

In the manuscript entitled “Physiological and behavioural resistance of malaria vectors in rural West-Africa : a data mining study to address their fine-scale spatiotemporal heterogeneity, drivers, and predictability” presents a modelling work taking advantage of a very large dataset to identify environmental drivers of insecticide resistance in malaria vectors. Among the insecticide resistance traits investigated, they are mutations in *kdr* and *ace-1* loci and also behavioural resistance phenotypes. As detailed in the ms, genetic basis of behavioural phenotypes are not characterized and the apparent resistant phenotypes have not been related to molecular mechanism. Due to the absence of evidence of inheritance of such behavioural phenotypes, we cannot clearly qualify these as resistance. Therefore the discussion related to this should be more developed. Overall the ms is well written and provide clear explanations to understand their complex models so that their work is quite accessible to a large audience.

Here are some comments to help improve the ms.

The use of the term “development” for an adaptive traits in the field of ecology and evolution is misleading. Indeed, development is a very complex process more often used at the individual level that does not describe an adaptive process that occurs at the population level. The term selection is more appropriate and should be used along the manuscript (for instance but not limited to selection “of physiological mechanism of resistance”, l72; selection “of resistant phenotypes”, l77; “of physiological and behavioral resistances”, l125; “of the *kdr-e* mutation”, l559; “of resistances”, l737)

L190: It is not clearly specified in this section whether mosquitoes from IC were genotyped for *kdr-w* and *-e* and *ace1 G119S*. Authors should add this information with some brief justification here.

L254: Streams are used as proxy of breeding sites but several stream characteristics (such as the width and the inter connections) are important factors for mosquito oviposition and density. Authors should more information on the streams in the studied area and provide evidence or reference that such streams are primary breeding sites for *Anopheles gambiae*?

L297: I wonder how relevant/important is to model separately for each site; authors should provide a clearer justification for this strategy. One can question the generalization of their results to other similar sites which could decrease the relevance for the scientific community.

L321: Authors should provide examples of empirically known collinear variables.

L397: Authors presented a detailed results of mosquito collections in both sites. However, overall percentage of mosquito species did not reach 100%: 98% in Ivory Coast and 86% in Burkina Faso. What other vectors were found?

Table 2: To what part of the table this computation refers to? Description of the computation of standard deviation may be more relevant in the mat & met section.

L440: An explanation/justification should be provided on the removing of dependent variable with low number of resistant (i.e. “small size of their resistant class”). I would understand

that when sample size is very small but having few or no resistant mosquito in a village is still informative and should be considered.

Figure 3: The presentation of the effect of other variables should be better organized, probably splitting the insecticide effect and the environmental in two separate panels. Attention should be paid to the square indicators that are not clearly presented in the figure caption. There are two types of squares in the figures that should be both presented.

In the result section, the influence of *kdr-w* genotypes on the probability of collecting a resistant mosquitoes shown by orange squares in figure 3 is not presented clearly.

Related to figure 4, the difference between the inference made from glmm (explanatory) and RF (predictive) should be made clearer by providing more detailed explanation or by providing examples. To illustrate this point, the explanatory power for exophagy in *An. gambiae* from IC is very low, suggesting that none of the tested variables can explained exophagy variation or that these variables captured very little of this variation. Thus how could they explain (or predict) well exophagy ?

Generally, it should be clearly stated that non-significant variables are not presented.

L553: in the title, probably replace and by of

L554: One interesting result is the increase of *kdr-e* associated with the time of LLIN distribution. However, it is not challenged enough against the literature. Several reports showed that ageing of LLIN reduce their efficacy thus the insecticide selective pressure is reduced. So how do authors discuss that *kdr-e* increases if the selective pressure decreases?

L571: remove the bracket

L575: "As stated previously, weather may impact the fitness or the activity of mosquitoes carrying resistant genotypes; and may therefore in fine impact the probability of collecting a physiologically resistant mosquito". As exactly stated, this is repetitive and it may not be necessary for clarity unless it is discussed with different angle.

L577: Authors did discuss weather impacting fitness but only as a cost. Could the associations captured would possibly traduce an advantage of resistant individuals? (for instance rainfall) or is this related only to the current analysis? in such case more detailed information should be provided.

L581: Decrease of mutated allele is discussed as associated with hot season. Seasonality is different from hot (or hotter) vs cold (less hotter) season. Thus authors should define better the hot season in the context of west Africa.

L582: "Carrying a *kdr* mutation might be associated with a reduced ability to seek out optimal temperatures". Authors should rephrase this sentence to make it clearer.

L595: "The relative seasonal ..." Authors should rephrase this sentence to make it clearer.

L607: "to" should be replaced by "of"

L609: While genetic basis of behavioural phenotypes may be indeed found, it is difficult to understand how larval stage may support this. Maternal/paternal effect should better support a genetic basis of behavioural phenotypes and their associated adaptative changes (i.e. resistance) due to the inheritance of alleles to the next generation. This part of the discussion needs more arguments/clarifications.

L610: Authors should provide the ranges or confidence intervals with the average exophagy rates.

L613: Authors should provide estimates of the outdoor biting levels from their analysis and the literature ("past levels")

L622-625: Authors discuss the association between time and behavioral resistance with two opposite examples in the literature. They should provide details on the difference and similarities between these two studies and particularly vector species and insecticide resistance.

L632: Authors should explain what is the "activity" of the phenotypes.

L697: This study suggested more a correlative relation between LLIN and the rise of insecticide resistance than evidence.

L700: Authors should provide or recall the data to support the growing of resistance in a susceptible population.

L715: Clarifications are needed to better understand how managing vector control would be beneficial. For instance, why different strategy? why at small scale only?

L718: Authors should remove "such spatiotemporal scales" that is repeated at the beginning of the sentence.

L723: It would be important to explain why sampling occurred during the dry season when mosquito density is low.