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Detection of a serious error in the paper: "On identifiability of nonlinear ODE models and applications in viral dynamics"

Agostino Martinelli*

January 26, 2024

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Abstract

This note highlights a serious error in a paper published by SIAM Review (SIREV) in 2011. The error is in Section 6.2 of [1]. It is important to notify this error because of the following two reasons: (i) [1] is one of the most cited contributions in the field of identifiability of viral dynamics models, and (ii) the error is relevant because, as a result of it, a popular viral model (perhaps the most popular in the field of HIV dynamics) has been classified as identifiable. In contrast, three of its parameters are not identifiable, even locally. This note first proves the non uniqueness of the three unidentifiable parameters by exhibiting infinitely many distinct but indistinguishable values of them. The non uniqueness is even local. Then, this note details the error made by the authors of [1] which produced the claimed (but false) local identifiability of all the model parameters.

This note was first submitted and rejected by the SIAM Review Journal (SIREV), and then published on arXiv [5]. In this document, with respect to the version published on

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arXiv, we also include the feedback obtained from the editor of the Survey and Review section of SIREV and from the two reviewers selected by the editor. This feedback clearly highlights the technical inadequacy of the editor and reviewers and more generally shows how the editor has dramatically failed to correctly manage the review of a simple erratum. This is a serious and damaging problem for our scientific community.

1 Introduction

Section 6.2 of [1] provided an identifiability analysis of a popular viral model that describes the HIV/AIDS dynamics. The model is characterized by six parameters ($\lambda, \delta, \eta, \rho, N, c$) and the analysis concerned the case when one of them (η) is time varying. The model is characterized by the following equations:

$$\begin{cases} \dot{T}_U &= \lambda - \rho T_U - \eta(t)T_U V \\ \dot{T}_I &= \eta(t)T_U V - \delta T_I \\ \dot{V} &= N\delta T_I - cV \\ y &= [V, T_U + T_I], \end{cases} \quad (1)$$

which provide the dynamics and the outputs. The above equations are Equations (6.15-6.17) in Section 6.2 of [1]. The reader is addressed to Section 6.2 of [1] for the definition of all the quantities that appear in these equations.

Unfortunately, the result of the identifiability analysis in Section 6.2 of [1] is wrong. Specifically, when η is time varying, it is not true that all the model parameters are locally identifiable, as concluded by the authors of [1] at the end of Section 6.2. The result of a thorough identifiability analysis shows that only three of the five constant parameters are locally identifiable. The remaining two constant parameters (δ , and N), and the time varying parameter (η) cannot be uniquely identified, even locally.

In this note, we prove the non uniqueness of δ , N , and η by exhibiting infinitely many distinct but indistinguishable values of these parameters (Section 2). The non uniqueness is even local. Then, in Section 3 we detail the technical error in Section 6.2 of [1] that produced the claimed (but false) local identifiability of all the model parameters.

This note was submitted and rejected by the SIAM Review Journal (SIREV), and then published on arXiv [5]. In Section 4, we report (in red) the feedback obtained from the editor of the Survey and Review section of SIREV and from the two reviewers selected by the editor. We provide a discussion of this feedback by showing both the poor technical ability of the editor and the reviewers in carrying out simple and basic calculations and the inadequacy of the editor in taking a final decision.

2 Non uniqueness of δ , N , and η

Let us refer to the viral model in Section 6.2 of [1]. The constant parameters $\lambda, \delta, \rho, N, c$, the three states $T_U(t), T_I(t), V(t)$, and the time varying parameter $\eta(t)$ satisfy the three dynamical equations in (1). Starting from the above parameters and states, we introduce the following new constant parameters, the following new states, and the following new time varying parameter, for any $\tau \in \mathbb{R}$:

$$\begin{cases} \lambda' &= \lambda \\ \delta' &= \delta'(\tau) = \frac{\delta\rho}{(\rho-\delta)e^{\rho\tau} + \delta} \\ \rho' &= \rho \\ N' &= N'(\tau) = Ne^{\rho\tau} \\ c' &= c, \end{cases} \quad (2)$$

