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Estimation of demo-genetic model probabilities with Approximate Bayesian Computation using linear discriminant analysis on summary statistics

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Abstract

Comparison of demo-genetic models using Approximate Bayesian Computation (ABC) is an active research field. Although large numbers of populations and models (i.e. scenarios) can be analysed with ABC using molecular data obtained from various marker types, methodological and computational issues arise when such numbers become too large. Moreover, Robert *et al.* (2011) have shown that the conclusions drawn on ABC model comparison cannot be trusted per se and required further simulation analyses. Monte Carlo inferential techniques to empirically evaluate confidence in scenario choice are very time consuming, however, when the numbers of summary statistics (Ss) and scenarios are large. We here describe a methodological innovation to process efficient ABC scenario probability computation using linear discriminant analysis (LDA) on Ss before computing logistic regression. We used simulated pseudo-observed datasets (*pods*) to assess the main features of the method (precision and computation time) in comparison to more traditional probability estimation using raw (i.e. not LDA-transformed) Ss. We also illustrate the method on real microsatellite datasets produced to make inferences about the invasion routes of the coccinelid *Harmonia axyridis*. We found that scenario probabilities computed from LDA-transformed and raw Ss were strongly correlated. Type I and II errors were similar for both methods. The faster probability computation that we observed (speed gain around a factor 100 for LDA-transformed Ss) substantially increases the ability of ABC practitioners to analyze large numbers of *pods* and hence provides a manageable way to empirically evaluate the power to discriminate among a large set of complex scenarios.

Introduction

One prospect of current biology is that molecular data will help us to reveal the complex demographic processes that have acted on natural populations. The extensive availability of various molecular markers and increased computer power have promoted the development of inferential methods and associated softwares (e.g. Beaumont & Rannala 2004; Excoffier & Heckel 2006). Among these novel methods, Approximate Bayesian Computation method (ABC; Beaumont *et al*. 2002) is increasingly used to make inferences from large datasets for complex models in population and evolutionary biology (e.g. Estoup *et al.* 2004; Fagundes *et al.* 2007; Jakobsson *et al.* 2006; Rosenblum *et al.* 2007; Neuenschwander *et al.* 2008; Toni *et al.* 2009; Verdu *et al.* 2009; Bazin *et al.* 2010; Estoup & Guillemaud 2010; Ascundes *et al.* 2011). The use of ABC techniques has also been envisaged and successfully processed in other research fields, such as infectious disease epidemiology (e.g. Luciania *et al.* 2009) and systems biology (e.g. Ratmann *et al.* 2009).

General statistical features, practical aspects, and applications of ABC in evolutionary biology have been reviewed in at least three recent papers (Bertorelle *et al.* 2010; Csilléry *et al.* 2010; Beaumont 2010). Briefly, ABC constitutes a recent approach to carrying out model-based inference in a Bayesian setting in which model likelihoods are difficult to calculate (due to the complexity of the models considered) and must be estimated by massive simulations. In ABC, the posterior probabilities of different models and/or the posterior distributions of the demographic parameters under a given model are determined by measuring the similarity between the observed dataset (i.e. the target) and a large number of simulated datasets; all raw datasets (i.e. multilocus genotypes or individual sequences) are summarized by so called summary statistics (Ss). Examples of such Ss in population genetics are the mean number of alleles or heterozygosity per population and F_{ST} or genetic distances between pairs of populations. In practice, ABC users can base their analysis on simulation programs and then use statistical software to post-process their

simulation outputs. Several ABC programs have recently been developed to provide non-specialist users with integrated solutions. They vary in the extent to which they are user-friendly and they can be used for both data simulation and some post-processing steps (see Table 1 in Bertorelle *et al*. 2010).

Although the methodology presented here is of more general interest, the present work focuses on population genetics applications and applies to the model choice question. In this context, models are evolutionary scenarios for which relative supports are compared through their posterior probabilities. Choosing among a finite set of scenarios is crucial when doing inferences about evolutionary history and processes for at least two reasons: (i) it allows making general conclusions about major evolutionary events (e.g. admixture between populations, occurrence of bottleneck events or identification of source populations) and (ii) it makes it possible to estimate posterior probabilities of parameters assuming a single scenario if the later is strongly supported (see the reviews of Bertorelle *et al.* 2009, Csilléry *et al.* 2010 and Estoup & Guillemaud 2010 for various illustrations regarding model choice). When processing ABC analyses, all the models are generally simulated the same number of times. This is equivalent to giving the same prior probability to each model under comparison and zero probability to any other model. In the final set of retained simulations (those that have Ss close to the target's), the datasets produced by the more supported models will be overrepresented and the datasets produced by other models will be under-represented or even absent. Intuitively, the probability of a model is related to the relative frequency of the datasets it produces that are among the retained simulations (Weiss & von Haeseler 1998; Pritchard *et al*. 1999). This frequency may be taken as an estimate of the posterior probability of a model, but this estimate is rarely accurate in complex models when, inevitably, the retained simulations are either too few or also contain datasets not closely matching the observed data (e.g. Guillemaud *et al.* 2010).

Recently, Leuenberger & Wegmann (2010) proposed the use of a parametric General Linear Model to adjust the model frequencies in the retained simulations. However, the most used and tested method, also available in integrated ABC packages such as DIYABC (Cornuet *et al*. 2008, 2010), is the adjustment based on the polychotomous logistic regression introduced by Beaumont (2008) (see also Fagundes *et al*. 2007; Cornuet *et al*. 2008). The coefficients for the regression between a model indicator (response) variable and the simulated Ss (the explanatory variables) can be estimated, allowing the estimation of the posterior probability for each model at the intercept condition where observed and simulated Ss coincide. Confidence intervals (i.e. 95 % CI) of the probabilities can be computed as suggested by Cornuet *et al*. (2008).

