

Lack of confidence in approximate Bayesian computation model choice

Christian P. Robert^{a,b,c,1}, Jean-Marie Cornuet^d, Jean-Michel Marin^e, and Natesh S. Pillai^f

^aUniversité Paris-Dauphine, 75775 Paris cedex 16, France; ^bInstitut Universitaire de France, France; ^cCentre de Recherche en Économie et Statistique (CREST), 92245 Malakoff cedex, France; ^dCentre de Biologie pour la Gestion des Populations (CBGP), French National Institute for Agricultural Research (INRA), 34988 Montpellier-sur-Lez cedex, France; ^eUnité Mixte de Recherche Centre National de la Recherche Scientifique (CNRS) 5149, Université Montpellier 2, 34095 Montpellier, France; and ^fDepartment of Statistics, Harvard University, Cambridge, MA 02138-2901

Edited by Stephen E. Fienberg, Carnegie Mellon University, Pittsburgh, PA, and approved July 21, 2011 (received for review February 23, 2011)

Approximate Bayesian computation (ABC) have become an essential tool for the analysis of complex stochastic models. Grelaud et al. [(2009) *Bayesian Anal* 3:427–442] advocated the use of ABC for model choice in the specific case of Gibbs random fields, relying on an intermodel sufficiency property to show that the approximation was legitimate. We implemented ABC model choice in a wide range of phylogenetic models in the Do It Yourself-ABC (DIY-ABC) software [Cornuet et al. (2008) *Bioinformatics* 24:2713–2719]. We now present arguments as to why the theoretical arguments for ABC model choice are missing, because the algorithm involves an unknown loss of information induced by the use of insufficient summary statistics. The approximation error of the posterior probabilities of the models under comparison may thus be unrelated with the computational effort spent in running an ABC algorithm. We then conclude that additional empirical verifications of the performances of the ABC procedure as those available in DIY-ABC are necessary to conduct model choice.

Bayes factor | Bayesian model choice | likelihood-free methods | sufficient statistics | consistent tests

Inference on population genetic models such as coalescent trees is one representative example of cases when statistical analyses such as Bayesian inference cannot easily operate because the likelihood function associated with the data cannot be computed in a manageable time (1–3). The fundamental reason for this impossibility is that the model associated with coalescent data has to integrate over trees of high complexity.

In such settings, traditional approximation tools such as Monte Carlo simulation (4) from the posterior distribution are unavailable for practical purposes. Indeed, due to the complexity of the latent structures defining the likelihood (like the coalescent tree), their simulation is too unstable to bring a reliable approximation in a manageable time. Such complex models call for a practical if cruder approximation method, the approximate Bayesian computation (ABC) methodology (1, 5). This rejection technique bypasses the computation of the likelihood via simulations from the corresponding distribution (see refs. 6 and 7 for recent surveys, and ref. 8 for the wide and successful array of applications based on implementations of ABC in genomics and ecology).

We argue here that ABC is a generally valid approximation method for doing Bayesian inference in complex models. However, without further justification, ABC methods cannot be trusted to discriminate between two competing models when based on insufficient summary statistics. We exhibit simple examples in which the information loss due to insufficiency leads to inconsistency, i.e., when the ABC model selection fails to recover the true model, even with infinite amounts of observation and computation. On the one hand, ABC using the entire data leads to a consistent model-choice decision, but it is clearly infeasible in most settings. On the other hand, too much information loss due to insufficiency leads to a statistically invalid decision procedure. The challenge is in achieving a balance between information loss and consistency.

Theoretical results that mathematically validate model choice for insufficient statistics are currently lacking on a general basis.

Our conclusion at this stage is to opt for a cautionary approach in ABC model choice, handling it as an exploratory tool rather than trusting the Bayes factor approximation. The corresponding degree of approximation cannot be evaluated, except via Monte Carlo evaluations of the model selection performances of ABC. More empirical measures such as those proposed in the DIY-ABC software (3) and in ref. 9 thus seem to be the only available solution at the current time for conducting model comparison.

We stress that, although refs. 10 and 11 repeatedly expressed reservations about the formal validity of the ABC approach in statistical testing, those criticisms were rebutted in refs. 12–14 and are not relevant for the current paper.

Statistical Methods

The ABC Algorithm. The setting in which ABC operates is the approximation of a simulation from the posterior distribution $\pi(\theta|\mathbf{y}) \propto \pi(\theta)f(\mathbf{y}|\theta)$ when distributions associated with both the prior π and the likelihood f can be simulated (the latter being unavailable in closed form). The first ABC algorithm was introduced by ref. 5 as follows: Given a sample \mathbf{y} from a sample space \mathcal{D} , a sample $(\theta_1, \dots, \theta_M)$ is produced by

Algorithm 1: ABC sampler

```
for  $i = 1$  to  $N$  do
  repeat
    Generate  $\theta'$  from the prior distribution  $\pi(\cdot)$ 
    Generate  $\mathbf{z}$  from the likelihood  $f(\cdot|\theta')$ 
  until  $\rho\{\eta(\mathbf{z}), \eta(\mathbf{y})\} \leq \epsilon$ 
  set  $\theta_i = \theta'$ 
end for
```

