International Congress Series 1239 (2003) 637–638

Mutations and the probabilistic approach to incompatible paternity tests

A.P. Dawid [a], J. Mortera [b], M. Dobosz [c], V.L. Pascali [c,*]

[a] *Department of Statistical Science, University College London, UK*
[b] *Dipartimento di Economia, Università Roma Tre, Italy*
[c] *Immunohematology Laboratory, Istituto di Medicina Legale, Università Cattolica del S. Cuore, Largo F. Vito, 1 00168 Rome, Italy*

Paternity tests are currently carried out by typing a set of microsatellite loci (STRs). This class of polymorphisms is known to be prone to germline mutations. The gametic mutability of those STR loci that are most often used for paternity tests has been closely examined in studies [1,3] which have estimated overall mutation rates per locus, μ, from a considerable volume of segregations. On the basis of these studies, there is now general consensus in defining mutations as non-sporadic events in human lineages.

In the evidentiary context of a typical forensic test, mutations may lead to apparent paternal/parental exclusions. This poses problems in the interpretation of the underlying biological evidence, and the soundness of some ad hoc rules traditionally used to manage incompatible tests (such as: ''non-fatherhood is certain after the occurrence of two/more than two exclusions'') is not guaranteed.

We have recently shown how a probabilistic analysis can be applied to incompatible genetic evidence in paternity tests, leading to its quantification in terms of a likelihood ratio, LR, for paternity vs. non-paternity.

Our approach incorporates the following ingredients.

(a) ''Incompatible'' genotype triplets explicable by assuming a single mutation are considered.

(b) Arbitrary, possibly different, mutation rates μ in paternal and maternal germlines are allowed.

(c) For each locus, allele-specific mutation transition rates (i.e. for allele x to mutate to allele y) are derived in terms of μ, based on reasonable biological assumptions including stepwise mutation and stationarity of gene frequencies [2].

(d) For each locus showing incompatibility, the probability (given the parental genotypes) of obtaining the child's genotype under the hypothesis of paternity (assuming a

* Corresponding author. Tel.: +39-635-507-031; fax: +39-635-507-033.
E-mail address: vince.pascali@rm.unicatt.it (V.L. Pascali).

0531-5131/03
PII: S0531-5131(02)00845-2

single mutation), and the corresponding probability under the alternative non-paternity hypothesis (assuming no mutation), are computed and combined to form a likelihood ratio.

(e) The overall likelihood ratio is obtained by multiplying together these LRs for incompatible segregations with the LRs from compatible loci.

Our proposed mutation model is compared with other mutation models suggested in the literature, and sensitivity analysis is performed on model parameters. We also show how to compute upper bounds on the LR in the very general case when one does not want to adopt any particular mutation model.

Our results, appropriately modified, could be used to obtain estimates or bounds on LRs allowing for other sources of false exclusion (e.g. laboratory errors or falsifications), thus pointing the way towards a general computational solution to the problem of uncertain paternity.

References

[1] B. Brinkmann, et al., Am. J. Hum. Genet. 62 (1998) 1408–1415.
[2] A.P. Dawid, J. Mortera, V.L. Pascali, D.W. Van Boxel, Scand. J. Statist. (in preparation).
[3] L. Henke, J. Henke, Am. J. Hum. Genet. 64 (1999) 1473.