Large numbers of populations and loci can be analysed with ABC, and there is no limit to the number and complexity of the models (hereafter named scenarios) considered. However, several issues arise when the number of populations becomes too large. The number of Ss to be manipulated increases considerably with the number of populations. This is especially true when different types of markers requiring different types of Ss are considered in the same analysis. A too large number of Ss may be of concern because ABC algorithms attempt to sample from a small multidimensional sphere around the observed statistics. The more Ss, the more difficult it becomes to match the observations closely and increasing the number of simulations may not be sufficient to deal with this issue (Beaumont *et al.* 2002). This phenomenon, which may potentially degrade the estimations of posterior distributions of demo-genetic parameter as well as those of model posterior probabilities, is often referred to as the “curse of dimensionality” (e.g. Beaumont *et al.* 2002; Blum & François 2009). There may be also a problem of co-linearity among explanatory variables (Ss) resulting in instability of the regression when (too) many Ss are introduced (Besley *et al*. 2004; Bazin *et al*. 2010). Recent improvements of ABC get round

these problems by using dimension reduction techniques, including a non-linear feed-forward neural network (Blum & François, 2009) and partial least squares (PLS) regression (Wegmann *et al.* 2009; see also Bazin *et al.* 2010). At least some algorithms of this type have been implemented in the package ABCtoolbox (Wegmann *et al*. 2010). The added value of such algorithms in the context of complex models and large datasets remains, however, to be thoroughly tested (Bertorelle *et al*. 2010). Most importantly, although the model itself can be considered as an additional parameter to infer, the PLS dimension reduction technique applies to a continuous response variable. Therefore, this technique can be applied to the estimation of posterior distributions of demographic and genetic parameters under a given model and not to the computation of posterior probabilities of models, the latter corresponding to a discrete response variable. Initially developed for the estimation of posterior distributions of demographic and genetic parameters, neural networks might theoretically be applied to model choice (Ripley 1996), but, to our knowledge, this has not been tested and achieved in practice, at least in the context of complex models and large datasets.

Robert *et al.* (2011) have shown that, because ABC algorithms involve an unknown loss of information induced by the use of insufficient summary statistics, the conclusions drawn on model comparison cannot be trusted per se and required further simulation analyses. As pointed by Bertorelle *et al.* (2010) and Robert *et al*. (2011) among others, confidence in model choice may be nevertheless empirically evaluated by processing Monte Carlo evaluation of false allocation rates (type I and II errors) based on ABC posterior probabilities computed from simulated pseudo-observed datasets. A version of this exploratory analysis is already provided in the DIYABC software (Cornuet *et al*. 2008, 2010). This evaluation, based on the simulation and analysis of pseudo-observed datasets (hereafter named *pods*), represents a useful and manageable quality assessment for

practitioners but is very time consuming. The polychotomous logistic regression used to estimate scenario probabilities requires the computation of a matrix involving a very large number of loops (i.e. [number of compared scenarios]² x [number of Ss]^2 x [number of selected simulated datasets close to the target dataset]) at each iteration of the Newton-Raphson method (Cornuet *et al*. 2008). This makes computation particularly time consuming when the number of scenarios and Ss become large. Moreover, computations involve several large matrices and probabilities that are sometimes simply not computable when the computer memory space is not large enough. This is of particular concern when type I and type II errors have to be computed from a large number of *pods*. As previously stressed, such computations are nevertheless more and more requested by ABC experts for assessing the power to discriminate among scenarios (e.g. Fagundes *et al*. 2007; Verdu *et al*. 2009; Bertorelle *et al*. 2010; Lombaert *et al*. 2010; Robert *et al*. 2011).

In this paper, we describe a methodological innovation to process more efficient ABC scenario probability estimation using linear discriminant analysis (LDA) transformations on Ss before computing logistic regression. We first describe the principle and goals of the method. We then use simulated *pods* to assess its main features (precision and computation time) in comparison to probability estimation using logistic regression on raw (i.e. not LDA-transformed) Ss. Finally, we illustrate the method on real microsatellite datasets produced by Lombaert *et al*. (2011) to make inferences about the worldwide routes of invasion of the coccinelid *Harmonia axyridis*.

Materials and Methods

Linear discriminant analysis

The Linear Discriminant Analysis (LDA) is a standard technique for supervised classification. For a modern and comprehensive presentation of LDA, we invite readers to refer to classical textbooks such as Ripley (1996), McLachlan (2004) or Hastie *et al.* (2009). The LDA dates back to Fisher (1936) who proposed the dimension reduction technique that contributed to the popularity of LDA. Actually, the classifier estimated with the LDA depends only on some linear projection of the dataset onto a linear subspace whose dimension is smaller than the number of groups, denoted by K. It is not our purpose here to explain how this low-dimensional projection of the data can further leads to a LDA classifier which provides automatic rules to classify a new data point to the class with the largest posterior probability. As a matter of fact, we are here only interested in the dimension reduction part of LDA and hence in the construction of the $(K-1)$ discriminant variables. Those discriminant variables are non-correlated, linear combinations of the original variables that maximise the between-class variance relative to the within-class variance, which is assumed identical among the different classes. This minimizes the overlap between the classes when projected on the discriminant subspace if the within-class distribution were Gaussian. Note that the discriminant variables are ordered with respect to their ability to move the classes further apart.

In the methodological framework considered here (i.e. that of computing posterior probabilities of scenarios using ABC), we used LDA to transform the set of usually large number J of summary statistics (Ss) into $(K-1)$ independent variables maximizing the differences among the K compared scenarios (assuming $K < J$). The goal was to reduce the dimension of the set of explanatory variables from J non-independent to $(K-1)$ independent variables, and this whatever the value of J. Certainly, variance of the Ss varies among the different scenarios. Even in that case, however, the projection onto the

discriminant subspace was proved relevant as a dimension reduction technique; see the classical textbooks cited above. It is worth noting that we also weighted the simulated datasets to give more importance to the ones that are closer to the observed dataset. The LDA functions were used to transform both the (raw) simulated and observed Ss. Details on LDA computations and transformation of Ss are given in the Appendix S1

Let us recapitulate how computation of the discriminant variables was included in practice as a single additional step of the ABC process allowing the computation of posterior probabilities of scenarios.

Step 1: We selected a subset of x % (typically 1 %) best simulations in a standard ABC reference table (i.e. the table where parameter values drawn from priors and corresponding simulated Ss have been recorded) usually including 10^6 simulations for each of the *K* compared scenarios. This selection was based on the standard normalized Euclidian distance computed between the observed and simulated "raw" (i.e. not transformed) Ss (e.g. Beaumont *et al*. 2002) and hence corresponded to the x % simulations with the smallest Euclidian distances.