The parameters of the ABC algorithm are the so-called summary statistic $\eta(\cdot)$, the distance $\rho\{\cdot, \cdot\}$, and the tolerance level $\epsilon > 0$. The approximation of the posterior distribution $\pi(\theta|\mathbf{y})$ provided by the ABC sampler is to instead sample from the marginal in θ of the joint distribution

$$\pi_\epsilon(\theta, \mathbf{z}|\mathbf{y}) = \frac{\pi(\theta)f(\mathbf{z}|\theta)\mathbb{I}_{A_{\epsilon, \mathbf{y}}}(\mathbf{z})}{\int_{A_{\epsilon, \mathbf{y}} \times \Theta} \pi(\theta)f(\mathbf{z}|\theta)d\mathbf{z}d\theta},$$

where $\mathbb{I}_B(\cdot)$ denotes the indicator function of B and

Author contributions: C.P.R., J.-M.M., and N.S.P. designed research; C.P.R., J.-M.M., and N.S.P. performed research; J.-M.C. and J.-M.M. analyzed data; and C.P.R., J.-M.C., and J.-M.M. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

Freely available online through the PNAS open access option.

¹To whom correspondence should be addressed. E-mail: Christian.Robert@ceremade.dauphine.fr.

This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1102900108/-DCSupplemental.

$$A_{\epsilon, \mathbf{y}} = \{\mathbf{z} \in \mathcal{D} | \rho\{\eta(\mathbf{z}), \eta(\mathbf{y})\} \leq \epsilon\}.$$

The basic justification of the ABC approximation is that, when using a sufficient statistic η and a small (enough) tolerance ϵ , we have

$$\pi_{\epsilon}(\boldsymbol{\theta} | \mathbf{y}) = \int \pi_{\epsilon}(\boldsymbol{\theta}, \mathbf{z} | \mathbf{y}) d\mathbf{z} \approx \pi(\boldsymbol{\theta} | \mathbf{y}).$$

In practice, the statistic η is necessarily insufficient (because only exponential families enjoy sufficient statistics with fixed dimension; see ref. 15) and the approximation then converges to the less informative $\pi(\boldsymbol{\theta} | \eta(\mathbf{y}))$ when ϵ goes to zero. This loss of information is a necessary price to pay for the access to computable quantities and $\pi(\boldsymbol{\theta} | \eta(\mathbf{y}))$ provides a convergent inference on $\boldsymbol{\theta}$ when $\boldsymbol{\theta}$ is identifiable in the distribution of $\eta(\mathbf{y})$ (16). While acknowledging the gain brought by ABC in handling Bayesian inference in complex models, and the existence of involved summary selection mechanisms (17, 18), we demonstrate here that the loss due to the ABC approximation may be arbitrary in the specific setting of Bayesian model choice via posterior model probabilities.

ABC Model Choice. The standard Bayesian tool for model comparison is the marginal likelihood (19)

$$w(\mathbf{y}) = \int_{\Theta} \pi(\boldsymbol{\theta}) f(\mathbf{y} | \boldsymbol{\theta}) d\boldsymbol{\theta},$$

which leads to the Bayes factor for comparing the evidences of models with likelihoods $f_1(\mathbf{y} | \boldsymbol{\theta}_1)$ and $f_2(\mathbf{y} | \boldsymbol{\theta}_2)$,

$$B_{12}(\mathbf{y}) = \frac{w_1(\mathbf{y})}{w_2(\mathbf{y})} = \frac{\int_{\Theta_1} \pi_1(\boldsymbol{\theta}_1) f_1(\mathbf{y} | \boldsymbol{\theta}_1) d\boldsymbol{\theta}_1}{\int_{\Theta_2} \pi_2(\boldsymbol{\theta}_2) f_2(\mathbf{y} | \boldsymbol{\theta}_2) d\boldsymbol{\theta}_2}.$$

As detailed in ref. 12, it provides a valid criterion for model comparison that is naturally penalized for model complexity.

Bayesian model choice proceeds by creating a probability structure across M models (or likelihoods). It introduces the model index \mathcal{M} as an extra unknown parameter, associated with its prior distribution, $\pi(\mathcal{M} = m)$ ($m = 1, \dots, M$), whereas the prior distribution on the parameter is conditional on the value m of the \mathcal{M} index, denoted by $\pi_m(\boldsymbol{\theta}_m)$ and defined on the parameter space Θ_m . The choice between those models is then driven by the posterior distribution of \mathcal{M} ,

$$\mathbb{P}(\mathcal{M} = m | \mathbf{y}) = \pi(\mathcal{M} = m) w_m(\mathbf{y}) / \sum_k \pi(\mathcal{M} = k) w_k(\mathbf{y}),$$

where $w_k(\mathbf{y})$ denotes the marginal likelihood for model k .

