

Identifiability Analysis Report

April 24, 2025

1 Introduction

The goal was to determine which parameters in the lettuce growth model are most identifiable and suitable for estimation. To do this, a sensitivity-based identifiability analysis was performed, combining both sensitivity and correlation methods. These steps helped distinguish which parameters should be estimated and which could be fixed, based on their influence on the model output and their degree of correlation with other parameters. After this, a structural analysis of those parameters was done using GenSSI matlab toolbox to assess whether those parameters can, in principle, be uniquely estimated from the model output.

2 Identifiability Analysis

Identifiability analysis is the first step in determining unknown parameters in ODE models. There are several methods to evaluate identifiability in nonlinear ODE models: structural identifiability analysis, practical identifiability analysis and sensitivity-based identifiability analysis. The methods discussed in this section are well described in [2].

2.1 Sensitivity-Based Identifiability Analysis

Sensitivity analysis

This method evaluates the impact of individual parameter changes on the model output. To do so, a simulation was run (using as parameters values the one in the paper by Van Henten [1]) over a period of $t = 40$ days to obtain the final total dry weight ($DW_{nom,final}$). The initial non-structural dry weight (X_{nsdw}) was set to 0.5 g m^{-2} and the initial structural dry weight (X_{sdw}) was set to 1.0 g m^{-2} .

Each parameter p was individually perturbed by adding 10% to its nominal value. The model was then re-simulated with the perturbed parameter set. The relative sensitivity S_{rel} for each parameter p was calculated as the ratio of the relative change in the final total dry weight to the relative change in the parameter:

$$S_{rel}(p) = \frac{(DW_{pert,final} - DW_{nom,final})/DW_{nom,final}}{(p_{pert} - p_{nom})/p_{nom}} = \frac{\Delta DW_{final}/DW_{nom,final}}{0.10}$$

where $DW_{pert,final}$ is the final total dry weight obtained from the simulation with the perturbed parameter. The result of the analysis, sorted by their absolute magnitude in descending order are showed in the Table 1.

Parameters that show negligible sensitivity suggest that they might be difficult to identify from measurements of the final total dry weight under these specific conditions, while parameters with higher sensitivity values are considered more influential and potentially more identifiable.

Correlation method

Another approach for practical identifiability analysis is to examine the correlations between model parameters. A strong correlation between two parameters indicates that one parameter strongly depends on another parameter and these two parameters cannot be separately estimated.

The methodology involved the following steps:

Table 1: Relative sensitivity of final total dry weight to a 10% increase in each parameter.

Parameter	Relative Sensitivity (S_{rel})
c_α	+1.0228
c_ϵ	+0.7798
c_β	+0.7562
c_{car2}	+0.2435
c_{resp_sht}	-0.2155
c_w	+0.2092
c_Γ	-0.1652
c_{car1}	-0.1561
c_{Q10_resp}	+0.1047
c_{bnd}	+0.0936
c_{car3}	-0.0731
c_K	+0.0669
c_{lar}	+0.0669
c_{gr_max}	+0.0342
c_γ	+0.0258
c_{stm}	+0.0186
c_τ	+0.0055
c_{resp_rt}	-0.0055
c_{Q10_gr}	+0.0000
c_{10_Gamma}	+0.0000

1. **Output trajectory:** The total dry weight trajectory, $DW(t) = X_{nsdw}(t) + X_{sdw}(t)$, was calculated over the 40 day simulation period at 100 equally spaced time points (t_{eval}). Inputs and initial conditions were the same as in the sensitivity analysis.
2. **Sensitivity matrix:** A sensitivity matrix $S \in R^{100 \times N_p}$ was computed, where N_p is the number of parameters. Each element S_{ij} represents the sensitivity of the total dry weight at time t_i to a change in parameter p_j :

$$S_{ij} = \frac{\partial DW(t_i)}{\partial p_j} \approx \frac{DW(t_i, p_j + \delta p_j) - DW(t_i, p_j - \delta p_j)}{2\delta p_j}$$

3. **Rank of sensitivity matrix:** theoretical derivations based on a first-order Taylor expansion of the model output show that if this matrix is rank deficient, the parameters are not locally identifiable, indicating linear dependencies among the sensitivity vectors.

The rank of $S^T S$ was found to be 5, significantly less than the number of parameters. This suggests that the parameters are locally non-identifiable.

4. **Pairwise correlation:** The Pearson correlation coefficient matrix $R = \text{corrcoef}(S)$ was computed to measure the correlation between each pair of parameters. A heatmap visualizing the absolute correlation matrix $|R|$ is shown in Figure 1.

A large number of pair of parameters exhibited very high absolute correlations and some pairs even showed perfect correlation:

- **Light interception parameters c_K vs c_{lar} ($R = 1.0000$) .**

Because they only influence the model through their product $c_K \times c_{lar}$, their effects are perfectly substitutable, leading to $R = 1.0$. Only the value of the product $c_K \cdot c_{lar}$ can be determined from the model output.