Step 2 (LDA step; see Appendix S1 for details): we used LDA to transform the raw Ss of this subset of x % best simulations into $(K-1)$ discriminant variables maximizing the differences among the *K* compared scenarios. When computing LDA functions, we weighted the simulated datasets with the Epanechnikov kernel commonly used in the local regression (equation 5 in Beaumont *et al.* 2002).

Step 3: We estimated the posterior probabilities of each competing scenario by polychotomous logistic regression (Cornuet *et al.* 2008) on the x % best simulated datasets now summarized by $(K-1)$ discriminant variables instead of *J* non-independent variables (i.e. raw Ss statistics). Confidence intervals (i.e. 95% CI) were computed for each posterior probability using the $(s-1)$ independent variables following Cornuet *et al*. (2008).

Hence, our proposal included only a single additional step (i.e. Step 2) when compared to the computation traditionally proposed by different authors (e.g. Beaumont 2008; Fagundes *et al*. 2007; Cornuet *et al*. 2008 & 2010). Processing Step 2 substantially decreases the number of explanatory variables through the production of LDA variables maximizing the differences among the compared scenarios. This provides three main advantages. First, computation of scenario probabilities using the polychotomous regression of Step 3 becomes (much) faster and sometimes simply feasible. Second, a lower number of explanatory variables may also improve the accuracy of the ABC approximation, particularly when the number of simulations is not large enough to offset the number of Ss. Finally, using LDA-transformed Ss avoids correlations among explanatory variables.

Tests on simulated datasets

Pseudo-observed datasets (*pods*) were simulated from a set of known scenarios and prior distributions to compare posterior probabilities obtained through the logistic regression performed on both LDA-transformed and raw Ss. The *pods* were defined to mimic the real microsatellite dataset of the ABC analysis 1 processed by Lombaert *et al*. (2011) on the invasive coccinelid *Harmonia axyridis*. The *pods* hence included 18 microsatellites genotyped in five population samples (18 to 35 individuals per population samples). This dataset was produced to make inferences about the origin of the invasive *H. axyridis* population established in Eastern North America in 1988 (ENA), considering altogether two populations from the native range, two strains used for biocontrol release and one (target) population from the introduction range (ENA). In this analysis, Lombaert *et al*. (2011) defined ten competing scenarios considering a native or biocontrol population as a

source for ENA or admixture between them (see Lombaert *et al*. 2010 and 2011 for details).

As in analysis 1 of Lombaert *et al*. (2011), genetic variation within and between populations was summarized in the *pods* using a set of (raw) statistics traditionally employed in ABC (Cornuet *et al*. 2008 & 2010; Guillemaud *et al*. 2010). For each population and each population pair we used the mean number of alleles per locus, the mean expected heterozygosity and the mean allelic size variance. The other statistics used were the mean ratio of the number of alleles over the range of allele sizes, pairwise F_{ST} values, mean individual assignment likelihoods of population *i* assigned to population *j* and the maximum likelihood estimate of admixture proportion. The total number of Ss was 86.

We choose this particular scenarios-priors-Ss setting because it had the potential to fairly illustrate our new methodological developments based on LDA-transformed Ss. This setting was characterized by relatively high (mean) type I error rates (ca. 0.40, due to the large prior parameter space used to generate *pods*, this space including "areas" for which the discrimination among scenarios was difficult) and relatively small (mean) type II error rates (ca. 0.07). High type I error rates corresponds to situations where probability values of the target scenario can be small to high depending on the parameter values of the analysed *pod*, hence virtually including the all spectrum of probabilities between 0 and 1. This allows a better (and fairer) comparison of results between raw and LDA-transformed Ss (cf. it is difficult to compare probability estimations when all values are between say 0.95 and 1.0). Moreover, this particular setting was chosen because it corresponded to complex evolutionary models and large datasets that nevertheless could be analyzed for a large number of *pods* using logistic regression on both LDA-transformed and raw Ss. More complex data and scenario settings (with larger number of scenarios and/or raw Ss) were

computationally too heavy to obtain probability estimations on a large enough number of *pods* in a manageable time using logistic regression on raw Ss "(i.e. < 15 min per *pod* on a single standard biprocessor computer; see below). The results presented here were however qualitatively similar to those obtained considering various alternative settings (with smaller or larger numbers of scenarios and/or raw Ss) that we have also tested with our methodological innovation (results not shown).

The ABC analyses of the *pods* were performed using parameter values drawn from the prior distributions described in Table S1 and by simulating 10^6 datasets for each of the ten competing scenarios. For each *pod* we estimated the posterior probabilities of the scenarios using a polychotomous logistic regression on the 1% of simulated datasets closest to the observed dataset, considering either LDA-transformed or raw Ss.

We produced a first set of 500 *pods* under scenario 5 (the scenario selected after ABC treatment by Lombaert *et al.* 2011), drawing parameters values into the distributions described in table S1. This scenario 5 is presented graphically in figure S1; the nine other competing scenarios correspond to alternative source(s) of the target introduced population (see Lombaert *et al.* 2011 for details). For each *pod*, we used the logistic regression on either the 9 LDA-transformed or the 86 raw Ss to estimate the posterior probability and 95% CI of scenario 5 relatively to the set of ten compared scenarios. The number of iterations of the Newton-Raphson algorithm used by the logistic regression computations and the mean time of each iteration were also recorded for each *pod*.

We then produced a second set of 1,000 *pods* including 10 subsets of 100 *pods* simulated under each of the ten compared scenarios, drawing parameter values from the same distributions (Table S1). Each *pods* subset was used to estimate type I and type II

errors on scenario choice using either the 9 LDA-transformed or the 86 raw Ss. Type I error of a given scenario is the proportion of *pods* simulated from this scenario for which this scenario does not have the highest posterior probability. Type II error is the proportion of *pods* for which the scenario with the highest posterior probability is not the given true one.

