ECRONICON OPEN ACCESS

EC CLINICAL AND MEDICAL CASE REPORTS

Research Article

Ab Initio Whole Cell Kinetic Model of *Corynebacterium accolens* DSM 44278 (caccSM26)

Sohnnakshee Murugesu[1,2], Tristan Zhi Xian Tay[1,2], Magaa Lakshmi Dhinakaran[1,2], Aguilar Normi Luisa Cinco[1,2], Pandiyan Srinithiksha[1,2] and Maurice Han Tong Ling[2,3,4]*

[1]*School of Health and Life Sciences, Teesside University, UK*

[2]*Management Development Institute of Singapore, Singapore*

[3]*Newcastle Australia Institute of Higher Education, University of Newcastle, Australia*

[4]*HOHY PTE LTD, Singapore*

***Corresponding Author:** Maurice Han Tong Ling, Newcastle Australia Institute of Higher Education, University of Newcastle, Australia.

Received: January 09, 2026; **Published:** January 28, 2026

Abstract

Corynebacterium accolens DSM 44278 is a nasal commensal with emerging probiotic potential and relevance to respiratory health, including interactions with respiratory pathogens in the upper airway. These properties make *C. accolens* a promising candidate for metabolic engineering, which can benefit from a whole-cell kinetic model to evaluate various engineering proposals *in silico*. However, there is currently no reported whole-cell kinetic model for *C. accolens*. Therefore, this study constructs a whole-cell simulatable kinetic model of *C. accolens* DSM 44278 using an *ab initio* approach by identifying enzymes from its reference genome. The resulting model, caccSM26, comprises 1097 metabolites, 407 enzymes with associated transcription and translation processes, and 1182 enzymatic reactions represented as ordinary differential equations using representative kinetic parameters. This whole-cell kinetic model serves as a foundational framework for future refinement with organism-specific data and for *in silico* exploration of growth behaviour, regulatory mechanisms, and metabolic engineering strategies in this clinically relevant commensal.

Keywords: *Whole-Cell Model; Kinetic Model; Differential Equations; AdvanceSyn Toolkit*

Introduction

Corynebacterium accolens DSM 44278 is a Gram-positive, non-spore-forming, lipophilic actinobacterium that predominantly colonises the human nasal cavity and upper respiratory tract as a commensal [1]. It produces TAG lipases (e.g. LipS1) that hydrolyse host triacylglycerols, releasing free fatty acids that have antimicrobial activity against important respiratory pathogens such as *Streptococcus pneumoniae* [2]. Improved respiratory health and a lower risk of pathogen acquisition have been associated with a nasal microbiome profile dominated by *Corynebacterium* species, including *C. accolens* [3,4]. Recent studies also suggest that *C. accolens* may influence host factors such as ACE2 and TMPRSS2 expression, potentially reducing susceptibility to viral infections like SARS-CoV-2 through both lipase activity and receptor modulation [5], indicative of probiotic potential [6]. Furthermore, probiotic evaluations of *C. accolens* strains from healthy human nasal cavities demonstrate adhesion to epithelial cells, competition with pathogens such as *Staphylococcus aureus*, and safety *in vivo*, supporting translational applications aimed at correcting sinonasal dysbiosis [7]. As the interest to engineer probiotic strains increases [8], *C. accolens* may likely be considered for potential metabolic engineering in the foreseeable future.

Mathematical models continue to underpin decision-making in metabolic engineering, guiding the exploration of genetic modifications long before experimental validation [9,10]. Two modelling paradigms dominate [11,12]: GSMs and KMs. GSMs, built on constraint-based principles, primarily predict flux distributions. KMs, however, extend beyond rates to include yield predictions [13]; and are typically more straightforward for simulating gene knock-ins [14]. These differences make KMs particularly attractive for evaluating competing engineering strategies in silico. Recognising this utility, many researchers have highlighted the growing importance of developing more comprehensive kinetic models to support future metabolic engineering work [15,16].

However, there is no whole-cell KM of *C. accolens* to-date. Hence, this study aims to construct a KM of *C. accolens* DSM 44278 using *ab initio* approach by identifying enzymes from its genome, and identifying the corresponding reaction from KEGG [17]. The result is a whole cell KM of *C. accolens* DSM 44278, named as caccSM26, using the nomenclature proposed by Cho and Ling [18], which consists of 1097 metabolites, 407 enzymes with corresponding transcriptions and translations, and 1182 enzymatic reactions.

