SUPPLEMENTARY MATERIAL

A. Detailed Mass Balances

General Reaction

$$\text{Glycerol (FC)} + \text{Ammonia (FN)} + O_2 \rightarrow X + P + CO_2 + H_2O + \Delta H_R$$

General Mass Balance Formulation

$$\text{Accumulation} = \text{In} - \text{Out} + \text{Generation} - \text{Consumption}$$

Batch Process: $F_{\text{in}} = F_{\text{out}} = 0$ and $V = \text{constant}$, thus:

$$\text{Accumulation} = \text{Generation} - \text{Consumption}$$

Biomass Balance

$$\frac{d}{dt}(X \cdot V) = \mu \cdot X \cdot V$$
$$\frac{dX}{dt} \cdot V = \mu \cdot X \cdot V$$
$$\frac{dX}{dt} = \mu \cdot X$$

Including the death rate constant k_d, the specific net growth rate becomes:

$$\frac{dX}{dt} = (\mu - k_d) \cdot X$$

Substrate and Product Balances

For any substrate or product S, assuming only microbial consumption or generation and constant volume V:

$$\frac{d}{dt}(S \cdot V) = -r_S \cdot V$$

The yield coefficient is defined as:

$$Y_{S/X} = \frac{r_X}{-r_S} = \frac{\mu X}{-r_S}$$

Therefore, the general expression becomes:

$$\frac{dS}{dt} = \pm \frac{\mu X}{Y_{S/X}}$$

where the sign depends on whether S is a substrate (negative) or a product (positive).

B. Ionic Balance

$$[\text{OH}^-] = \frac{K_{a6}}{[H^+]} \tag{8}$$

$$[\text{KHPO}_4^-] = \frac{\text{KH}_2\text{PO}_4^{\text{tot}}}{\left(1 + \frac{[H^+]}{K_{a1}}\right)} \tag{9}$$

$$[\text{C}_6\text{H}_5\text{O}_7^{3-}] = \frac{\text{C}_6\text{H}_8\text{O}_7^{\text{tot}}}{\frac{[H^+]^3}{K_{a2}K_{a3}K_{a4}} + \frac{[H^+]^2}{K_{a3}K_{a4}} + \frac{[H^+]}{K_{a4}} + 1} \tag{10}$$

$$[\text{C}_6\text{H}_6\text{O}_7^{2-}] = \frac{[H^+] \cdot [\text{C}_6\text{H}_5\text{O}_7^{3-}]}{K_{a4}} \tag{11}$$

$$[\text{C}_6\text{H}_7\text{O}_7^-] = \frac{[H^+] \cdot [\text{C}_6\text{H}_6\text{O}_7^{2-}]}{K_{a3}} \tag{12}$$

$$[\text{HCO}_3^-] = \frac{\text{CO}_2^{\text{tot}}}{\left(\frac{[H^+]}{K_{a7}} + 1\right)} \tag{13}$$

$$[\text{H}^+] = [\text{OH}^-] + [\text{KHPO}_4^-] + 3[\text{C}_6\text{H}_5\text{O}_7^{3-}] + 2[\text{C}_6\text{H}_6\text{O}_7^{2-}] + [\text{C}_6\text{H}_7\text{O}_7^-] + [\text{HCO}_3^-] - [pH_{\text{alk}}]$$