Finally, we evaluated the impact of the dimensionality of the simulated dataset (i.e. the "curse of dimensionality" mentioned in the *Introduction* section), using either the 9 LDA-transformed or the 86 raw Ss. For different amount of simulated datasets, we estimatied the type I and II error rates from 500 *pods* simulated under scenario 5 (type I error for scenario 5) and 500 *pods* simulated under scenario 1 (type II error for scenario 5 which in this case corresponds to the proportion of times that scenario 5 was selected when *pods* have been produced under scenario 1). Scenario 1 was chosen to evaluate type II errors because this scenario has shown the largest type II errors in the abovementioned analyses. To consider different dimensionalities of simulated datasets, we decreased the number of datasets simulated for each of the ten compared scenarios from 10^6 to 10^4, keeping the proportions of datasets closest to the observed dataset selected for the logistic regression at 1% of the total number of simulated datasets

All analyses were processed on a 2 CPU Intel Xeon X5472 computer (Windows XP platform, 32 bits system, 4 Go of RAM) using a modified version of the package DIYABC V1. This modified version is available under request from AE. LDA-transformation of Ss before logistic regression will be implemented in a new multiplatform version of DIYABC that will be freely available later in 2012.

Tests on real datasets

We used the real microsatellite datasets of Lombaert *et al*. (2011) to compare scenario choice and probability estimation computing logistic regression on both LDA-transformed and raw Ss. These datasets, which included 18 microsatellites genotyped on five to eight population samples (18 to 42 individuals per population samples), were used to make five consecutive ABC analyses about the worldwide routes of invasion of the coccinelid *H. axyridis*, considering altogether populations from the native range, the introduction range and biocontrol release actions, with potential admixture between them (see Lombaert *et al*. 2010 and 2011 for details).

We used prior distributions and Ss identical to those described in the previous section (*Tests on simulated datasets*; Table S1). Following Lombaert *et al*. (2010 and 2011), we performed five consecutive ABC analyses of invasion scenarios involving successive *H. axyridis* outbreaks that were successively recorded in the invaded range. As previously detailed, analysis 1 dealt with the introduction pathway for the first recorded outbreak in eastern North America in 1988, defining ten competing scenarios. Analysis 2 dealt with the second outbreak recorded in western North America in 1991, taking into account the scenario selected in analysis 1, hence defining 15 competing scenarios. The European and South American outbreaks in 2001 were addressed in analyses 3 and 4, respectively (15 scenarios for each outbreak), taking into account the scenario selected in analysis 1 and 2. Finally, the African outbreak in 2004 was considered in analysis 5 (28 scenarios), taking into account the scenarios selected in analyses 1, 2, 3 and 4. The total number of raw Ss varied from 86 (analysis 1) to 223 (analysis 5), whereas the total number of LDA-transformed Ss varied from 9 (analysis 1) to 27 (analysis 5).

The ABC analyses were performed by simulating 10^6 microsatellite datasets for each competing scenario in the first four analyses and $5x10^5$ datasets per scenario in analysis 5 because of the high number of scenarios (28) and raw summary statistics (223) which made a larger analysis computationally too heavy, even when using LDA-transformed Ss. For each of the five analyses, we estimated the posterior probabilities of the competing scenarios using a polychotomous logistic regression on the 1% of simulated datasets closest to the observed dataset, considering either LDA-transformed or raw Ss. Computation times were also recorded to illustrate the gain obtained in computation speed when using LDA-transformed Ss.

Finally, we evaluated the impact of the number of simulated datasets recorded in the reference table for analysis 1 on the estimation of the probability of scenario 5 using either LDA-transformed or raw Ss. To this aim, we decreased the number of datasets simulated for each of the ten compared scenarios from 10^6 to 10^4, keeping the proportions of datasets closest to the observed dataset selected for the logistic regression at 1% of the total number of simulated datasets.

All analyses were processed on a 2 CPU Intel Xeon E5540 computer (Windows XP platform, 32 bits system, 4 Go of RAM) using a modified version of the package DIYABC V1 (available under request from AE).

Results

Tests on simulated datasets

Figure 1A illustrates the strong correlation between the probability values of scenario 5 obtained from *pods* computing logistic regression on LDA-transformed Ss and raw Ss (Pearson's correlation coefficient = 0.940). One can see, however, a trend for a globally slightly lower scenario probability with LDA-transformed Ss (see linear regression equation in the legend of Figure 1A). Figure 1B shows that 95% CI are almost always smaller with LDA-transformed Ss.

Figure 2 summarizes the type I and II error rates obtained with LDA-transformed and raw Ss. We found that these error rates substantially varied among scenarios but were to a large extent similar for both methods for a given scenario. P-values computed using Fisher exact test were higher than 0.6 for all scenarios for mean type II errors and were lower than 5% for a single scenario for type I errors ($p = 0.047$ for scenario 7; p-value non significant after applying the false discovery rate correction method of Benjamini & Hochberg 1995).

The gain in computation time with LDA-transformed Ss was high. First, the number of iterations needed to reach convergence during the logistic regression analysis was lower with LDA-transformed Ss (mean = 7.320, SD = 1.420) than with raw Ss (mean = 9.190, SD = 2.250). Second, the mean time of each such iteration was considerably smaller with LDA-transformed Ss (mean = 7.034 sec, SD = 0.791) than with raw Ss (mean = 888.146 sec, SD = 65.374). This translated into a computation speed increase by a mean factor 128.128 (SD = 19.482) per iteration and 163.601 (SD = 46.456) for a completed logistic regression analysis. The computation time for the LDA-transformation of raw Ss before the regression was negligible.

Results summarized in Table 1 indicate that we did not face the curse of dimensionality problem (see definition in the *Introduction* section) at least in the present setting. Even for a large number of Ss and a strongly degraded number of simulated datasets including only 10^4 datasets per scenario (total of 10^5 datasets for the ten compared scenarios in this case), the error rates did not dramatically increase. The increase of type I and II error rates with smaller datasets is (only) slightly faster for raw SS than for LDA-transformed Ss.

Tests on real datasets

As will be further illustrated below on real datasets, our methodological innovation is particularly attractive when practitioners have to deal with a large number of complex scenarios involving a large number of Ss. Table 2 summarizes our results on scenario choice and probability estimation computing logistic regression on both LDA-transformed and raw Ss obtained on the real microsatellite datasets of Lombaert *et al*. (2011). For each of the five consecutive analyses, the same scenario had the highest probability and was hence selected using either LDA-transformed or raw Ss. The probabilities of the most likely scenarios were slightly smaller with LDA-transformed Ss for analyses 1, 3 and 4, and slightly larger for analysis 2. In contrast to computation based on LDA-transformed Ss, analysis 5 could not be processed with raw Ss due to computer memory overflow. In all analyses the 95% CI of the most likely scenario never overlapped those of competing scenarios. As found with simulated *pods*, 95% CI with LDA-transformed Ss were smaller than those with raw Ss.