Although this posterior distribution is straightforward to interpret, it offers a challenging computational conundrum in Bayesian analysis. When the likelihood is not available, ABC represents the almost unique solution. Ref. 5 describes the use of model choice based on ABC for distinguishing between different mutation models. The justification behind the method is that the average ABC acceptance rate associated with a given model is proportional to the posterior probability corresponding to this approximative model, when identical summary statistics, distance, and tolerance level are used over all models. In practice, an estimate of the ratio of marginal likelihoods is given by the ratio of observed acceptance rates. Using Bayes formula, estimates of the posterior probabilities are straightforward to derive. This approach has been widely implemented in the literature (see, e.g., refs. 20–23).

A representative illustration of the use of an ABC model-choice approach is given by ref. 21, which analyses the European invasion of the Western corn rootworm, North America's most destructive corn pest. Because this pest was initially introduced

in Central Europe, it was believed that subsequent outbreaks in Western Europe originated from this area. Based on an ABC model-choice analysis of the genetic variability of the rootworm, the authors conclude that this belief is false: There have been at least three independent introductions from North America during the past two decades.

The above estimate is improved by regression regularization (24), where model indices are processed as categorical variables in a polychotomous regression. When comparing two models, this involves a standard logistic regression. Rejection-based approaches were lately introduced by refs. 3, 25, and 26, in a Monte Carlo simulation of model indices as well as model parameters. Those recent extensions are already widely used in population genetics, as exemplified by refs. 27–36. Another illustration of the popularity of this approach is given by the availability of four softwares implementing ABC model-choice methodologies:

- ABC-SysBio, which relies on a sequential Monte Carlo (SMC)-based ABC for inference in system biology, including model choice (26).
- ABCToolbox, which proposes SMC and Markov chain Monte Carlo implementations, as well as Bayes factor approximation (37).
- DIY-ABC, which relies on a regularized ABC model choice (ABC-MC) algorithm on population history using molecular markers (3).
- PopABC, which relies on a regular ABC-MC algorithm for genealogical simulation (38).

As exposed in, e.g., refs. 25, 39, or 40, once \mathcal{M} is incorporated within the parameters, the ABC approximation to its posterior follows from the same principles as in regular ABC. The corresponding implementation is as follows, using for the summary statistic a statistic $\eta(\mathbf{z}) = \{\eta_1(\mathbf{z}), \dots, \eta_M(\mathbf{z})\}$ that is the concatenation of the summary statistics used for all models (with an obvious elimination of duplicates):

Algorithm 2: ABC-MC

```

for  $i = 1$  to  $N$  do
  repeat
    Generate  $m$  from the prior  $\pi(\mathcal{M} = m)$ 
    Generate  $\boldsymbol{\theta}_m$  from the prior  $\pi_m(\boldsymbol{\theta}_m)$ 
    Generate  $\mathbf{z}$  from the model  $f_m(\mathbf{z} | \boldsymbol{\theta}_m)$ 
  until  $\rho\{\eta(\mathbf{z}), \eta(\mathbf{y})\} \leq \epsilon$ 
  Set  $m^{(i)} = m$  and  $\boldsymbol{\theta}^{(i)} = \boldsymbol{\theta}_m$ 
end for

```

The ABC estimate of the posterior probability $\pi(\mathcal{M} = m | \mathbf{y})$ is then the frequency of acceptances from model m in the above simulation $\hat{\pi}(\mathcal{M} = m | \mathbf{y}) = N^{-1} \sum_{i=1}^N \mathbb{I}_{m^{(i)}=m}$. This also corresponds to the frequency of simulated pseudodatasets from model m that are closer to the data \mathbf{y} than the tolerance ϵ . In order to improve the estimation by smoothing, ref. 3 follows the rationale that motivated the use of a local linear regression in ref. 2 and relies on a weighted polychotomous regression to estimate $\pi(\mathcal{M} = m | \mathbf{y})$ based on the ABC output. This modeling is implemented in the DIY-ABC software.

The Difficulty with ABC-MC. There is a fundamental discrepancy between the genuine Bayes factors/posterior probabilities and the approximations resulting from ABC-MC.

The ABC approximation to a Bayes factor, B_{12} say, resulting from Algorithm 2, is

$$\widehat{B}_{12}(\mathbf{y}) = \pi(\mathcal{M} = 2) \sum_{i=1}^N \mathbb{I}_{m^{(i)}=1} / \pi(\mathcal{M} = 1) \sum_{i=1}^N \mathbb{I}_{m^{(i)}=2}.$$