$$\begin{cases} T'_U &= T'_U(t, \tau) = T_U(t) + T_I(t) - \frac{T_I(t)}{\rho} (\delta e^{-\rho\tau} + \rho - \delta) \\ T'_I &= T'_I(t, \tau) = \frac{T_I(t)}{\rho} (\delta e^{-\rho\tau} + \rho - \delta) \\ V' &= V'(t) = V(t) \end{cases} \quad (3)$$

$$\eta' = \eta'(t, \tau) = \frac{\eta(t)T_U(t)V(t)\rho e^{\rho\tau} + [T_I(t)\delta^2 - T_I(t)\delta\rho - \eta(t)T_U(t)V(t)\delta][e^{\rho\tau} - 1]}{V(t)[T_I(t)\delta + T_U(t)\rho]e^{\rho\tau} - V(t)T_I(t)\delta} \quad (4)$$

We claim that all the above new constant parameters, the new states, and the new time varying parameter, are indistinguishable from the original ones, and this holds for any choice of $\tau \in \mathbb{R}$.

Our statement can be easily checked by a direct substitution.

First, the outputs $y_1(t) = T_U(t) + T_I(t)$ and $y_2(t) = V(t)$ remain the same because $T'_U(t, \tau) + T'_I(t, \tau) = T_U(t) + T_I(t)$ and $V'(t) = V(t)$.

Second, from (1) and (2-4) it is possible to check, by a simple substitution, the validity of the following dynamics of the new three states (see all the details in Appendix A):

$$\begin{cases} \frac{d}{dt}T'_U(t, \tau) &= \lambda' - \rho'T'_U(t, \tau) - \eta'(t, \tau)T'_U(t, \tau)V'(t) \\ \frac{d}{dt}T'_I(t, \tau) &= \eta'(t, \tau)T'_U(t, \tau)V'(t) - \delta'T'_I(t, \tau) \\ \frac{d}{dt}V'(t) &= N'\delta'T'_I(t, \tau) - c'V'(t) \end{cases} \quad (5)$$

In other words, the new three states, satisfy exactly the same dynamical equations in (1) with the new parameters.

We conclude that $T'_U, T'_I, V', \eta', \lambda', \delta', \rho', N'$, and c' cannot be distinguished from $T_U, T_I, V, \eta, \lambda, \delta, \rho, N$, and c , respectively. Regarding the model parameters, as $\eta' \neq \eta, \delta' \neq \delta$, and $N' \neq N$, we conclude that η, δ , and N are not identifiable. Finally, we remark that τ can take infinitesimal values and that, in the limit of $\tau \rightarrow 0$, we have: $T'_U \rightarrow T_U, T'_I \rightarrow T_I, V' \rightarrow V, \eta' \rightarrow \eta, \delta' \rightarrow \delta$, and $N' \rightarrow N$. Therefore, we conclude that the three parameters η, δ , and N are not even locally identifiable.

In Chapter 6 of [2], we also provided a numerical test for the validity of the above fundamental new result (Section 6.6 of [2]). In particular, we adopted the same data set introduced in [4]. Finally, in Section 6.7 of [2] we characterized the minimal information that must be added to the knowledge of the two outputs, in order to make identifiable all the model parameters (and to make observable all the states).

We wish to emphasize that our claim was here easily proved by a simple substitution. What is not trivial is the analytic derivation of the expressions in (2-4). These expressions were analytically determined in [2], starting from the analytic solution of a fundamental problem, strongly connected with the problem of determining the identifiability of time varying parameters. This is the unknown input observability problem, whose general analytic solution was recently introduced in [3]. The analytic solution given in [2] is strongly based on the solution in [3] and provides the identifiability of any ODE model, even in the presence of time varying parameters and in the presence of any type of nonlinearity (and not necessarily polynomial, as for the methods discussed in [1]). Additionally, in contrast with the methods discussed in [1], it works automatically (i.e., by following the steps of a systematic procedure). Finally, in the presence of unidentifiability, it also provides, automatically, the local indistinguishable states and parameters (i.e., for the specific case, the non trivial expressions in (2-4), for infinitesimal τ).