C. Complementary Tables

TABLE II
MODEL PARAMETERS USED IN THE DYNAMIC SIMULATION OF *M. smegmatis* GROWTH

Parameter	Description	Value
t_{lag}	Lag phase duration [h]	7
k_C	Monod constant for glycerol [g/L]	0.3828
k_N	Monod constant for ammonia [g/L]	1.0027×10^{-4}
$Y_{X/C}$	Biomass yield on glycerol [g/g]	0.484
$Y_{X/N}$	Biomass yield on ammonia [g/g]	21.575
$Y_{X/CD}$	CO_2 yield [g/g]	0.3687
Y_{X/O_2}	O_2 yield [g/g]	1.352
X_{max}	Maximum biomass concentration [g/L]	1.4462
μ_{max}	Maximum specific growth rate [1/h]	0.19
k_d	Death rate constant [1/h]	0.001
pH_{LL}	Lower limit of pH tolerance [-]	3.4687
pH_{UL}	Upper limit of pH tolerance [-]	7.4
pH_{alk}	Constant ions in pH charge balance [-]	7.2
pK_{a1} to pK_{a9}	Acid dissociation constants [-]	See Table III
$[KH_2PO_4]$	Phosphate buffer (monobasic) [mol/L]	2.18
$[C_6H_8O_7]$	Citric acid (tricarboxylic acid) [mol/L]	2.00
I_{val}	pH inhibition shape parameter [-]	4.0413
$O_{2,\text{sat}}$	O_2 saturation concentration [g/L]	7.267×10^{-3}
k_La	Oxygen transfer coefficient [1/h]	86.26
k_O	Monod constant for oxygen [g/L]	4.5×10^{-3}

TABLE III
ACID DISSOCIATION CONSTANTS (pK_a) USED IN THE PH MODEL

Parameter	Chemical species or group	Value
pK_{a1}	KH_2PO_4 (phosphate buffer)	6.86
pK_{a2}	Citric acid ($C_6H_8O_7$)	3.13
pK_{a3}	Mono-deprotonated citric acid $(C_6H_7O_7)^-$	4.76
pK_{a4}	Di-deprotonated citric acid $(C_6H_7O_7)^{2-}$	6.40
pK_{a5}	Ammonium (NH_3)	9.25
pK_{a6}	Glycerol ($C_3H_8O_3$)	14.15
pK_{a7}	Carbon dioxide (CO_2)	6.35
pK_{a8}	Bicarbonate (HCO_3^-)	10.33
pK_{a9}	Water (H_2O)	14.00

TABLE IV
INITIAL CONDITIONS USED IN THE SIMULATION OF *M. smegmatis* GROWTH FOR THE FITTING DATA

Variable	Description	Initial Value
X_0	Biomass concentration [g/L]	0.229
C_0	Glycerol concentration [g/L]	5.389
N_0	Ammonium concentration [g/L]	0.951
$CO_{2,0}$	Carbon dioxide concentration [g/L]	4.39×10^{-4}
$O_{2,0}$	Dissolved oxygen concentration [g/L]	7.267×10^{-3}

TABLE V
INITIAL CONDITIONS USED IN THE SIMULATION OF *M. smegmatis* GROWTH FOR THE VALIDATION DATA

Variable	Description	Initial Value
X_0	Biomass concentration [g/L]	0.223
C_0	Glycerol concentration [g/L]	5.922
N_0	Ammonium concentration [g/L]	1.027
$CO_{2,0}$	Carbon dioxide concentration [g/L]	4.39×10^{-4}
$O_{2,0}$	Dissolved oxygen concentration [g/L]	7.267×10^{-3}

TABLE VI
HIGHLY CORRELATED PARAMETER PAIRS ($|\rho| > 0.95$), GROUPED BY CORRELATION SIGN

Parameter A	Parameter B	Correlation
Positively correlated pairs		
t_{lag}	k_C	0.9702
Y_{X/CO_2}	k_d	0.9955
Y_{X/O_2}	pH_{LL}	0.9977
I_{val}	k_{La}	0.9975
μ_{max}	k_O	0.9686
Negatively correlated pairs		
t_{lag}	pH_{UL}	-0.9704
t_{lag}	k_N	-0.9543
k_N	μ_{max}	-0.9801
Y_{X/O_2}	I_{val}	-0.9976
Y_{X/O_2}	k_{La}	-1.0000
pH_{LL}	I_{val}	-1.0000
pH_{LL}	k_{La}	-0.9975

