JOURNAL OF CLINICAL IMMUNOLOGY AND MICROBIOLOGY

E-ISSN: 3068-5168
Journal of Clinical Immunology & Microbiology

ATHENAEUM SCIENTIFIC PUBLISHERS

Research Article

Ab initio Whole Cell Kinetic Model of *Streptomyces murinus* CR-43 (smuLA26)

Aguilar Normi Luisa Cinco[1,2], Pandiyan Srinithiksha[1,2], Sohnnakshee Murugesu[1,2], Tristan Zhi Xian Tay[1,2], Magaa Lakshmi Dhinakaran[1,2], 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

***Correspondence author:** Maurice HT Ling, Management Development Institute of Singapore, Singapore and Newcastle Australia Institute of Higher Education, University of Newcastle, Australia and HOHY PTE LTD, Singapore; Email: mauriceling@acm.org

Citation: Cinco ANL, et al. *Ab Initio* Whole Cell Kinetic Model of *Streptomyces murinus* CR-43 (smuLA26). J Clin Immunol Microbiol. 2026;7(1):1-5.

https://doi.org/10.46889/JCIM.2026.

Received Date: 04-01-2026

Accepted Date: 12-02-2026

Published Date: 20-02-2026

Abstract

Streptomyces species are known for the synthesis of bioactive compounds ranging from antibiotics, antifungals and enzymes with industrial value. *Streptomyces murinus* CR-43 has been shown to produce antinematodal fatty acids and may be potential for future metabolic engineering for fatty acid production. Mathematical kinetic models can inform and guide metabolic engineering strategies; however, there has been no whole-cell kinetic model of *S. murinus* CR-43 to-date. In this study, the *ab initio* whole-cell kinetic model of *S. murinus* CR-43 is constructed. Enzymatic genes were identified from the complete genome sequence of *S. murinus* CR-43 and mapped to metabolic reactions using KEGG enzyme nomenclature, enabling systematic reconstruction of the organism's metabolic reactome. The resulting simulatable model, smuLA26, comprises of 1009 metabolites and 425 unique enzymes with 1385 enzymatic reactions. This model can be a preliminary framework for *S. murinus* CR-43, which serves as a platform for future refinement and exploration of metabolic engineering strategies targeting fatty acid and secondary metabolite production.

Keywords: Whole-Cell Model; Kinetic Model; Antinematodal Fatty Acids; Differential Equations; Advancesyn Toolkit

Introduction

The *Streptomyces* species are generally known as a prolific source of antibiotics and antifungal compounds and *Streptomyces murinus*, a Gram-positive and filamentous soil bacteria, is one of its members [1-5]. Other isolates of the *S. murinus* species are known to produce pentamycin and actinomycin D-antifungal compounds that possess broad spectrum activity against plant pathogens suggesting promise in agricultural applications [1,6,7]. Due to the ability of the *Streptomyces* species to secrete proteins efficiently and to thrive under fermentation conditions, the species has been generally explored as hosts for industrial enzyme production [8]. *S. murinus* CR-43, previously known as *Streptomyces costaricanus* CR-43T (T = type strain), produces antinematodal fatty acids [9,10]. This suggests that *S. murinus* may be potential for future metabolic engineering for fatty acid production [11].

Mathematical modelling supports metabolic engineering by providing a structured way to evaluate interventions before testing them experimentally [12,13]. Within this space, Genome-Scale Models (GSMs) and Kinetic Models (KMs) serve as the two primary modelling paradigms [14,15]. While GSMs have become widely adopted, they operate mostly at the level of flux

predictions. KMs provide a richer output by including yield predictions and are often simpler to modify for *in-silico* gene knock-ins [1617]. These strengths make KMs more suited for screening multiple engineering scenarios. As a result, there has been a noticeable rise in interest and advocacy for the construction of new and improved kinetic models [18,19].