3 The error in Section 6.2 of [1]

The derivation given in Section 6.2 of [1] contains a serious error that will be detailed in Section 3.2. To explain this serious error, we first need to highlight another minor error that could simply be a typo (Section 3.1).

3.1 Two typos in Equation (6.23) in [1]

Equation (6.23) was obtained from (6.21) and (6.22), which are correct. From (6.21) and (6.22), we obtain:

$$\begin{aligned} &\ddot{y}_1y_2\dot{y}_2 - \dot{y}_1y_2\ddot{y}_2 - \delta y_1y_2\ddot{y}_2 + \lambda y_2\ddot{y}_2 - (\delta + c)\dot{y}_1y_2\dot{y}_2 + (\delta\rho - \delta^2 - \delta c)y_1y_2\dot{y}_2 \\ &+ (\rho + \delta)\dot{y}_1y_2\dot{y}_2 + \lambda c y_2\dot{y}_2 + \rho c \dot{y}_1y_2^2 + (\rho\delta c - \delta^2 c)y_1y_2^2 - N\delta y_1\dot{y}_1y_2 \\ &+ c\dot{y}_1y_2^2 - N\delta(\rho + \delta)y_1\dot{y}_1y_2 - N\delta^2\rho y_1^2y_2 + N\delta^2\lambda y_1y_2 = 0 \end{aligned} \quad (6)$$

The differences between (6) and (6.23) are the following two:

1. The sixth term in (6.23) is not $(\delta\rho + \rho + \delta - \delta^2 - \delta c)y_1y_2\dot{y}_2$ but $(\delta\rho - \delta^2 - \delta c)y_1y_2\dot{y}_2 + (\rho + \delta)\dot{y}_1y_2\dot{y}_2$.

2. The seventh term in (6.23) is not $cy_2\dot{y}_2$ but $\lambda cy_2\dot{y}_2$.

3.2 The serious error made by the authors of [1]

Let us denote the expression in (6) by $\phi = \phi(y_1, \dot{y}_1, \ddot{y}_1, y_2, \dot{y}_2, \ddot{y}_2, \lambda, \delta, \rho, c, N)$. In this notation, Equation (6) becomes:

$$\phi = 0.$$

In Section 6.2 of [1], the local identifiability of all the parameters was claimed by referring to Equation (6.23). In particular, the authors suggested two methods to obtain the local identifiability: (i) by using the third statement of Theorem 3.8 in [1], and (ii) by using the implicit function Theorem (in accordance with the procedure given in Section 3.4 of [1]). We cannot comment the first method because the authors only provided the last polynomial (i.e., $B_n(u, y, \theta_1, \dots, \theta_q)$) of Theorem 3.8. They did not provide the remaining polynomials mentioned by the theorem (i.e., B_1, \dots, B_{n-1}).

Regarding the second method, the error is pointed out as follows. In accordance with the procedure in Section 3.4 of [1], we need, first of all, to compute the first 4 time derivatives of ϕ . In this manner, we obtain four additional equations, i.e.,

$$\phi^1 \equiv \frac{d}{dt}\phi = 0, \quad \dots, \quad \phi^4 \equiv \frac{d^4}{dt^4}\phi = 0$$

Then, we include all the above functions in the vector function Φ . In other words, we introduce the vector function $\Phi \equiv [\phi, \phi^1, \phi^2, \phi^3, \phi^4]^T$. As the parameters $\lambda, \delta, \rho, c, N$ are constant, Φ is a function of them and of the two outputs (y_1, y_2) and their time derivatives up to the sixth order. To check the identifiability of $\lambda, \delta, \rho, c, N$, the procedure in Section 3.4 of [1] uses the following equation:

$$\Phi = 0 \tag{7}$$

Now, by using the implicit function Theorem, we need to compute the Jacobian of Φ with respect to $\lambda, \delta, \rho, c, N$. By proceeding in this manner, we obtain a 5×5 matrix that we denote by M . The entries of M are expressed in terms of $\lambda, \delta, \rho, c, N, y_1, y_2$, and the time derivatives of y_1, y_2 , up to the sixth order.