TABLE VII
t-VALUES OF ESTIMATED PARAMETERS

Parameter	t-Value	New Value
pH_{UL}	50674.90	7.571
X_{max}	4098.99	1.174 g/L

TABLE VIII
NRMSE FOR MODEL FITTING UNDER DIFFERENT PARAMETER SETS FOR ADJUSTING BASED ON THE SENSITIVITY ANALYSIS

Variable	1 parameter adjusted	2 parameter adjusted	3 parameter adjusted	4 parameter adjusted
Biomass	30.37 %	19.73 %	19.73 %	19.93 %
Ammonia	27.30 %	28.68 %	28.68 %	28.81 %
Glycerol	22.12 %	15.95 %	15.95 %	16.26 %
pH	14.38 %	11.77 %	11.77 %	12.13 %

TABLE IX
PARAMETER ESTIMATION — RESULTS

Set	pH_{UL}	X_{max}	μ_{max}	I_{val}
1 Parameter	6.52	–	–	–
2 Parameters	7.571	1.174	–	–
3 Parameters	7.400	1.446	0.113	–
4 Parameters	7.751	1.1545	0.111	4.9

D. Complementary Figures

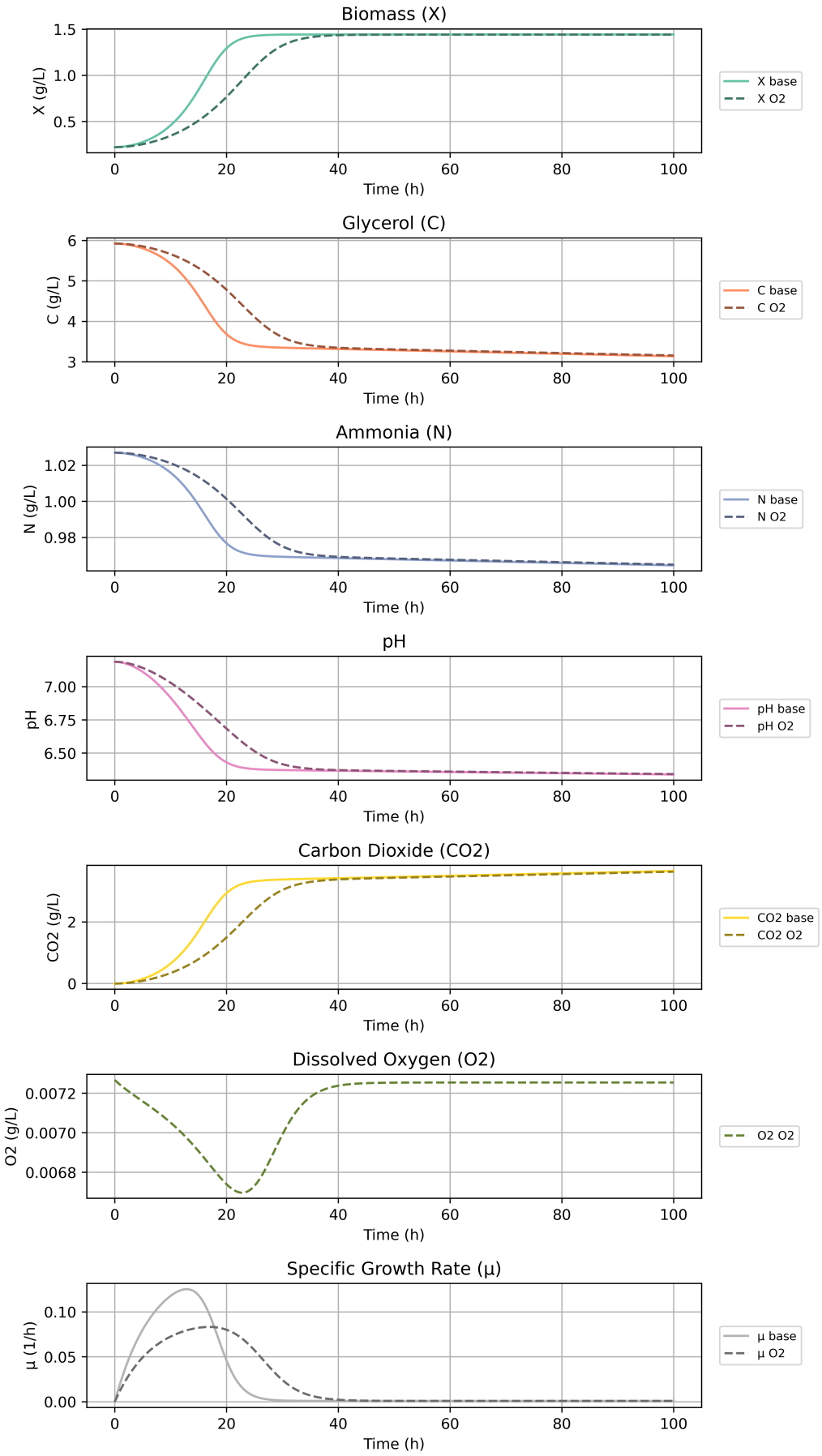

Fig. 1. Comparison between original model without oxygen, and the updated model with oxygen consumption on hypoxic conditions.

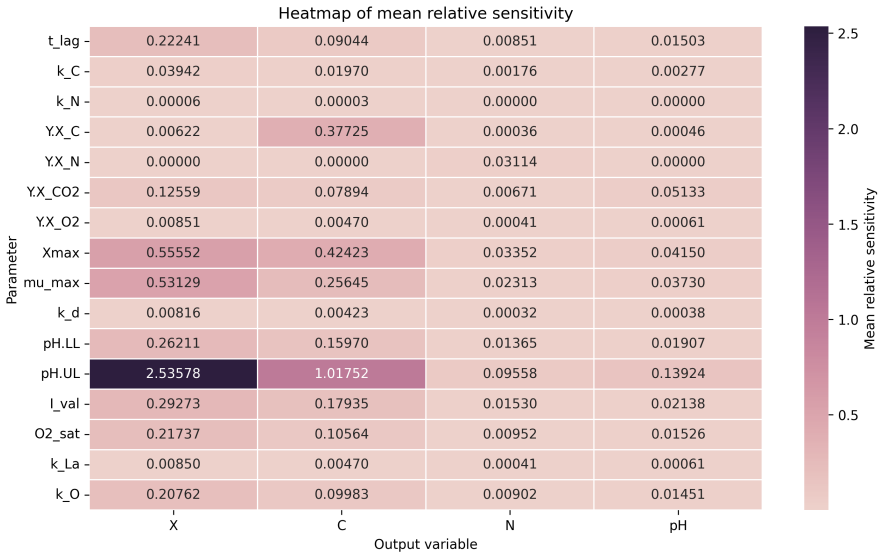

Fig. 2. Heatmap of the mean relative sensitivity of each parameter with respect to the model outputs.

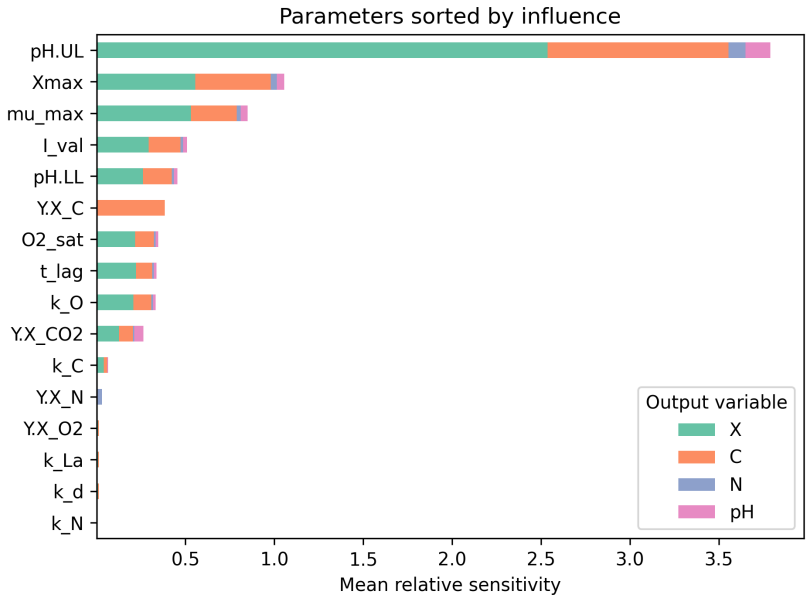

Fig. 3. Mean relative sensitivity of all model parameters, sorted by overall influence and disaggregated by output variable.