Materials and Methods

Identification of reactome: The genome of *C. accolens* DSM 44278 (NCBI RefSeq assembly GCF_023520795.1; NCBI GenBank Accession NZ_CP046605.1) was used as source to identify enzymatic genes using the process previously described [14,19,20]. Briefly, each enzymatic gene was identified as a presence of complete Enzyme Commission (EC) number in the GenBank record and mapped into reaction IDs via KEGG Ligand Database for Enzyme Nomenclature [17]. For example, EC 1.1.1.23 (https://www.genome.jp/entry/1.1.1.23) catalyses reactions R01158, R01163, and R03012; where the substrates and products of each rection can be identified.

Model development: The model was developed using methodology in Sim., *et al.* [21]. From BioNumbers, *Escherichia coli* typically carries around 3000 RNA polymerases (BioNumbers 106199) [22], with only 25% actively extending transcripts (BioNumbers 111676) [23]. At 22 nt/s (BioNumbers 104109) [24] and 339.5 Da per nucleotide, this results in about 5600 kDa per second of RNA synthesis or 9.3e-18 grams per second. Adjusting this rate to a cell volume of 7e-16 litres [25] and dividing it among 4225 protein-coding genes (BioNumbers 105443) [26] gives a production estimate of 2.92 micromolar per gene per second. With an average mRNA lifetime of about 108 seconds (BioNumbers 107666) [27], corresponding to 0.93% degradation per second, the governing equation is d[mRNA]/dt = 0.00292 - 0.0093[mRNA]. On the translation side, mammalian estimates of 1000 peptides per hour per transcript yield 0.278 peptides per second (BioNumbers 106382) [28]; *E. coli* protein degradation at 1% per hour (2.78e-16 per second) (BioNumbers 109924) [29] gives d[peptide]/dt = 0.278[mRNA] - 0.00000278[peptide]. The system was built as a set of ODEs [19,30] with representative kinetic constants (kcat = 13.7 per second, Km = 1 mM) [31], written according to the AdvanceSyn Model Specification [32].

Model simulation: The constructed model was tested for simulatability using AdvanceSyn Toolkit [32]. Initial concentrations of all mRNA and enzymes were set to 0 mM. Initial concentrations of all metabolites were set to 1 mM except the following which were set to 1000 mM: (I) C00001 (Water), (II) C00002 (ATP), (III) C00003 (NAD+), (IV) C00004 (NADH), (V) C00005 (NADPH), (VI) C00006 (NADP+), (VII) C00007 (Oxygen), (VIII) C00011 (Carbon Dioxide), (IX) C00014 (Ammonia), (X) C00025 (L-Glutamate), (XI) C00031 (D-Glucose), (XII) C00037 (Glycine), (XIII) C00041 (L-Alanine), (XIV) C00047 (L-Lysine), (XV) C00049 (L-Aspartate), (XVI) C00064 (L-Glutamine), (XVII) C00065 (L-Serine), (XVIII) C00073 (L-Methionine), (XIX) C00097 (L-Cysteine), (XX) C00133 (D-Alanine), (XXI) C00148 (L-Proline). The model was simulated using the fourth-order Runge-Kutta method [33,34] from time zero to 3600 seconds with timestep of 0.1 second, and the concentrations of metabolites were bounded between 0 millimolar and 1000 millimolar. The simulation results were sampled every 2 seconds.

Results and Discussion

The annotated genome of *C. accolens* DSM 44278 consists of 2337 genes, including 2216 protein coding sequences. 407 unique EC numbers consisting of 1182 enzymatic reactions involving 1097 metabolites were identified and developed into a model based on AdvanceSyn Model Specification [32]. In addition, 814 ODEs acting as placeholder for enzyme transcriptions and translations were added.

We evaluated the caccSM26 model using AdvanceSyn Toolkit [32], and Figure 1 shows that the model runs as intended, demonstrating structural soundness and absence of syntax errors as argued in recent model constructions [14,20,35-39]. Whole-cell kinetic models often fail during early simulation attempts due to minor inconsistencies, so achieving a successful run is an essential milestone. The accumulation of formate and UDP may arise from using uniform median enzyme kinetics [31], which simplify the system for testing but distort biological realism. Therefore, the simulation patterns should be interpreted only in the context of model operability. What we put forward is a functional whole-cell kinetic backbone for *C. accolens* DSM 44278, offering a starting point for extensions involving growth coupling, regulatory influences, or calibrated enzyme parameters based on empirical measurements [40-42].