The serious error made by the authors of [1] was to consider independent all the above quantities, i.e., $\lambda, \delta, \rho, c, N, y_1, y_2$, and the time derivatives of y_1, y_2 , up to the sixth order. By doing this we obtain that the rank of M is equal to 5 (and the authors concluded that all the model parameters are identifiable).

On the other hand, the two output functions, $y_1(t), y_2(t)$, and their time derivatives up to any order, cannot take arbitrary values. **They must satisfy the constraints due to the system dynamics.** In accordance with the dynamics constraints, we must express the two outputs (y_1, y_2) and their time derivatives up to the sixth order, in terms of the state (T_U, T_I, V), the model parameters $\lambda, \delta, \rho, c, N$, and the time varying parameter η and its time derivatives up to the fifth order. We obtain all these expressions by repetitively using (1). Finally, we compute the rank of M and, by a direct computation, we obtain the following fundamental property. Independently of the values of $\lambda, \delta, \rho, c, N, T_U, T_I, V, \eta, \eta^{(1)}, \eta^{(2)}, \eta^{(3)}, \eta^{(4)}, \eta^{(5)}$ (with $\eta^{(k)} \equiv \frac{d^k \eta}{dt^k}$), this rank cannot exceed $4 < 5$. As a result, it is erroneous to conclude that Equation (7) allows us to locally identify all the five parameters $\lambda, \delta, \rho, c, N$.

4 Feedback of the review from SIREV

This note was first submitted and rejected by the SIAM Review Journal (SIREV), and then published on arXiv [5]. This section reports the feedback obtained during the review process made by SIREV and provides a discussion on the technical ability of the editor and the two reviewers selected by the editor.

Sections 4.1 and 4.2 provide the comments from the first and the second reviewer. The second reviewer is one of the authors of [1]¹. Section 4.3 provides the final decision taken by

¹This clearly appears from his review.

the editor. Finally, Section 4.4 provides a thorough analysis of the entire review feedback, which clearly highlights the poor technical ability of the two reviewers (in particular the second) and the inadequacy of the editor both for the poor technical ability in carrying out simple and basic calculations and the ineptitude in taking a final decision.

4.1 Report of the first reviewer

This note proposes a correction of a well-known paper on "Identifiability of nonlinear ODE models and applications in viral dynamics", by Miao et al. (reference [1] from now on). In [1], it was claimed that a model of host HIV/AIDS dynamics containing a time-varying parameter is structurally unidentifiable. The submitted note argues that the opposite is true. This note is relevant because the original paper [1] is one of the most popular and cited references in the topic of structural identifiability analysis, and the HIV model has been used as a case study in later works. Hence it is important to clarify the correctness of those results. The present note attempts to do so by means of three main claims:

(1) That three parameters of the model have infinitely many equivalent solutions. This is argued in Section 1 of the note, by showing a set of parameter transformations, depending on a "tau" parameter, that allegedly yields a solution with dynamics indistinguishable from the original one. (2) That there is an error in equation (6.23) of [1], which may have been the cause of the wrong result. This is shown in Section 2 of the note. (3) That the implicit function Theorem, when applied to the model under study, yields a 5x5 matrix M which has a rank of at most $4 < 5$, which indicates non-identifiability.

Claim (2) above is indeed true. However, I have not been able to confirm claims (1) and (3). As a matter of fact, when attempting to replicate the results reported in the present note, I obtained instead results that seem to support the conclusions in [1]: in regard to claim (1), I was unable to recover the original model equations by direct substitution of the transformed parameters; instead I obtained different ones. As for claim (3), when applying the similarity transform method, I obtained a 5x5 matrix with rank 5, which would indicate full identifiability.