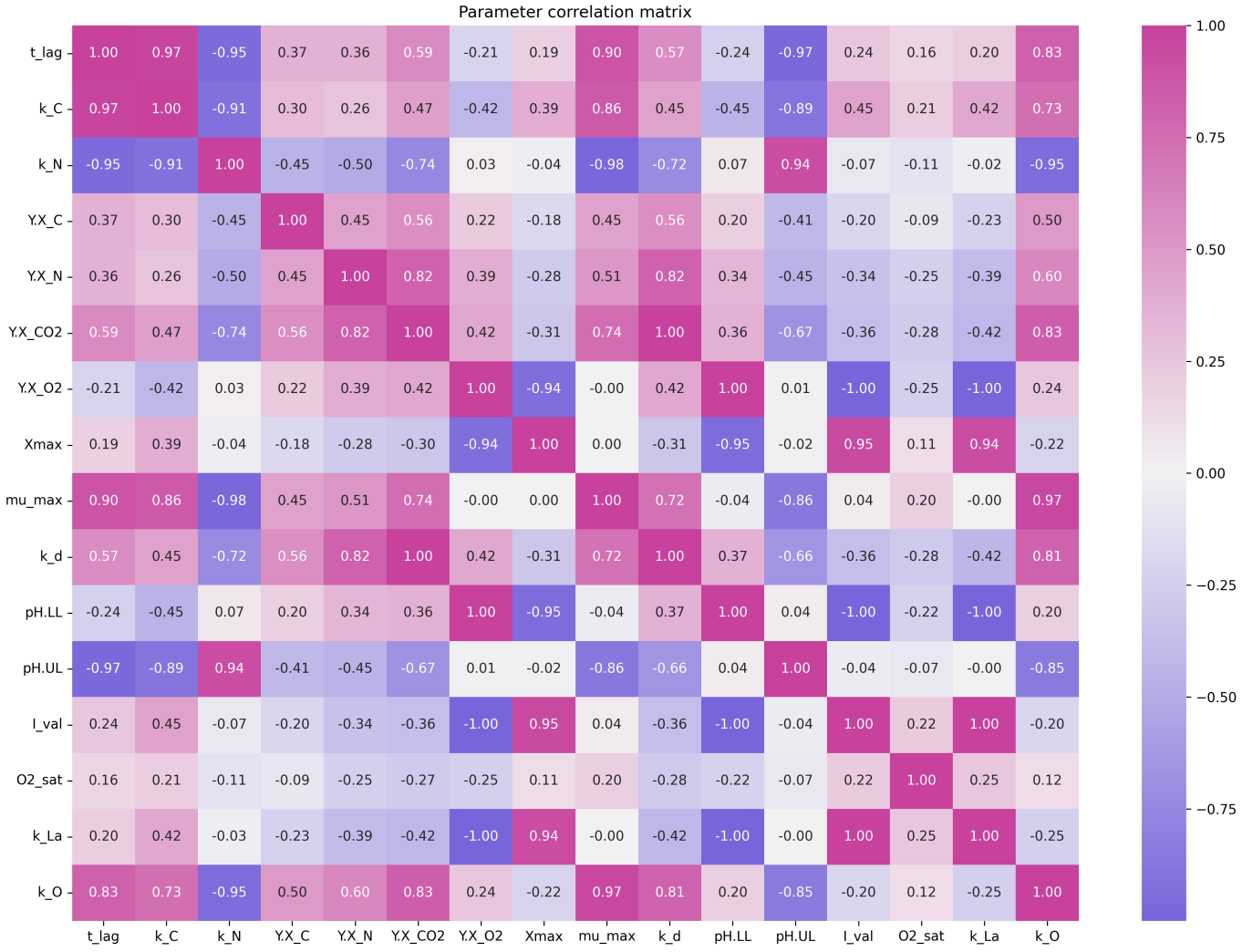

Fig. 4. Correlation matrix between the parameters.

