same observations assuming unrelatedness, considering each of the different mutation models and also the absence of mutation ("Null"

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mutation model). In the case of full-siblings, the comparison assuming half-sibship as the alternative pedigree was also considered. The LR results obtained for each pedigree and mutation model were then compared between them through simple ratios. This allowed for an insight on the impact of (a.) using different mutation models, and (b.) considering the occurrence of the so-called hidden mutations, which are those that do not lead to Mendelian incompatibilities.

3. Results and discussion

The results of the ratios between each of the models and all others are summarized in Table 1 below.

Considering the complete set of 17 independent STRs, the average ratios observed for all kinship problems revealed little impact on the (final) LR results depending on the mutation model considered, when pedigrees simulated under the assumption of the main kinship hypothesis were considered. For example, when pedigrees simulated as parent-child (undoubted mother available for testing or not) were considered the average ratio between the LR obtained considering the "Equal" model ("Equal" row, "PC vs U" column) and the "Extended Stepwise" mutation model equaled 0.9824 (in trios) and an average ratio of 1.1103 was achieved when the LR considering the "Equal" model was compared with the one obtained assuming the "Stepwise" model (in duos). For this case, the other comparisons revealed intermediate average ratios. Moreover, the proportions of ratios that were lower than 1/1.1 or higher than 1.1 were smaller than 6% for all models' comparisons and kinship problems. Considering again the case-example where parent-child duos and trios were simulated and "Equal" mutation model assumed, ratios between LRs differing in 10% were verified in a proportion of 0.0192 when the "Proportional" model (in duos) was considered, and a proportion of 0.031 was reached for comparison with the "Stepwise" model (in trios). The same is true for comparisons between the Null model and the others, which indicates that, under the aforementioned assumptions, there is little impact on the results depending on whether or not hidden mutations are considered. Nevertheless, despite the low frequencies, some sporadic cases were found where the use of different models (or the consideration or disregarding of hidden mutations) led to substantially different results, in all cases.

Preliminary results show that greater impact is observed when genotypic information of pedigrees simulated as unrelated are considered. Indeed, future work should be developed to measure the impact on the cases where individuals are related by a different pedigree than the one assumed in the main hypothesis.

Conflict of interests

All authors declare no conflict of interests.

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Table 1
General summary of the ratios between LRs assuming each of the models considered and the others. The models indicated correspond to the numerators in the ratios, over each of the remaining models. The Null mutation model was considered only for pedigrees with no mendelian incompatibilities.

		PC vs U	FS vs U	HS vs U	FS vs HS
Null	Average ratio (r)	1.0088–1.0203	0.9995–1.0136	0.9996–1.0023	0.9904–1.0135
	Proportion of $r < 1/1.1$ or $r > 1.1$	0–0.0041	0–0.0556	0–0.0319	0–0.0438
Equal	Average ratio (r)	0.9824–1.1103	0.9909–1.0167	0.9997–1.0013	1.0013–1.0154
	Proportion of $r < 1/1.1$ or $r > 1.1$	0.0192–0.031	0.0426–0.057	0.0234–0.0332	0.0268–0.0385
Proportional	Average ratio (r)	0.9929–1.2170	1.0002–1.0301	1.0001–1.0033	1–1.0275
	Proportion of $r < 1/1.1$ or $r > 1.1$	0.0172–0.0306	0.0133–0.0535	0.0058–0.0332	0.0093–0.0385
Stepwise	Average ratio (r)	0.9939–1.2057	0.999–1.0587	0.9996–1.0031	0.9988–1.0533
	Proportion of $r < 1/1.1$ or $r > 1.1$	0.0068–0.031	0.0137–0.057	0.0098–0.0327	0.0108–0.0379
Extended Stepwise	Average ratio (r)	1.0369–1.3386	1.001–1.0797	1.0004–1.0044	1.0009–1.0747
	Proportion of $r < 1/1.1$ or $r > 1.1$	0.0068–0.03048	0.0133–0.0516	0.0058–0.0311	0.0093–0.0364

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