In agreement with *pods* analyses, the gain in computation time with LDA-transformed Ss was substantial. For all analyses, both the number of iterations needed to reach convergence during the logistic regression and the mean computation time for each such iteration was smaller with LDA-transformed Ss. This translated into a computation speed increase by a factor 72 to 101 per iteration and 93 to 159 for a completed logistic regression analysis.

Figure 3 indicates that analysis 1, processed either on LDA-transformed or raw Ss, is rather robust to the potential difficulties associated with the curse of dimensionality. Estimations of the probability of scenario 5 start to fluctuate substantially and 95% CIs to increase considerably for simulation efforts including less than $2x10^5$ datasets per scenarios. No obvious differences could be observed between LDA-transformed and raw Ss.

Discussion

Model comparison is an active research field among the widespread developments currently undergone in ABC (e.g. Beaumont *et al*. 2009; Bertorelle *et al.* 2010; Csilléry *et al.* 2010; Beaumont 2010; Robert *et al*. 2011). Here, we propose a methodological innovation to deal with the discrimination among a large set of complex scenarios through more efficient ABC probability computation using a linear discriminant analysis (LDA) on Ss before the logistic regression analysis. Statistical methods to select appropriate Ss to optimize model selection are still under development and discussed (see for instance

Fearnhead & Prangle 2012 and associated discussions). Our LDA-based transformation of Ss represents a practical and straightforward way to tackle this question.

We show, using both simulated and real datasets, that posterior probabilities of scenarios computed from LDA-transformed and raw Ss are strongly correlated. LDA-transformed Ss tend, however, to provide slightly lower probability values and hence to be somewhat conservative with respect to scenario discrimination. On the other hand, model probabilities estimated from LDA-transformed Ss are characterized by smaller 95% CI. The later feature is expected to decrease the number of inconclusive results if non-overlapping of CI is taken as a criterion to select a scenario. When scenario selection is made on the basis of the highest probability, type I and II errors were nevertheless similar for both methods. The lower number of LDA variables used for the logistic regression analysis (e.g. 9 LDA-transformed Ss versus 86 raw Ss in the *pods* we analyzed) is likely to explain, to a large extent, both the smaller 95% CIs of probability estimates and the smaller number of iterations needed to reach convergence during the regression.

A major practical advantage of using LDA-transformed Ss is that it substantially decreases the dimension of explanatory variables making computation of scenario probability (much) faster and sometimes simply feasible when the memory space is not large enough to compute the matrix of second partial derivatives of the likelihood (p1 of Supplementary material in Cornuet *et al.* 2008), as in Analysis 5 using the real dataset of Lombaert *et al.* (2011). This allows larger data-scenarios settings to be analyzed. It is worth stressing, however, that because LDA-transformation only plays on the number of Ss and not on the number of parameters of the models, such transformation should not motivate ABC practitioners to over-parameterize their models.

Faster probability computation increases the ability of ABC practitioners to analyze large numbers of *pods* (for instance using the option “Evaluate confidence in scenario choice” in the package DIYABC). It hence makes it easier to process a manageable empirical evaluation of the power to discriminate among a given set of scenarios by computing type I and II errors from sufficiently large number of *pods*, especially for large sets of complex scenarios (see e.g. Robert *et al*. 2011 for theoretical arguments in favor of such experimental explorations). Several authors have suggested to use scenario probabilities computed from *pods* to evaluate type I and II errors to estimate the posterior probability of a model among a set of *k* models given the observed posterior probability of a real dataset, $P(M_k \text{ is the true model} \mid \text{observed estimated posterior probability} = x)$. Such computation can then be used to adjust the posterior probabilities estimated from the real dataset, taking part of the errors associated with ABC into account (see Fagundes *et al*. 2007; Lombaert *et al*. 2011).

Other potential advantages of LDA-transformation of raw Ss include reducing the difficulties associated with the curse of dimensionality and avoiding correlation among explanatory variables (i.e. multi-co-linearity) during the regression step. At least theoretically the dimensionality issue might be offset by increasing the number of simulations, but the amount of time then needed for concrete implementation might be unreasonable. It is worth stressing, however, that the actual impact of such potential issues remains difficult to assess in a generic manner as it probably differs depending on the analyzed observed dataset, as well as on the Ss and/or scenario settings. Table 1 and Figure 3 both indicate a good robustness to the numbers of simulated datasets, as a substantial effect could be observed only for particularly low (and in practice rarely used) number of simulated datasets. Analyses carried on *pods* suggest a slightly better robustness when

using LDA-transformed rather than raw Ss, at least when using type I and II error rates as criterion (cf. the slightly smaller increase of errors with smaller datasets for LDA-transformed than raw Ss). It is difficult to know, however, to which extent this result reflects the lower number of LDA variables used for the regression and/or the fact that a substantial number of raw Ss are non-independent variables.

We believe that our LDA-based methodological innovation will usefully enlarge the tool box available to biologists to make ABC inferences on more complex and hence more realistic demographic processes that have acted on natural populations.

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606

Figures legends

Figure 1. Probability estimations of scenario 5 computed using LDA-transformed or raw summary statistics for 500 pods simulated under scenario 5 (ten scenarios compared).
Note: (A) Pearson's correlation coefficient between probability estimations = 0.940 (95% CI = [0.928, 0.949]). Solid line: y = x; dotted line: linear regression line y = 0.818436 x + 0.004878. (B) 95% CIs (i.e. 2.5% and 97.5% quantiles) for each probability values obtained from either LDA-transformed summary statistics (black lines) or raw summary statistics (grey lines).

Figure 2. Confidence in discriminating scenarios using LDA-transformed or raw summary statistics.
Note: Type I error: exclude scenario x when it is actually scenario x. Type II error: choose scenario x when it is not scenario x. Results are based on 100 *pods* per scenario (total of ten compared scenarios). The compared scenarios correspond to variants of the scenario 5, the latter being detailed in Figure S1.