While my results contradict those presented in the correction, the correction does provide a convincing rationale and it raises some - at least - intriguing concerns. Therefore, I think that the underlying claims deserve more investigation. To obtain these results I did some calculations by hand, and others on a computer. Although I double-checked them, I might have made a mistake somewhere; likewise, there might be an error in the calculations performed by the author of the submitted note. To avoid any possibility of confusion, it would be very helpful if the author provided some code that performs the necessary calculations, so that it would be easier to spot any differences in methodology as well as possible errors.

To sum up, my suggestion would be that the correction is resubmitted along with further details and code to reproduce the results.

4.2 Report of the second reviewer (most likely one of the authors of [1])

We thank Dr. Martinelli for pointing out an error in Eq. (6.23) of Miao et al. (2011). However, there are several misunderstandings in the derivations and arguments in this submission such that the conclusions on parameter identifiability are not justified. We thus do not recommend publication of this submission in SIAM REV, but all the authors of Miao et al. (2011) are willing to work with the SIAM REV editorial office to publish an erratum on Eq. (6.23).

1. We appreciate that Dr. Martinelli pointed out an error in the coefficients of Eq. (6.23). While Eq. (2.1) derived by Dr. Martinelli is correct, it can be further simplified by combining the 5th and the 7th terms of Eq. (2.1) to yield:

$$\begin{aligned} & \ddot{y}_1 y_2 \dot{y}_2 - \dot{y}_1 y_2 \ddot{y}_2 - \delta y_1 y_2 \dot{y}_2 + \lambda y_2 \ddot{y}_2 + (\rho - c) \dot{y}_1 y_2 \dot{y}_2 + (\delta \rho - \delta^2 - \delta c) y_1 y_2 \dot{y}_2 \\ & + \lambda c y_2 \dot{y}_2 + \rho c \dot{y}_1 y_2^2 + (\rho \delta c - \delta^2 c) y_1 y_2^2 - N \delta y_1 \dot{y}_1 y_2 + c \dot{y}_1 y_2^2 \\ & - N \delta (\rho + \delta) y_1 \dot{y}_1 y_2 - N \delta^2 \rho y_1^2 y_2 + N \delta^2 \lambda y_1 y_2 = 0. \end{aligned}$$

It is easy to show from the revised Eq. (2.1) by the methods in our paper that the model parameters are all identifiable as claimed in our original paper. Specifically, let Φ denote the left side of Eq. (2.1) and let $\theta_c = (\lambda, \rho, N, \delta, c)^T$ denote the constant parameter vector, we have $\Phi = \Phi(\theta_c, y_1, \dot{y}_1, \ddot{y}_1, y_2, \dot{y}_2, \ddot{y}_2)$ and $\Phi^{(n)} = \frac{d^n}{dt^n} \Phi(y_1, \dot{y}_1, \ddot{y}_1, y_2, \dot{y}_2, \ddot{y}_2)$, where n is a positive integer. The Jacobian matrix we obtained is as follows:

$$\begin{bmatrix} \frac{\partial \Phi}{\partial \lambda} & \frac{\partial \Phi}{\partial \rho} & \frac{\partial \Phi}{\partial N} & \frac{\partial \Phi}{\partial \delta} & \frac{\partial \Phi}{\partial c} \\ \frac{\partial \Phi^{(1)}}{\partial \lambda} & \frac{\partial \Phi^{(1)}}{\partial \rho} & \frac{\partial \Phi^{(1)}}{\partial N} & \frac{\partial \Phi^{(1)}}{\partial \delta} & \frac{\partial \Phi^{(1)}}{\partial c} \\ \frac{\partial \Phi^{(2)}}{\partial \lambda} & \frac{\partial \Phi^{(2)}}{\partial \rho} & \frac{\partial \Phi^{(2)}}{\partial N} & \frac{\partial \Phi^{(2)}}{\partial \delta} & \frac{\partial \Phi^{(2)}}{\partial c} \\ \frac{\partial \Phi^{(3)}}{\partial \lambda} & \frac{\partial \Phi^{(3)}}{\partial \rho} & \frac{\partial \Phi^{(3)}}{\partial N} & \frac{\partial \Phi^{(3)}}{\partial \delta} & \frac{\partial \Phi^{(3)}}{\partial c} \\ \frac{\partial \Phi^{(4)}}{\partial \lambda} & \frac{\partial \Phi^{(4)}}{\partial \rho} & \frac{\partial \Phi^{(4)}}{\partial N} & \frac{\partial \Phi^{(4)}}{\partial \delta} & \frac{\partial \Phi^{(4)}}{\partial c} \end{bmatrix}.$$