An alternative representation is given by

$$\widehat{B}_{12}(\mathbf{y}) = \frac{\pi(\mathcal{M} = 2) \sum_{t=1}^T \mathbb{I}_{m^t=1} \mathbb{I}_{\rho\{\eta(\mathbf{z}^t), \eta(\mathbf{y})\} \leq \epsilon}}{\pi(\mathcal{M} = 1) \sum_{t=1}^T \mathbb{I}_{m^t=2} \mathbb{I}_{\rho\{\eta(\mathbf{z}^t), \eta(\mathbf{y})\} \leq \epsilon}},$$

where the pairs (m^t, \mathbf{z}^t) are simulated from the joint prior and T is the number of simulations necessary for N acceptances in Algorithm 2. In order to study the limit of this approximation, we first let T go to infinity. (For simplification purposes and without loss of generality, we choose a uniform prior on the model index.) The limit of $\widehat{B}_{12}(\mathbf{y})$ is then

$$\begin{aligned} B_{12}^{\epsilon}(\mathbf{y}) &= \frac{\mathbb{P}\{\mathcal{M} = 1, \rho\{\eta(\mathbf{z}), \eta(\mathbf{y})\} \leq \epsilon\}}{\mathbb{P}\{\mathcal{M} = 2, \rho\{\eta(\mathbf{z}), \eta(\mathbf{y})\} \leq \epsilon\}} \\ &= \frac{\int \mathbb{I}_{\rho\{\eta(\mathbf{z}), \eta(\mathbf{y})\} \leq \epsilon} \pi_1(\boldsymbol{\theta}_1) f_1(\mathbf{z}|\boldsymbol{\theta}_1) d\mathbf{z} d\boldsymbol{\theta}_1}{\int \mathbb{I}_{\rho\{\eta(\mathbf{z}), \eta(\mathbf{y})\} \leq \epsilon} \pi_2(\boldsymbol{\theta}_2) f_2(\mathbf{z}|\boldsymbol{\theta}_2) d\mathbf{z} d\boldsymbol{\theta}_2} \\ &= \frac{\int \mathbb{I}_{\rho\{\eta, \eta(\mathbf{y})\} \leq \epsilon} \pi_1(\boldsymbol{\theta}_1) f_1^{\eta}(\boldsymbol{\theta}_1) d\boldsymbol{\theta}_1}{\int \mathbb{I}_{\rho\{\eta, \eta(\mathbf{y})\} \leq \epsilon} \pi_2(\boldsymbol{\theta}_2) f_2^{\eta}(\boldsymbol{\theta}_2) d\boldsymbol{\theta}_2}, \end{aligned}$$

where $f_1^{\eta}(\boldsymbol{\theta}_1)$ and $f_2^{\eta}(\boldsymbol{\theta}_2)$ denote the densities of $\eta(\mathbf{z})$ when $\mathbf{z} \sim f_1(\mathbf{z}|\boldsymbol{\theta}_1)$ and $\mathbf{z} \sim f_2(\mathbf{z}|\boldsymbol{\theta}_2)$, respectively. By L'Hospital formula, if ϵ goes to zero, the above converges to

$$B_{12}^{\eta}(\mathbf{y}) = \int \pi_1(\boldsymbol{\theta}_1) f_1^{\eta}(\boldsymbol{\theta}_1) d\boldsymbol{\theta}_1 / \int \pi_2(\boldsymbol{\theta}_2) f_2^{\eta}(\boldsymbol{\theta}_2) d\boldsymbol{\theta}_2,$$

namely the Bayes factor for testing model 1 versus model 2 based on the sole observation of $\eta(\mathbf{y})$. This result reflects the current perspective on ABC: The inference derived from the ideal ABC output when $\epsilon = 0$ uses only the information contained in $\eta(\mathbf{y})$. Thus, in the limiting case, i.e., when the algorithm uses an infinite computational power, the ABC odds ratio does not account for features of the data other than the value of $\eta(\mathbf{y})$, which is why the limiting Bayes factor depends only on the distribution of η under both models.

When running ABC for point estimation, the use of an insufficient statistic does not usually jeopardize convergence of the method. As shown, e.g., in ref. 16, Theorem 2, the noisy version of ABC as an inference method is convergent under usual regularity conditions for model-based Bayesian inference (41), including identifiability of the parameter for the insufficient statistic η . In contrast, the loss of information induced by η may seriously impact model-choice Bayesian inference. Indeed, the information contained in $\eta(\mathbf{y})$ is less than the information contained in \mathbf{y} and this even in most cases when $\eta(\mathbf{y})$ is a sufficient statistic for *both models*. In other words, $\eta(\mathbf{y})$ being sufficient for both $f_1(\mathbf{y}|\boldsymbol{\theta}_1)$ and $f_2(\mathbf{y}|\boldsymbol{\theta}_2)$ does not usually imply that $\eta(\mathbf{y})$ is sufficient for $\{m, f_m(\mathbf{y}|\boldsymbol{\theta}_m)\}$. To see why this is the case, consider the most favorable case, namely when $\eta(\mathbf{y})$ is a sufficient statistic for both models. We then have by the factorization theorem (15) that $f_i(\mathbf{y}|\boldsymbol{\theta}_i) = g_i(\mathbf{y}) f_i^{\eta}(\boldsymbol{\theta}_i|\eta(\mathbf{y}))$ ($i = 1, 2$); i.e.,