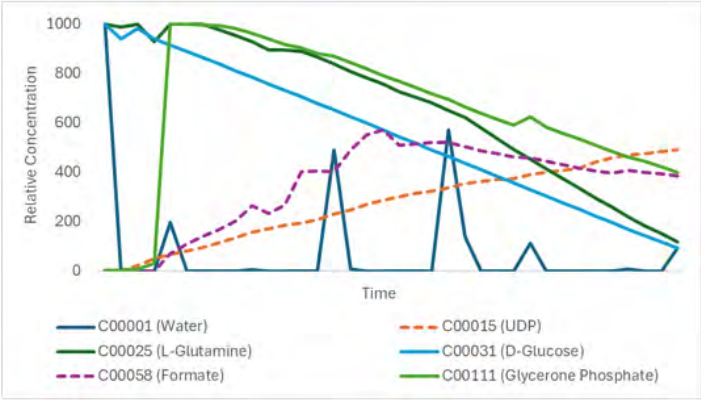

Figure 1: *Selection of simulation results.*

Conclusion

In this study, we present an *ab initio* whole cell kinetic model of *C. accolens* DSM 44278, caccSM26; comprising of 1097 metabolites, 407 enzymes with corresponding transcriptions and translations, and 1182 enzymatic reactions.

Supplementary Materials

Reaction descriptions and model can be download from https://bit.ly/caccSM26.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgements

The authors wish to thank the institute, Management Development Institute of Singapore, for its support towards this work. The cost of publication fees was borne by the authors.

Bibliography

1. Tran TH., *et al*. "Metabolic capabilities are highly conserved among human nasal-associated *Corynebacterium* species in pangenomic analyses". *mSystems* 9.12 (2024): e0113224.

2. Bomar L., *et al*. "*Corynebacterium accolens* releases antipneumococcal free fatty acids from human nostril and skin surface triacylglycerols". *mBio* 7.1 (2016): e01725-01715.

3. Man WH., *et al*. "The microbiota of the respiratory tract: gatekeeper to respiratory health". *Nature Reviews Microbiology* 15.5 (2017): 259-270.

4. Brugger SD., *et al*. "Commensal-pathogen interactions along the human nasal passages". *PLoS Pathogens* 12.7 (2016): e1005633.

5. Szabo D., *et al*. "Specific nasopharyngeal *Corynebacterium* strains serve as gatekeepers against SARS-CoV-2 infection". *GeroScience* 45.5 (2023): 2927-2938.

6. Shamsuzzaman M., *et al*. "Genome insight and probiotic potential of three novel species of the genus *Corynebacterium*". *Frontiers in Microbiology* 14 (2023): 1225282.

7. Menberu MA., *et al*. "*In vitro* and *in vivo* evaluation of probiotic properties of *Corynebacterium accolens* isolated from the human nasal cavity". *Microbiological Research* 255 (2022): 126927.

8. Duhan P., *et al*. "Gut microbiome engineering with probiotics: current trends and future directions". *Discover Applied Sciences* 7.11 (2025): 1354.

9. Khanijou JK., *et al*. "Metabolomics and modelling approaches for systems metabolic engineering". *Metabolic Engineering Communications* 15 (2022): e00209.

10. Gudmundsson S and Nogales J. "Recent advances in model-assisted metabolic engineering". *Current Opinion in Systems Biology* 28 (2021): 100392.

11. Richelle A., *et al*. "Towards a widespread adoption of metabolic modeling tools in biopharmaceutical industry: a process systems biology engineering perspective". *npj Systems Biology and Applications* 6.1 (2020): 6.

12. Lee YQ., *et al*. "Genome-scale metabolic model-guided systematic framework for designing customized live biotherapeutic products". *NPJ Systems Biology and Applications* 11.1 (2025): 73.

13. Prabhu S., *et al*. "Derivative-free domain-informed data-driven discovery of sparse kinetic models". *Industrial and Engineering Chemistry Research* 64.5 (2025): 2601-2615.

14. Yeo KY., *et al*. "*Ab initio* whole cell kinetic model of *Yarrowia lipolytica* CLIB122 (yliYKY24)". *Medicon Medical Sciences* 8.4 (2025): 01-06.

15. Foster CJ., *et al*. "Building kinetic models for metabolic engineering". *Current Opinion in Biotechnology* 67 (2021): 35-41.

16. Lázaro J., *et al*. "Enhancing genome-scale metabolic models with kinetic data: resolving growth and citramalate production trade-offs in *Escherichia coli*". *Bioinformatics Advances* 5.1 (2025): vbaf166.

17. Okuda S., *et al*. "KEGG Atlas mapping for global analysis of metabolic pathways". *Nucleic Acids Research* 36(Web Server issue) (2008): W423-W426.

18. Cho JL and Ling MH. "Adaptation of whole cell kinetic model template, UniKin1, to *Escherichia coli* whole cell kinetic model, ecoJC20". *EC Microbiology* 17.2 (2021): 254-260.

19. Kwan ZJ., *et al*. "Ab initio whole cell kinetic model of *Stutzerimonas balearica* DSM 6083 (pbmKZJ23)". *Acta Scientific Microbiology* 7.2 (2024): 28-31.