Note that y_1 and y_2 are observed and their arbitrary-order time derivatives ($y_1^{(n)}$ and $y_2^{(n)}$) are deemed as known. Also, according to the persistently exciting input assumption (see Page 5 in Miao et al. 2011), $y_1^{(n)}$ and $y_2^{(n)}$ will not vanish for the purpose of identifiability analysis. That is, y_1 , y_2 and their derivatives up to the sixth order in $\Phi^{(n)}$ are known and they will not vanish (e.g., degenerate to zeros); therefore, $\Phi^{(i)} \neq \Phi^{(j)}$ ($i \neq j$) is expected at certain time points in theory and the rank of the Jacobian matrix can be 5.

2. The derivations in Section 1 showing the model parameters are not all identifiable are not convincing for two reasons:
 - a. An additional parameter τ was introduced in Eqns. (1.1)~(1.3) to re-parameterize the original model. In general, it is not recommended to introduce additional (redundant) parameters into a model in the context of identifiability analysis as such practice is likely to change the given model structure and subsequently change the identifiability of existing model parameters.
 - b. The parameter identifiability problem here is to verify whether $\theta = (\eta, \lambda, \rho, N, \delta, c)^T$ is identifiable given the model structure in Eqns. (6.15)~(6.17) and given the observations $y_1 = T_U + T_I, y_2 = V$. This is different from the problem of verifying whether $(T_U, T_I, V, \eta, \lambda, \rho, N, \delta, c)^T$ is unique given the model structure and the observations. In short, directly including (T_U, T_I, V) in identifiability analysis is not appropriate, and $\theta = (\eta, \lambda, \rho, N, \delta, c)^T$ will not be unique when θ is locally identifiable.

4.3 Decision from the editor of the Survey and Review section of SIREV

Dear Agostino Martinelli,

I am emailing with regard to the manuscript "Correction to "On identifiability of nonlinear ODE models and applications in viral dynamics" submitted to the Survey and Review section of SIAM Review. We have now received sufficient referee feedback to allow me to make an editorial decision. Please find this feedback attached and/or appended below. Based on this material and my own reading, and keeping in mind the high standards of SIAM Review, I must reject your submission.

I will nevertheless ask the authors of the original manuscript to write a correction and acknowledge your hint to the error.

Thank you for considering SIAM Review as an outlet for your work.

Best wishes,

Regards,

*****,

Section Editor, SIREV Survey and Review

sirev@math.kit.edu

4.4 Discussion

From the comments of the editor and the two reviewers, we can easily remark the following evidences.

1. The two reviewers and the editor were unable to follow the simple derivation provided in Section 2. In particular, Reviewer 1 stated (see Section 4.1): **I was unable to recover the original model equations by direct substitution of the transformed parameters; instead I obtained different ones.** These computations are very easy and are now available in Appendix A.

Even worse, Reviewer 2, misunderstood the meaning of τ in Eqs (2) and (4) (see Item 2.a in Section 4.2). The introduction of τ does not change the model in (1). For any value of τ , we have a set of values for the parameters of the model in (1), which are distinct from the true values but indistinguishable from them. Specifically, these indistinguishable values are obtained from Eqs (2) and (4).

It is a very serious problem that the reviewers were unable to understand this trivial derivation. It only requires to perform very basic calculations (simple differentiation and substitutions). This type of computation is usually acquired during the high-school. It is definitely unacceptable that people who define themselves as theoretical researchers in technological sciences are unable to perform similar calculations.