$$\begin{aligned} B_{12}(\mathbf{y}) &= \frac{w_1(\mathbf{y})}{w_2(\mathbf{y})} = \frac{\int_{\Theta_1} \pi(\boldsymbol{\theta}_1) g_1(\mathbf{y}) f_1^{\eta}(\boldsymbol{\theta}_1|\eta(\mathbf{y})) d\boldsymbol{\theta}_1}{\int_{\Theta_2} \pi(\boldsymbol{\theta}_2) g_2(\mathbf{y}) f_2^{\eta}(\boldsymbol{\theta}_2|\eta(\mathbf{y})) d\boldsymbol{\theta}_2} \\ &= \frac{g_1(\mathbf{y}) \int \pi_1(\boldsymbol{\theta}_1) f_1^{\eta}(\boldsymbol{\theta}_1|\eta(\mathbf{y})) d\boldsymbol{\theta}_1}{g_2(\mathbf{y}) \int \pi_2(\boldsymbol{\theta}_2) f_2^{\eta}(\boldsymbol{\theta}_2|\eta(\mathbf{y})) d\boldsymbol{\theta}_2} = \frac{g_1(\mathbf{y})}{g_2(\mathbf{y})} B_{12}^{\eta}(\mathbf{y}). \quad [1] \end{aligned}$$

Thus, unless $g_1(\mathbf{y}) = g_2(\mathbf{y})$, as in the special case of Gibbs random fields detailed below, the two Bayes factors differ by the ratio $g_1(\mathbf{y})/g_2(\mathbf{y})$, which is equal to one only in a very small number of known cases. This decomposition is a straightforward proof that a modelwise sufficient statistic is usually not sufficient across models, hence for model comparison. An immediate corollary is that the ABC-MC approximation does not always converge to the exact Bayes factor.

The discrepancy between limiting ABC and genuine Bayesian inferences does not come as a surprise, because ABC is indeed an approximation method. Users of ABC algorithms are therefore prepared for some degree of imprecision in their final answer, a point stressed by refs. 16 and 42 when they qualify ABC as exact inference on a wrong model. However, the magnitude of the difference between $B_{12}(\mathbf{y})$ and $B_{12}^{\eta}(\mathbf{y})$ expressed by Eq. 1 is such that there is no direct connection between both answers. In a general setting, if η has the same dimension as one component of the n components of \mathbf{y} , the ratio $g_1(\mathbf{y})/g_2(\mathbf{y})$ is equivalent to a density ratio for a sample of size $O(n)$; hence it can be arbitrarily small or arbitrarily large when n grows. Contrastingly, the Bayes factor $B_{12}^{\eta}(\mathbf{y})$ is based on an equivalent to a single observation and hence does not necessarily converge with n to the correct limit, as shown by the Poisson and normal examples below and in *SI Text*. The conclusion derived from the ABC-based Bayes factor may therefore completely differ from the conclusion derived from the exact Bayes factor and there is no possibility of a generic agreement between both, or even of a manageable correction factor. This discrepancy means that a theoretical validation of the ABC-based model-choice procedure is currently missing and that, due to this absence, potentially costly simulation-based assessments are required when calling for this procedure.

Therefore, users must be warned that ABC approximations to Bayes factors do not perform as standard numerical or Monte Carlo approximations, with the exception of Gibbs random fields detailed in the next section. In all cases when $g_1(\mathbf{y})/g_2(\mathbf{y})$ differs from one, no inference on the true Bayes factor can be derived from the ABC-MC approximation without further information on the ratio $g_1(\mathbf{y})/g_2(\mathbf{y})$, most often unavailable in settings where ABC is necessary.

Ref. 40 also derived this relation between both Bayes factors in their formula 18. Although they still advocate the use of ABC model choice in the absence of sufficient statistic, we stress that no theoretical guarantee can be given on the validity of the ABC approximation to the Bayes factor and hence of its use as a model-choice procedure.

Note that the authors of ref. 43 resort to full allelic distributions in an ABC framework, instead of choosing summary statistics. They show how to apply ABC using allele frequencies to draw inferences in cases where selecting suitable summary statistics is difficult (and where the complexity of the model or the size of dataset prohibits the use of full-likelihood methods). In such settings, ABC-MC does not suffer from the divergence exhibited here because the measure of distance does not involve a reduction of the sample. The same comment applies to the ABC-SysBio software of ref. 26, which relies on the whole dataset. The theoretical validation of ABC inference in hidden Markov models by ref. 44 should also extend to the model-choice setting because the approach does not rely on summary statistics but instead on the whole sequence of observations.

Results

The Specific Case of Gibbs Random Fields. In an apparent contradiction with the above, ref. 25 showed that the computation of the posterior probabilities of Gibbs random fields under competition can be done via ABC techniques, which provide a converging approximation to the true Bayes factor. The reason for this result is that, for these models in the above ratio Eq. 1, $g_1(\mathbf{y}) = g_2(\mathbf{y})$. The validation of an ABC comparison of Gibbs random fields is thus that their specific structure allows for a sufficient statistic vector that runs across models and therefore leads to an exact (when $\epsilon = 0$) simulation from the posterior probabilities of the models. Each Gibbs random field model has its own sufficient statistic $\eta_m(\cdot)$, and ref. 25 exposed the fact that the vector of statistics $\boldsymbol{\eta}(\cdot) = (\eta_1(\cdot), \dots, \eta_M(\cdot))$ is also sufficient for the joint parameter $(\mathcal{M}, \boldsymbol{\theta}_1, \dots, \boldsymbol{\theta}_M)$.