Figure 3. Probabilities of scenario 5 computed from the real dataset of Lombaert et al. (2011) for different numbers of simulated datasets.
Note Black = LDA-transformed summary statistics. Grey = raw summary statistics. Plain and dotted lines are for probability estimations and 95% CIs, respectively. Probabilities of scenario 5 were estimated for number of datasets simulated for each of the ten compared scenarios decreasing from 10^6 to 10^4, keeping the proportions of datasets closest to the observed dataset selected for the logistic regression at 1% of the total number of simulated datasets.

Table 1. Type I and II error rates estimated for different numbers of simulated datasets.

		Number of simulated datasets for each of the 10 compared scenarios				
		10^6	10^5	$5x10^4$	$2x10^4$	10^4
Type I error	LDA-transformed Ss	0.560	0.556	0.584	0.592	0.622
	Raw Ss	0.450	0.492	0.530	0.536	0.624
Type II error	LDA-transformed Ss	0.056	0.056	0.052	0.062	0.080
	Raw Ss	0.060	0.062	0.072	0.088	0.116

Note: Type I error rates were estimated for scenario 5 from 500 *pods*. Type II errors were estimated for scenario 5 when simulating 500 *pods* under scenario 1. The number of datasets simulated for each of the ten compared scenarios decreased from 10^6 to 10^4, keeping the proportions of datasets closest to the observed dataset selected for the logistic regression at 1% of the total number of simulated datasets

Table 2. Scenario choice and posterior probability estimated from either LDA-transformed or raw summary statistics when considering the real microsatellite datasets of Lombaert et al. (2011).

	Logistic regression on raw summary statistics					Logistic regression on LDA-transformed summary statistics					Speed gain
Consecutive ABC analyses (nb simulations per scen. \ nb of scen.)	Nb of stats	Selected scenario #	Posterior probability [95% CI]	Mean time per NR iteration	Nb of NR iterations	Nb of stats	Selected scenario #	Posterior probability [95% CI]	Mean time per NR iteration	Nb of NR iterations	Per iteration \ over all iterations
Analysis 1 (10^6 \ 10 scenarios)	86	5	0.6242 [0.5767, 0.6717]	5' 05"	11	9	5	0.5420 [0.5325, 0.5516]	3"	7	101.7 \ 159.8
Analysis 2 (10^6 \ 15 scenarios)	124	1	0.4425 [0.3746, 0.5105]	38' 45"	11	14	1	0.5767 [0.5559, 0.5976]	31"	7	75.0 \ 117.9
Analysis 3 (10^6 \ 15 scenarios)	124	13	0.8134 [0.7107, 0.9160]	38' 38"	9	14	13	0.7487 [0.7214, 0.7760]	32"	6	72.4 \ 93.1
Analysis 4 (10^6 \ 15 scenarios)	124	4	0.9489 [0.9315, 0.9663]	33' 36"	9	14	4	0.9227 [0.9139, 0.9315]	27"	7	74.7 \ 96.0
Analysis 5 ($5x10^5$ \ 28 scenarios)	223	NC*	NC	NC	NC	27	4	0.6864 [0.6456, 0.7272]	6' 11"	7	NC

Note: The probabilities of the competing scenarios were computed using a logistic regression on the 1% of simulated datasets closest to the real *Harmonia axyridis* datasets. NR iterations = Newton-Raphton iterations (Cornuet *et al*. 2008). NC: not computable. * Because the full computation of analysis 5 was not feasible (Lombaert *et al.* 2011), an alternative method was used to compare scenarios by first setting aside 11 scenarios using the direct approach (Cornuet *et al*. 2008) on the 0.01% datasets closest to the observed dataset. The scenario 4 was then selected due to its highest posterior probability in a subsequent analysis (using polychotomous logistic regression and raw Ss) performed on the 19 remaining scenarios (see Lombaert *et al*. 2011 for details).

Fig. 1

(A)