2. The two reviewers and the editor were only able to understand the simple error (typo) mentioned in Section 3.1.

The authors published an erratum where this typo was acknowledged [6]. To this regard, there are two interesting aspects to be remarked:

- (a) The paper contains several other typos and the authors of [1] seem to be unaware of this fact.
- (b) The authors still concluded in [6] that the model is locally identifiable, which is false.

3. The two reviewers and the editor were unable to understand the derivation given in Section 3.2. They assumed that the two output functions, $y_1(t)$, $y_2(t)$, and their time derivatives up to any order, can take arbitrary values (see the second part of Item 1 in Section 4.2 and the comment about claim (3) in Section 4.1). They were unable to understand that these measurements (and their time derivatives) must satisfy the constraints due to the system dynamics. This fact is also unacceptable, especially from the authors of [1].

4. The first reviewer suggested to better discuss all the mentioned issues with the author of the correction. In particular, he/she said: **While my results contradict those presented**

in the correction, the correction does provide a convincing rationale and it raises some - at least - intriguing concerns. Therefore, I think that the underlying claims deserve more investigation. To obtain these results I did some calculations by hand, and others on a computer. Although I double-checked them, I might have made a mistake somewhere; likewise, there might be an error in the calculations performed by the author of the submitted note. To avoid any possibility of confusion, it would be very helpful if the author provided some code that performs the necessary calculations, so that it would be easier to spot any differences in methodology as well as possible errors.

The editor ignored this very wise suggestion (despite being asked to confirm if the decision was truly final), showing a serious ineptitude in doing the very important work of editor.

5 Conclusion

This note highlighted a very serious error on a paper published by SIAM Review in 2011. The error is in Section 6.2 of [1].

The error is relevant because, as a result of it, a very popular viral model (perhaps the most popular in the field of HIV dynamics) has been classified as identifiable. In contrast, three of its parameters are not identifiable, even locally.

This note first proved the non uniqueness of the three unidentifiable parameters by exhibiting infinitely many distinct but indistinguishable values of them (Section 2). The non uniqueness is even local. Then, this note detailed the very serious error made by the authors of [1] which produced the claimed (but false) local identifiability of all the model parameters (Section 3.2).

This note was first submitted and rejected by the SIAM Review Journal (SIREV), and then published on arXiv [5]. In this note, we also included the feedback obtained from the editor of the Survey and Review section of SIREV and from the two reviewers selected by the editor. This feedback clearly highlights the technical inadequacy of the editor and reviewers and more generally shows how the editor has dramatically failed to correctly manage the review of a simple erratum. This is a serious and very damaging problem for our scientific community.

A Technical details for the derivation of Eq. (5)

First equation

Let us prove the validity of the first equation in (5), i.e., the validity of

$$\frac{d}{dt}T'_U = \lambda' - \rho'T'_U - \eta'T'_UV'$$

We prove the equality of the two members.

First member

From the first equation in (3), we obtain:

$$\frac{d}{dt}T'_U = \frac{d}{dt}T_U + \frac{d}{dt}T_I - \frac{\frac{d}{dt}T_I}{\rho} (\delta e^{-\rho\tau} + \rho - \delta).$$

By using the first two equations in (1), we obtain:

$$\begin{aligned} \frac{d}{dt}T'_U &= \lambda - \rho T_U - \eta T_U V + \eta T_U V - \delta T_I - \frac{\eta T_U V - \delta T_I}{\rho} (\delta e^{-\rho\tau} + \rho - \delta) = \\ &= \lambda - \rho T_U - \delta T_I + \frac{\delta T_I - \eta T_U V}{\rho} (\delta e^{-\rho\tau} + \rho - \delta). \end{aligned} \quad (8)$$

Second member

The second member is $\lambda' - \rho'T'_U - \eta'T'_UV'$. By using (2), we obtain:

$$\lambda' - \rho'T'_U - \eta'T'_UV' = \lambda - \rho T'_U - \eta T'_U V'$$

By using the expression of T'_U and V' in (3), and by using the expression of η' in (4), after some simplifications, we obtain:

$$\lambda' - \rho'T'_U - \eta'T'_UV' = -\frac{T_I \delta^2 - \lambda \rho + T_U \rho^2 - T_I \delta^2 e^{-\rho\tau} - T_U V \delta \eta + T_U V \eta \rho + T_U V \delta \eta e^{-\rho\tau}}{\rho} \quad (9)$$