The validity of the importance sampling approximation can obviously be questioned in both experiments; however, [Figs. S3](#) and [S4](#) display a strong stability of the posterior probability IS approximation across 10 independent runs for 5 different datasets and give proper confidence in this approach. Increasing the number of loci to 50 and the sample size to 100 individuals per population (see [SI Text](#)) leads to posterior probabilities of the true scenario overwhelmingly close to one ([Fig. S5](#)), thus blur-

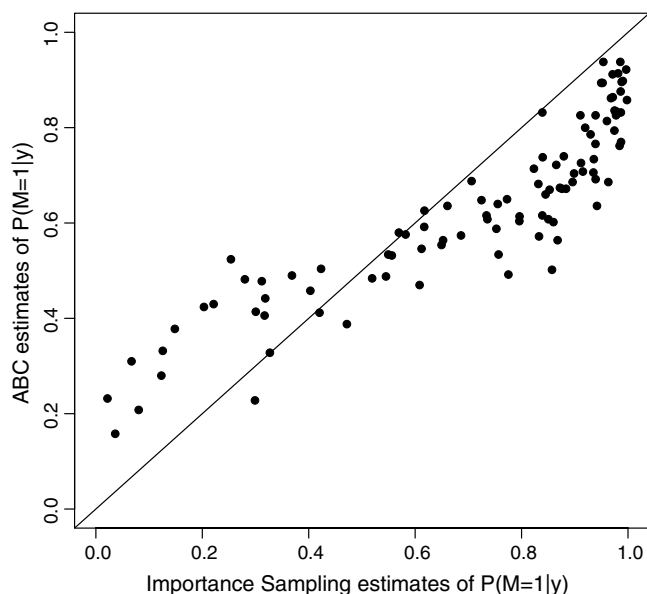


Fig. 1. Comparison of IS and ABC estimates of the posterior probability of scenario 1 in the first population genetic experiment, using 24 summary statistics.

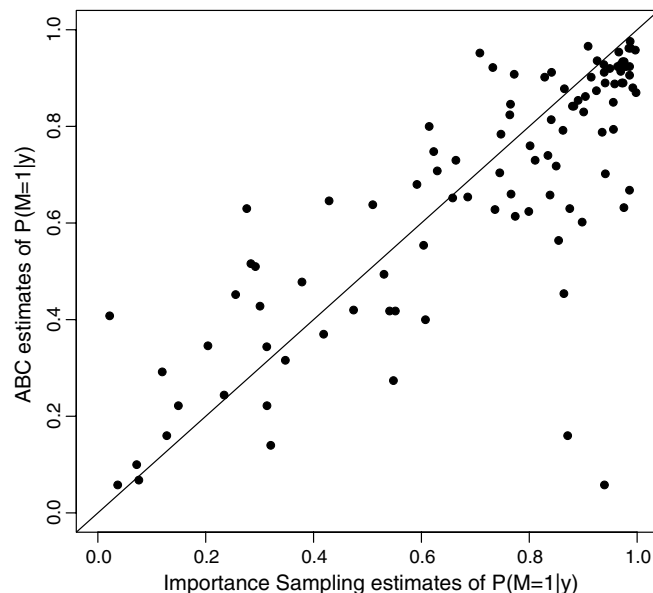


Fig. 2. Same caption as Fig. 1 when using 15 summary statistics.

ring the distinction between ABC and likelihood-based estimates but also reassuring the ability of ABC to provide the right choice of model with a higher information content of the data. We note that, for this experiment, all ABC-based decisions conclude in favor of the correct model. As shown in Fig. S6, this second experiment requires an increase in the number of importance sampling simulations because of a higher variability in the likelihood.

Discussion

Since its introduction by refs. 1 and 5, ABC has been extensively used in areas involving complex likelihoods, both for point estimation and testing of hypotheses. In realistic settings, with the exception of models such as Gibbs random fields, which are resilient with respect to their sufficient statistics, the conclusions drawn on model comparison cannot be trusted per se but require further simulation analyses as to the pertinence of the (ABC) Bayes factor based on the summary statistics. This paper has

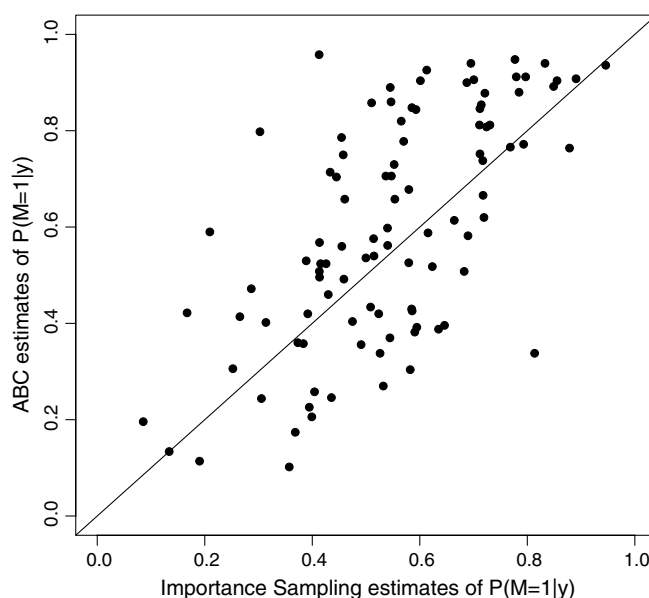


Fig. 3. Comparison of IS and ABC estimates of the posterior probability of scenario 1 in the second population genetic experiment.