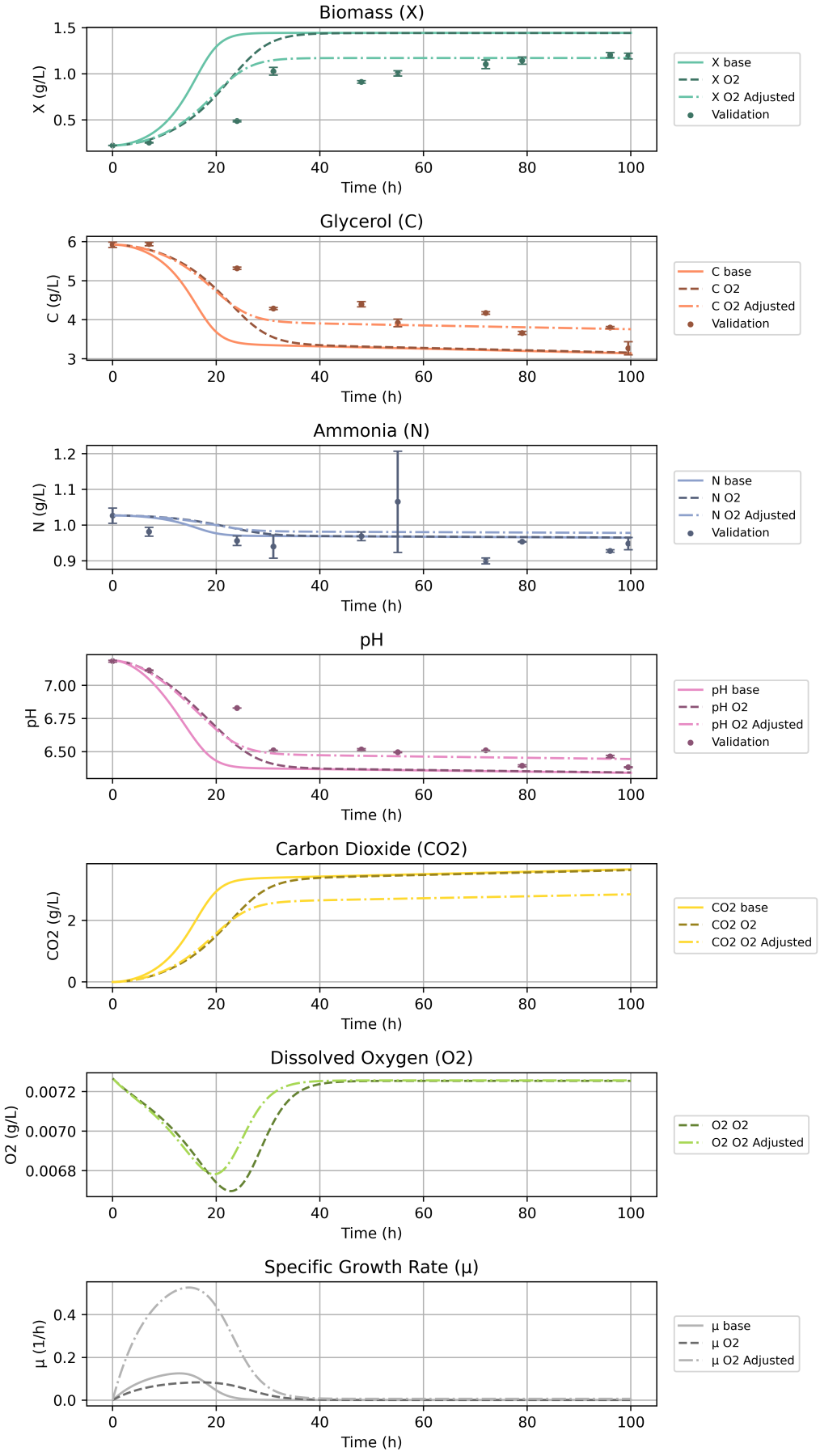

Fig. 5. Comparison between all the models tested, with the validation data. Error bars represent the relative deviation of experimental validation data.