By a direct computation it is easy to check that the two members (given in (8) and (9), respectively) coincide, i.e., the following equality holds

$$\lambda - \rho T_U - \delta T_I + \frac{\delta T_I - \eta T_U V}{\rho} (\delta e^{-\rho\tau} + \rho - \delta) = -\frac{T_I \delta^2 - \lambda \rho + T_U \rho^2 - T_I \delta^2 e^{-\rho\tau} - T_U V \delta \eta + T_U V \eta \rho + T_U V \delta \eta e^{-\rho\tau}}{\rho}$$

Second equation

Let us prove the validity of the second equation in (5), i.e., the validity of

$$\frac{d}{dt}T'_I = \eta'T'_UV' - \delta'T'_I$$

We prove the equality of the two members.

First member

From the second equation in (3), we obtain:

$$\frac{d}{dt}T'_I = \frac{\frac{d}{dt}T_I}{\rho} (\delta e^{-\rho\tau} + \rho - \delta).$$

From the second equation in (1), we obtain:

$$\frac{d}{dt}T'_I = \frac{\eta T_U V - \delta T_I}{\rho} (\delta e^{-\rho\tau} + \rho - \delta). \quad (10)$$

Second member

The second member is $\eta'T'_UV' - \delta'T'_I$. By using (2), we obtain:

$$\eta'T'_UV' - \delta'T'_I = \eta'T'_UV' - \frac{\delta\rho}{(\rho - \delta)e^{\rho\tau} + \delta}T'_I$$

By using the expression of T'_U , T'_I , and V' in (3), and by using the expression of η' in (4), after some simplifications, we obtain:

$$\eta'T'_UV' - \delta'T'_I = -\frac{e^{-\rho\tau}(T_I\delta - T_UV\eta)(\delta - \delta e^{\rho\tau} + \rho e^{\rho\tau})}{\rho} \quad (11)$$

By a direct computation it is easy to check that the two members (given in (10) and (11), respectively) coincide, i.e., the following equality holds

$$\frac{\eta T_U V - \delta T_I}{\rho} (\delta e^{-\rho\tau} + \rho - \delta) = -\frac{e^{-\rho\tau}(T_I\delta - T_UV\eta)(\delta - \delta e^{\rho\tau} + \rho e^{\rho\tau})}{\rho}$$

Third equation

Let us prove the validity of the third equation in (5), i.e., the validity of

$$\frac{d}{dt}V' = N'\delta'T'_I - c'V'$$

We prove the equality of the two members.

First member

From the third equation in (3), we obtain:

$$\frac{d}{dt}V' = \frac{d}{dt}V$$

From the third equation in (1), we obtain:

$$\frac{d}{dt}V' = N\delta T_I - cV \quad (12)$$

Second member

The second member is $N'\delta'T'_I - c'V'$. By using (2), we obtain:

$$N'\delta'T'_I - c'V' = Ne^{\rho\tau} \frac{\delta\rho}{(\rho - \delta)e^{\rho\tau} + \delta} T'_I - cV'$$

By using (3), we obtain:

$$N'\delta'T'_I - c'V' = Ne^{\rho\tau} \frac{\delta\rho}{(\rho - \delta)e^{\rho\tau} + \delta} \frac{T_I}{\rho} (\delta e^{-\rho\tau} + \rho - \delta) - cV \quad (13)$$

By a direct computation it is easy to check that the two members (given in (12) and (13), respectively) coincide, i.e., the following equality holds

$$N\delta T_I - cV = Ne^{\rho\tau} \frac{\delta\rho}{(\rho - \delta)e^{\rho\tau} + \delta} \frac{T_I}{\rho} (\delta e^{-\rho\tau} + \rho - \delta) - cV$$

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