20. Maiyappan S., *et al*. "Four *ab initio* whole cell kinetic models of *Bacillus subtilis* 168 (bsuLL25) 6051-HGW (bshSM25), N33 (bsuN33SS25), FUA2231 (bsuGR25)". *Journal of Clinical Immunology and Microbiology* 6.2 (2025): 1-6.

21. Sim BJH., *et al*. "Multilevel metabolic modelling using ordinary differential equations". Encyclopedia of Bioinformatics and Computational Biology (Second Edition), eds Ranganathan S, Cannataro M, Khan AM (Elsevier, Oxford) (2025): 491-498.

22. Müller-Hill B. "The lac Operon: A Short History of a Genetic Paradigm". (Berlin, Germany) (1996).

23. Churchward G., *et al*. "Transcription in bacteria at different DNA concentrations". *Journal of Bacteriology* 150.2 (1982): 572-581.

24. Gray WJ and Midgley JE. "The control of ribonucleic acid synthesis in bacteria. The synthesis and stability of ribonucleic acid in rifampicin-inhibited cultures of *Escherichia coli*". *The Biochemical Journal* 122.2 (1971): 161-169.

25. Kubitschek HE. "Cell volume increase in *Escherichia coli* after shifts to Richer media". *Journal of Bacteriology* 172.1 (1990): 94-101.

26. Hu P., *et al*. "Global functional atlas of *Escherichia coli* encompassing previously uncharacterized proteins". *PLoS Biology* 7.4 (2009): e96.

27. So L-H., *et al*. "General properties of transcriptional time series in *Escherichia coli*". *Nature Genetics* 43.6 (2011): 554-560.

28. Schwanhäusser B., *et al*. "Corrigendum: Global quantification of mammalian gene expression control". *Nature* 495.7439 (2013): 126-127.

29. Maurizi MR. "Proteases and protein degradation in *Escherichia coli*". *Experientia* 48.2 (1992): 178-201.

30. Murthy MV., *et al*. "UniKin1: A universal, non-species-specific whole cell kinetic model". *Acta Scientific Microbiology* 3.10 (2020): 04-08.

31. Bar-Even A., *et al*. "The moderately efficient enzyme: evolutionary and physicochemical trends shaping enzyme parameters". *Biochemistry* 50.21 (2011): 4402-4410.

32. Ling MH. "AdvanceSyn toolkit: An open source suite for model development and analysis in biological engineering". *MOJ Proteomics & Bioinformatics* 9.4 (2020): 83-86.

33. Yong B. "The comparison of fourth order Runge-kutta and homotopy analysis method for solving three basic epidemic models". *Journal of Physics: Conference Series* 1317 (2019): 012020.

34. Ling MH. "COPADS IV: Fixed time-step ODE solvers for a system of equations implemented as a set of python functions". *Advances in Computer Science: An International Journal* 5.3 (2016): 5-11.

35. Saisudhanbabu T., *et al*. "*Ab initio* whole cell kinetic model of *Limosilactobacillus fermentum* EFEL6800 (lfeTS24)". *EC Clinical and Medical Case Reports* 8.4 (2025): 01-04.

36. Arivazhagan M., *et al*. "*Ab initio* whole cell kinetic model of *Bifidobacterium bifidum* BGN4 (bbfMA24)". *Acta Scientific Nutritional Health* 9.1 (2025): 42-45.

37. Senthilkumar A., *et al*. "*Ab initio* whole cell kinetic model of *Lactobacillus acidophilus* NCFM (lacAS24)". *Journal of Clinical Immunology and Microbiology* 6.1 (2025): 1-5.

38. Wong TB., *et al*. "*Ab initio* whole cell kinetic models of *Escherichia coli* BL21 (ebeTBSW25) and MG1655 (ecoMAL25)". *Scholastic Medical Sciences* 3.2 (2025): 01-04.

39. Ambel WB., *et al*. "UniKin2 - A universal, pan-reactome kinetic model". *International Journal of Research in Medical and Clinical Science* 3.2 (2025): 77-80.

40. Ahn-Horst TA., *et al*. "An expanded whole-cell model of *E. coli* links cellular physiology with mechanisms of growth rate control". *npj Systems Biology and Applications* 8.1 (2022): 30.

41. Chagas M da S., *et al*. "Boolean model of the gene regulatory network of *Pseudomonas aeruginosa* CCBH4851". *Frontiers in Microbiology* 14 (2023): 1274740.

42. Hao T., *et al*. "Reconstruction of metabolic-protein interaction integrated network of *Eriocheir sinensis* and analysis of ecdysone synthesis". *Genes* 15.4 (2024): 410.

Volume 9 Issue 2 February 2026