- **Photosynthesis parameters c_α vs c_ϵ , c_Γ , c_{bnd} , c_{stm} , c_{car1} , c_{car2} , c_{car3} , c_w (all $|R| \approx 1.0000$).**
the parameters related to CO₂ transport and assimilation are highly correlated. This result can be motivated by looking at the model equations: those parameters interact with one

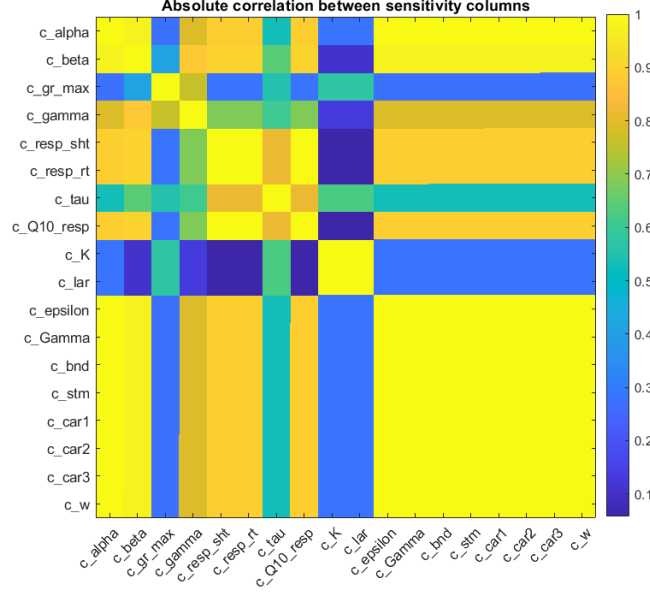


Figure 1: Heatmap of the absolute Pearson correlation coefficients ($|R|$) between parameter sensitivities.

another through a sequence of calculations involving multiplications and combined terms. This means that a change in one parameter early in the sequence can be cancelled out or compensated for by adjusting another parameter later in the sequence, since they results of a sequence of multiplications

- **Growth efficiency parameters c_β vs c_α , c_ϵ , ... ($|R| \approx 0.9769$).**

c_β is highly correlated with the photosynthesis parameters. The growth efficiency parameter c_β determines the fraction of assimilated carbon lost to growth respiration:

$$\frac{dX_{\text{nsdw}}}{dt} = \dots - \frac{1 - c_\beta}{c_\beta} r_{gr} X_{sdw}$$

It is highly correlated with the photosynthesis parameters because the growth depends strongly on both the *rate* of carbon intake (governed by $c_\alpha, \epsilon, g_{CO_2}$) and the *efficiency* (governed by c_β) with which that carbon is used for structural growth. This means that increasing the photosynthesis rate has a similar positive effect on net growth as increasing the efficiency c_β (which reduces the loss term), which explain their high correlation.

Similar considerations can be made for the other parameters with high correlations.

5. **Total correlation:** A total correlation index (TC_i) was calculated for each parameter p_i by summing the squared correlation coefficients with the other parameters p_j , considering only pairs where the absolute correlation $|R_{ij}|$ exceeded a threshold $\delta_{tc} = 0.95$:

$$TC_i = \sum_{j \neq i, |R_{ij}| \geq \delta_{tc}} R_{ij}^2$$

These results reinforced the findings from the pairwise analysis. The parameters with the highest values of TC were, as expected, those embedded within the complex sequence of multiplications and dependencies in the photosynthesis calculations. The results, sorted by TC value, are shown in Table 2.

2.2 Structural Identifiability Analysis

Structural Identifiability verify system identifiability by analysing the system structure. The basic idea of this approach is to directly use the identifiability definition to verify parameter identifiability. It is

Table 2: Total correlation index (TC) for each parameter, based on pairs with $|R_{ij}| \geq 0.95$.

Parameter	Total Correlation (TC)
c_{car2}	8.9543
c_ϵ	8.9543
c_α	8.9543
c_w	8.9543
c_{car1}	8.9543
c_{bnd}	8.9543
c_{car3}	8.9543
c_{stm}	8.9543
c_Γ	8.9543
c_β	8.5891
c_{resp_rt}	2.0000
c_{resp_sht}	2.0000
c_{Q10_resp}	2.0000
c_K	1.0000
c_{lar}	1.0000
c_{gr_max}	0.0000
c_γ	0.0000
c_τ	0.0000

used to investigate whether parameters can take on unique, finite, or infinite (thus termed structurally unidentifiable) values for the given model outputs

GenSSI toolbox

The structural identifiability analysis has been performed using GenSSI [3], a software toolbox for structural identifiability analysis of linear and non-linear ODE models. It couples the generating series approach with identifiability tableaux. Using Lie derivatives of the ODE model, a system of equations is generated, the solvability properties of which provide information about global and local structural identifiability as well as non-identifiability.

GenSSI allows for the analysis of the structural identifiability of a subset of parameters, and analyzing all of them can be computationally expensive. A subset of parameters has been chosen based on the outcomes of the previous sensitivity-based analysis. Additionally, as shown in (Table 1) and the results from the Correlation Method, particularly the low rank of $S^T S$ (Rank 5) and the numerous high pairwise correlations (Figure 1), it was evident that estimating all parameters of the original model is infeasible.

Parameter selection for structural analysis

The parameter selected were: c_α , c_β , c_{resp_sht} , c_{gr_max} . This selection prioritized parameters that demonstrated significant sensitivity and represented key physiological processes, while parameters that remained less sensitive or potentially still confounded in the model should be fixed to their nominal values for subsequent analysis.

A structural identifiability analysis using GenSSI was performed and confirmed that the selected parameters are structurally globally identifiable (see output file: results/structural_analysis_output.txt).

References

- [1] Van Henten, E. J. (1994). Sensitivity analysis of a dynamic growth model of lettuce.
- [2] Miao, H., Xia, X., Perelson, A. S., Wu, H. (2021). On Identifiability of nonlinear ODE models and applications in viral dynamics.

- [3] Ligon, T. S., Fröhlich, F., Chis, O. T., Banga, J. R., Balsa-Canto, E., Hass, H. (2018). GenSSI 2.0: multi-experiment structural identifiability analysis of SBML models.