examined in details only the case when the summary statistics are sufficient for both models, while practical situations imply the use of insufficient statistics. The rapidly increasing number of applications estimating posterior probabilities by ABC indicates a clear need for further evaluations of the worth of those estimations, especially because our population genetic experiments showed that those ABC approximations were selecting the proper model.

Further research is needed for producing trustworthy approximations to the posterior probabilities of models. At this stage, unless the whole data are involved in the ABC approximation as in ref. 43, our conclusion on ABC-based model choice is to exploit the approximations in an exploratory manner as measures of discrepancies rather than genuine posterior probabilities. This direction relates with the analyses found in ref. 9. Furthermore, a version of this exploratory analysis is already provided in the DIYABC software of ref. 3. An option in this software allows for the computation of a Monte Carlo evaluation of false allocation

rates resulting from using the ABC posterior probabilities in selecting a model as the most likely. For instance, in the setting of both our population genetic experiments, DIY-ABC gives false allocation rates equal to 20% (under scenarios 1 and 2) and 14.5% and 12.5% (under scenarios 1 and 2), respectively. This evaluation obviously shifts away from the performances of ABC as an approximation to the posterior probability toward the performances of the whole Bayesian apparatus for selecting a model, but this nonetheless represents a useful and manageable quality assessment for practitioners.

ACKNOWLEDGMENTS. The authors are grateful to the reviewers and to Michael Stumpf for their comments. Computations were performed on the INRA CBGP and MIGALE clusters. C.P.R., J.-M.C., and J.-M.M. have been partly supported by Agence Nationale de la Recherche via the 2009–2013 project EMILE (Études de Méthodes Inférentielles et Logiciels pour l'Évolution). N.S.P. gratefully acknowledges National Science Foundation Grant DMS 1107070.