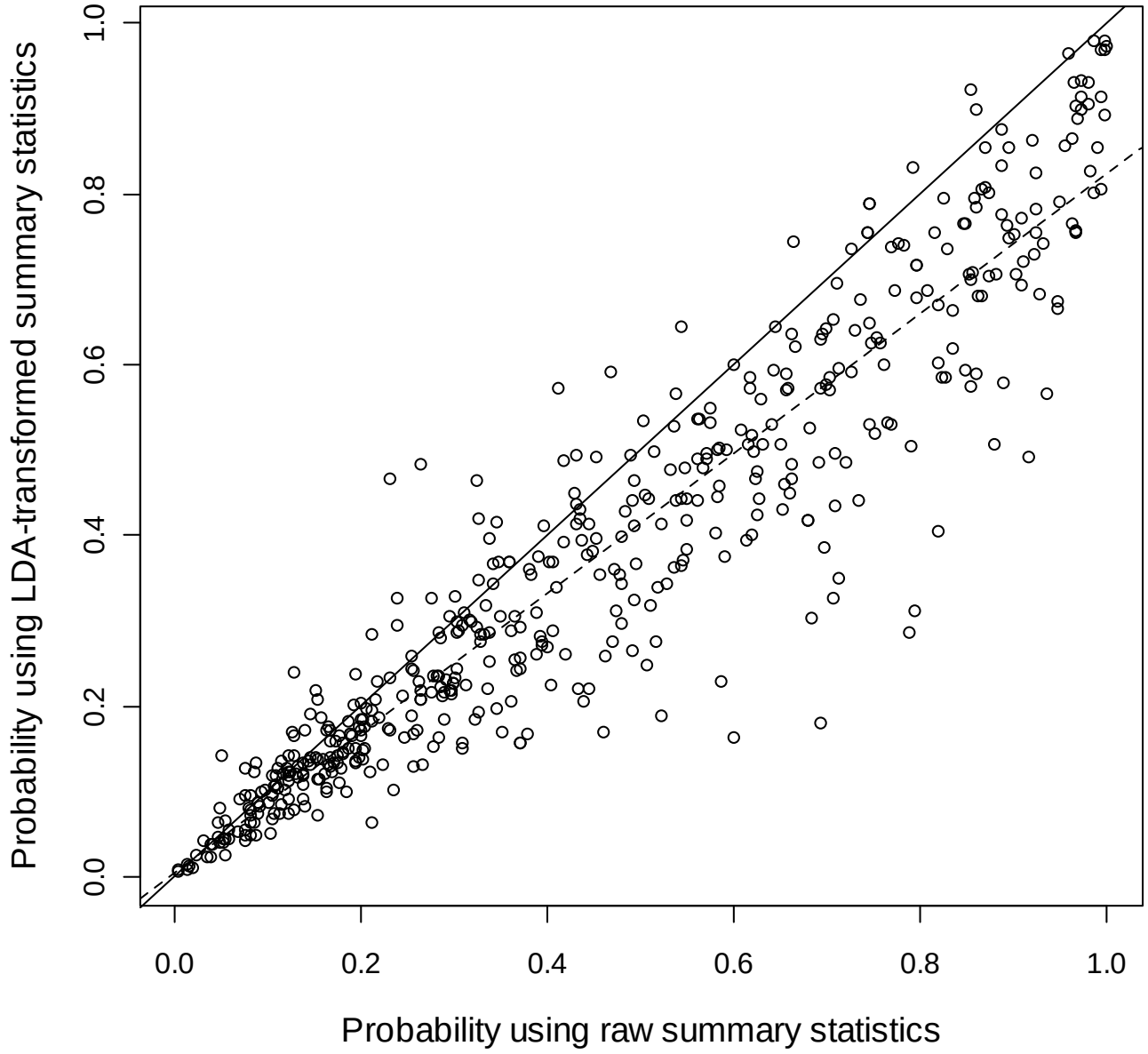

Probability using LDA-transformed summary statistics
0.0
0.2
0.4
0.6
0.8
1.0
Probability using raw summary statistics
0.0
0.2
0.4
0.6
0.8
1.0

Fig. 1 continued

(B)