- Tavaré S, Balding D, Griffith R, Donnelly P (1997) Inferring coalescence times from DNA sequence data. *Genetics* 145:505–518.
- Beaumont M, Zhang W, Balding D (2002) Approximate Bayesian computation in population genetics. *Genetics* 162:2025–2035.
- Cornuet JM, et al. (2008) Inferring population history with DIYABC: A user-friendly approach to Approximate Bayesian Computation. *Bioinformatics* 24:2713–2719.
- Robert C, Casella G (2004) *Monte Carlo Statistical Methods* (Springer, New York), 2nd Ed.
- Pritchard J, Seielstad M, Perez-Lezaun A, Feldman M (1999) Population growth of human Y chromosomes: A study of Y chromosome microsatellites. *Mol Biol Evol* 16:1791–1798.
- Beaumont M (2010) Approximate Bayesian computation in evolution and ecology. *Annu Rev Ecol Syst* 41:379–406.
- Lopes J, Beaumont M (2010) ABC: A useful Bayesian tool for the analysis of population data. *Infect Genet Evol* 10:825–832.
- Csilléry K, Blum M, Gaggiotti O, François O (2010) Approximate Bayesian computation (ABC) in practice. *Trends Ecol Evol* 25:410–418.
- Ratmann O, Andrieu C, Wuji F, Richardson S (2009) Model criticism based on likelihood-free inference, with an application to protein network evolution. *Proc Natl Acad Sci USA* 106:1–6.
- Templeton A (2009) Statistical hypothesis testing in intraspecific phylogeography: Nested clade phylogeographical analysis vs approximate Bayesian computation. *Mol Ecol* 18:319–331.
- Templeton A (2010) Coherent and incoherent inference in phylogeography and human evolution. *Proc Natl Acad Sci USA* 107:6376–6381.
- Beaumont M, et al. (2010) In defense of model-based inference in phylogeography. *Mol Ecol* 19:436–446.
- Csilléry K, Blum M, Gaggiotti O, François O (2010) Invalid arguments against ABC: A reply to A. R. Templeton. *Trends Ecol Evol* 25:490–491.
- Berger J, Fienberg S, Raftery A, Robert C (2010) Incoherent phylogeographic inference. *Proc Natl Acad Sci USA* 107:E57.
- Lehmann E, Casella G (1998) *Theory of Point Estimation (revised edition)* (Springer, New York).
- Fearnhead P, Prangle D Semi-automatic approximate Bayesian computation. *J Royal Statist Soc*, in press.
- Joyce P, Marjoram P (2008) Approximately sufficient statistics and Bayesian computation. *Stat Appl Genet Mol Biol* 7:article 26.
- Nunes MA, Balding DJ (2010) On optimal selection of summary statistics for approximate Bayesian computation. *Stat Appl Genet Mol Biol* 9:article 34.
- Jeffreys H (1939) *Theory of Probability* (Clarendon Press, Oxford, UK), 1st Ed.
- Estoup A, Beaumont M, Sennedot F, Moritz C, Cornuet J (2004) Genetic analysis of complex demographic scenarios: Spatially expanding populations of the cane toad, *Bufo marinus*. *Evolution* 58:2021–2036.
- Miller N, et al. (2005) Multiple transatlantic introductions of the Western corn rootworm. *Science* 310:992.
- Pascual M, et al. (2007) Introduction history of *Drosophila subobscura* in the New World: A microsatellite-based survey using ABC methods. *Mol Ecol* 16:3069–3083.
- Sainudiin R, et al. (2011) Experiments with the site frequency spectrum. *Bull Math Biol* 73:829–872.
- Fagundes N, et al. (2007) Statistical evaluation of alternative models of human evolution. *Proc Natl Acad Sci USA* 104:17614–17619.
- Grelaud A, Marin JM, Robert C, Rodolphe F, Tally F (2009) Likelihood-free methods for model choice in Gibbs random fields. *Bayesian Anal* 3:427–442.
- Toni T, Welch D, Strelkowa N, Ipsen A, Stumpf M (2009) Approximate Bayesian computation scheme for parameter inference and model selection in dynamical systems. *J R Soc Interf* 6:187–202.
- Belle E, Benazzo A, Ghirotto S, Colonna V, Barbujani G (2008) Comparing models on the genealogical relationships among Neandertal, Cro-Magnon and modern Europeans by serial coalescent simulations. *Heredity* 102:218–225.
- Cornuet JM, Ravigné V, Estoup A (2010) Inference on population history and model checking using DNA sequence and microsatellite data with the software DIYABC (v10). *BMC Bioinformatics* 11:401.
- Excoffier C, Leuenberger D, Wegmann L (2009) Bayesian computation and model selection in population genetics. *arXiv:0901.2231*.
- Ghirotto S, et al. (2010) Inferring genealogical processes from patterns of bronze-age and modern DNA variation in Sardinia. *Mol Biol Evol* 27:875–886.
- Guillemaud T, Beaumont M, Ciosi M, Cornuet JM, Estoup A (2009) Inferring introduction routes of invasive species using approximate Bayesian computation on microsatellite data. *Heredity* 104:88–99.
- Leuenberger C, Wegmann D (2010) Bayesian computation and model selection without likelihoods. *Genetics* 184:243–252.
- Patin E, et al. (2009) Inferring the demographic history of African farmers and Pygmy hunter-gatherers using a multilocus resequencing data set. *PLoS Genetics* 5:e1000448.
- Ramakrishnan U, Hadly E (2009) Using phylogenetics to reveal cryptic population histories: Review and synthesis of 29 ancient DNA studies. *Mol Ecol* 18:1310–1330.
- Verdu P, et al. (2009) Origins and genetic diversity of Pygmy hunter-gatherers from western central Africa. *Curr Biol* 19:312–318.
- Wegmann D, Excoffier L (2010) Bayesian inference of the demographic history of chimpanzees. *Mol Biol Evol* 27:1425–1435.
- Wegmann D, Leuenberger C, Neuenschwander S, Excoffier L (2010) ABCtoolbox: A versatile toolkit for approximate Bayesian computations. *BMC Bioinformatics* 11:116–123.
- Lopes JS, Balding D, Beaumont MA (2009) PopABC: A program to infer historical demographic parameters. *Bioinformatics* 25:2747–2749.
- Toni T, Stumpf M (2010) Simulation-based model selection for dynamical systems in systems and population biology. *Bioinformatics* 26:104–110.
- Didelot X, Everitt R, Johansen A, Lawson D (2011) Likelihood-free estimation of model evidence. *Bayesian Anal* 6:1–28.
- Bernardo J, Smith A (1994) *Bayesian Theory* (John Wiley, New York).
- Wilkinson RD (2008) Approximate Bayesian computation (ABC) gives exact results under the assumption of model error. *arXiv:0811.3355*.
- Sousa V, Fritz M, Beaumont M, Chikhi L (2009) Approximate Bayesian computation without summary statistics: the case of admixture. *Genetics* 181:1507–1519.
- Dean T, Singh S, Jasra A, Peters G (2011) Parameter estimation for hidden Markov models with intractable likelihoods. *arXiv:1103.5399*.
- Marin J, Pudlo P, Robert C, Ryder R (2011) Approximate Bayesian computational methods. *Stat Comput*, in press.
- Estoup A, Clegg S (2003) Bayesian inferences on the recent island colonization history by the bird *Zosterops lateralis lateralis*. *Mol Ecol* 12:657–674.
- Lombaert E, et al. (2010) Bridgehead effect in the worldwide invasion of the biocontrol *Harlequin Ladybird*. *PLoS ONE* 5:e9743.
- Stephens D, Donnelly P (2000) Inference in population genetics (with discussion). *J R Stat Soc Series B Stat Methodol* 62:602–655.