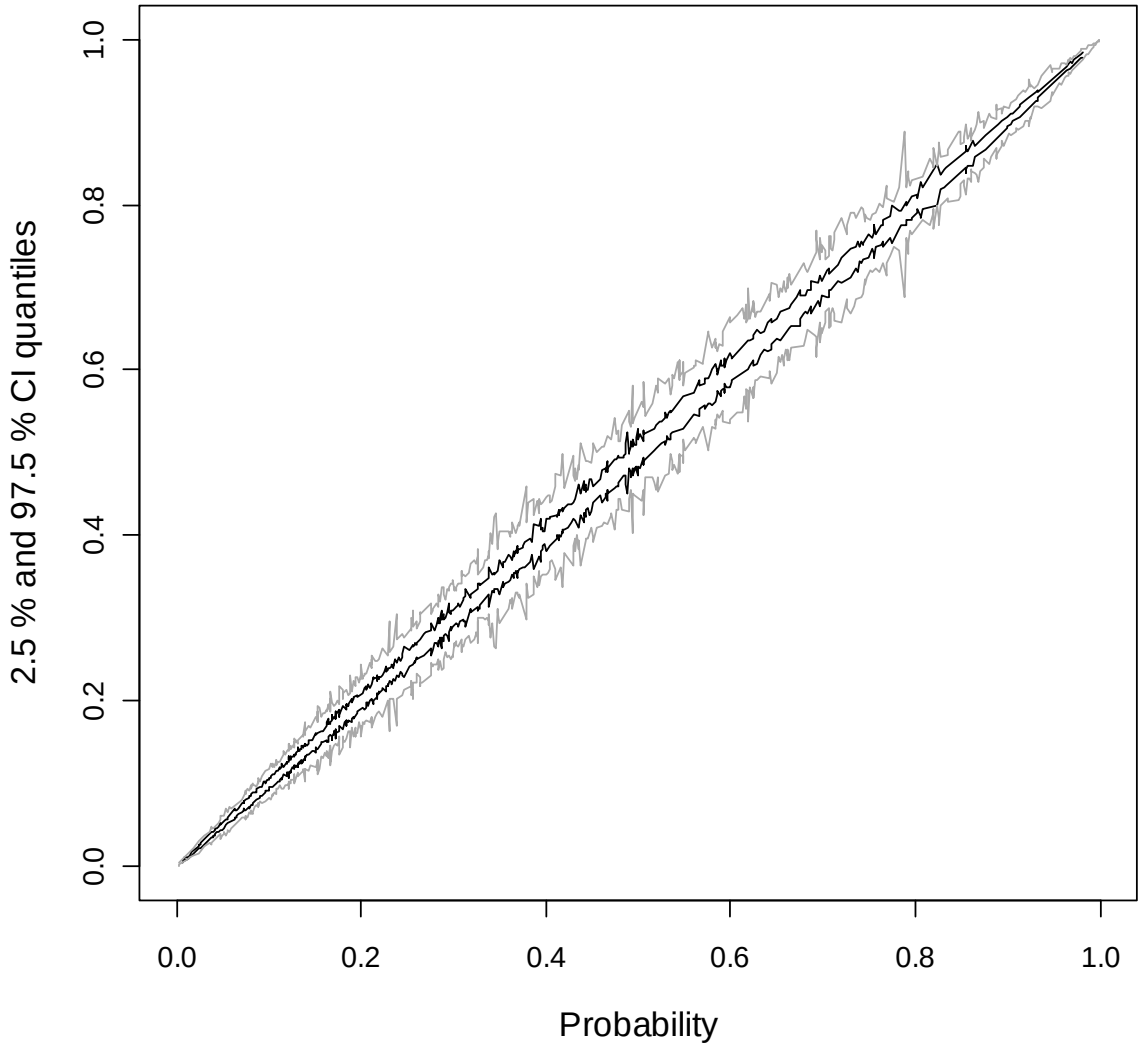


Fig. 2

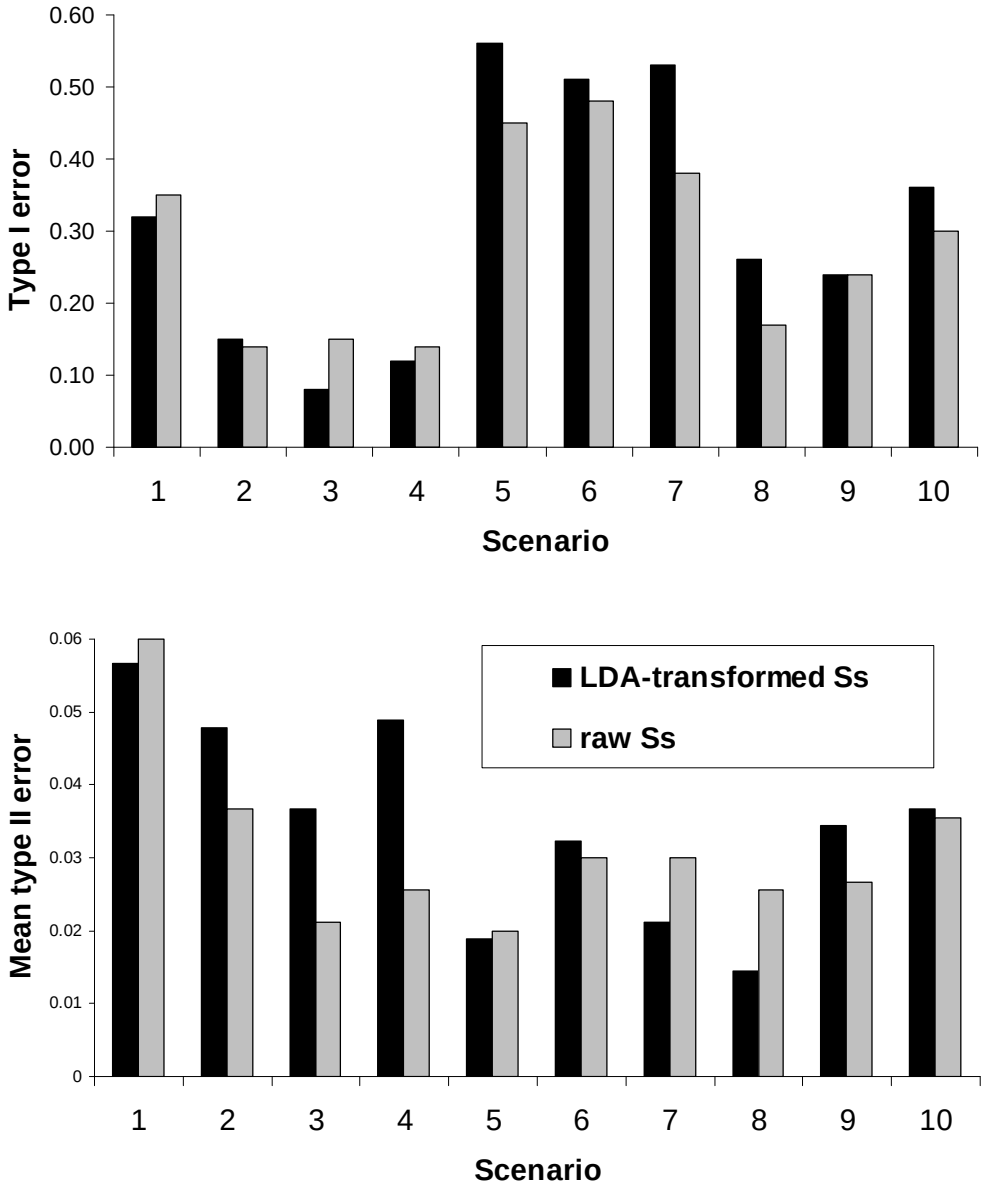
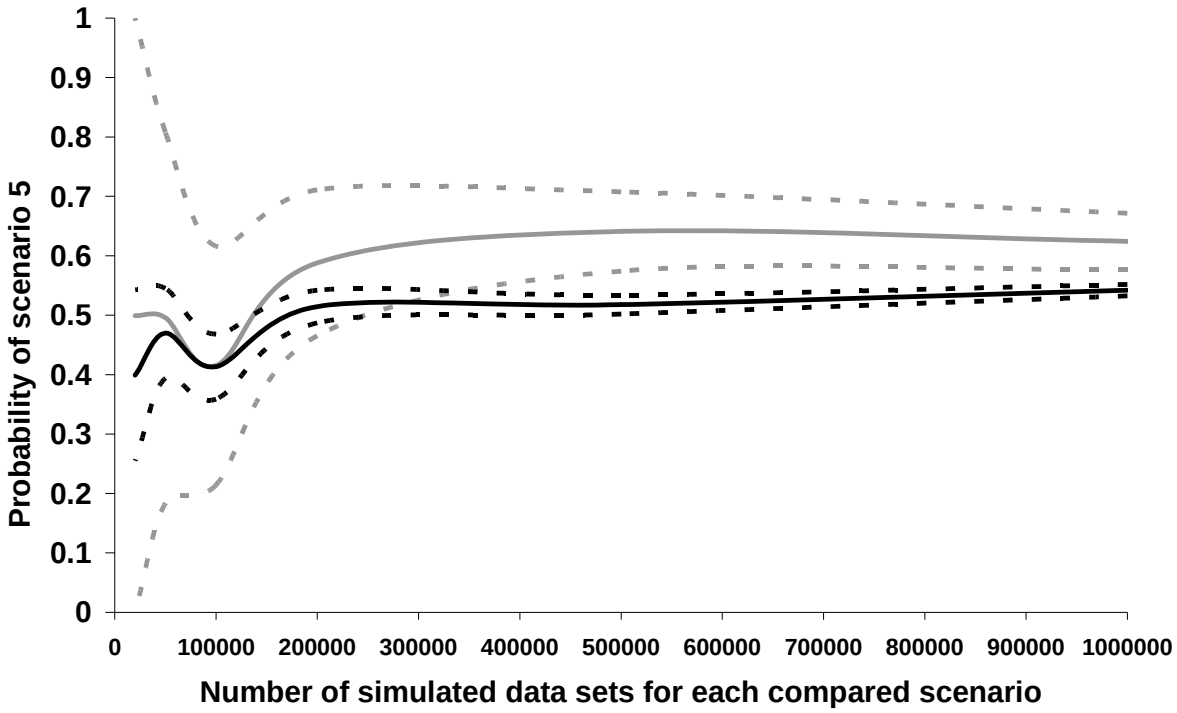

0.60
0.50
0.40
0.30
0.20
0.10
0.00
Type I error
1
2
3
4
5
6
7
8
9
10
Scenario
0.06
0.05
0.04
0.03
0.02
0.01
0
Mean type II error
LDA-transformed Ss
raw Ss
1
2
3
4
5
6
7
8
9
10
Scenario

Fig. 3


Probability of scenario 5
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
100000
200000
300000
400000
500000
600000
700000
800000
900000
1000000
Number of simulated data sets for each compared scenario