However, there is no whole-cell KM of *S. murinus* to-date. Hence, this study aims to construct a KM of *S. murinus* CR-43 using *ab initio* approach by identifying enzymes from its genome and identifying the corresponding reaction from Kyoto Encyclopedia of Genes and Genomes (KEGG) [20]. The result is a whole cell KM of *S. murinus* CR-43, named as smuLA26, using the nomenclature proposed by Cho and Ling, which consists of 1009 metabolites, 425 enzymes with corresponding transcriptions and translations and 1385 enzymatic reactions [21].

Materials and Methods

Identification of Reactome

The genome of *Streptomyces murinus* CR-43 (NCBI RefSeq assembly GCF_025231465.1; NCBI GenBank Accession NZ_CP046623.1) was used as source to identify enzymatic genes using the process previously described [17,22,23]. 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 [20]. 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. [24]. Using standard BioNumbers values, transcriptional output in Escherichia coli can be estimated from about 3000 total RNA polymerases (BioNumbers 106199) of which 25% are elongating (BioNumbers 111676) at 22 nucleotides per second (BioNumbers 104109) [25-27]. At 339.5 Daltons per nucleotide, this leads to about 5600 kDa of mRNA produced each second. Converted into mass (9.3e-10 grams per second) and normalized to the 7e-16 litres per cell environment and 4225 protein-coding genes (BioNumbers 105443), we obtain 2.92 micromolar per gene per second [28,29]. With the average transcript surviving 107.56 seconds, the decay constant is 0.0093 per second (BioNumbers 107666), yielding: d[mRNA]/dt = 0.00292 - 0.0093[mRNA] [30]. For translation, about 1000 peptides per transcript per hour correspond to 0.278 peptides/s (BioNumbers 106382) and degradation occurs at 2.78e-1 per second (BioNumbers 109924) [31,32]. Hence: d[peptide]/dt = 0.278[mRNA] - 0.00000278[peptide]. The model was implemented as an Ordinary Differential Equations (ODE) system with standard median kinetic constants (kcat = 13.7 per second, Km = 1 mM), aligned with AdvanceSyn's modelling structure [22,33-35].

Model Simulation

The constructed model was tested for simulatability using AdvanceSyn Toolkit [35]. 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) C00008 (ADP), (IX) C00011 (Carbon Dioxide), (X) C00014 (Ammonia), (XI) C00025 (L-Glutamate), (XII) C00031 (D-Glucose), (XIII) C00037 (Glycine), (XIV) C00041 (L-Alanine), (XV) C00047 (L-Lysine), (XVI) C00049 (L-Aspartate), (XVII) C00064 (L-Glutamine), (XVIII) C00065 (L-Serine), (XIX) C00073 (L-Methionine), (XX) C00097 (L-Cysteine), (XXI) C00133 (D-Alanine), (XXII) C00148 (L-Proline). The model was simulated using the fourth-order Runge-Kutta method 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 [36,37].

Results and Discussion

The annotated genome of *Streptomyces murinus* CR-43 consists of 1928 genes, including 1775 protein coding sequences. 425 unique EC numbers consisting of 1385 enzymatic reactions involving 1009 metabolites were identified and developed into a model based on AdvanceSyn Model Specification [35]. In addition, 850 ODEs acting as placeholder for enzyme transcriptions and translations were added.

The smuLA26 model, when loaded into AdvanceSyn Toolkit and simulated, produced clean, error-free trajectories (Fig. 1), underscoring that the model is structurally sound and properly encoded, as previously argued in recent model constructions [17,23,36-42]. Given the complexity of a whole-cell kinetic network, this is nontrivial. That said, the simulated fluxes suggesting that the concentration of tetrahydrofolate (C00101) plateau at about half the concentration of coenzyme A (C00010) but about double the concentration of formate (C00058) may be the result of simplifying assumption that all enzymes share median kinetic parameters [34]. Those uniform parameters compress natural variation; thus, distort quantitative flux balances. Nonetheless, this model constitutes a robust starting point, a "blank-slate" whole-cell KM for *S. murinus* CR-43, upon which more realistic kinetics, additional metabolic pathways or regulatory and growth dynamics may be layered in future work to aid engineering efforts for metabolite productions [11,43-45].

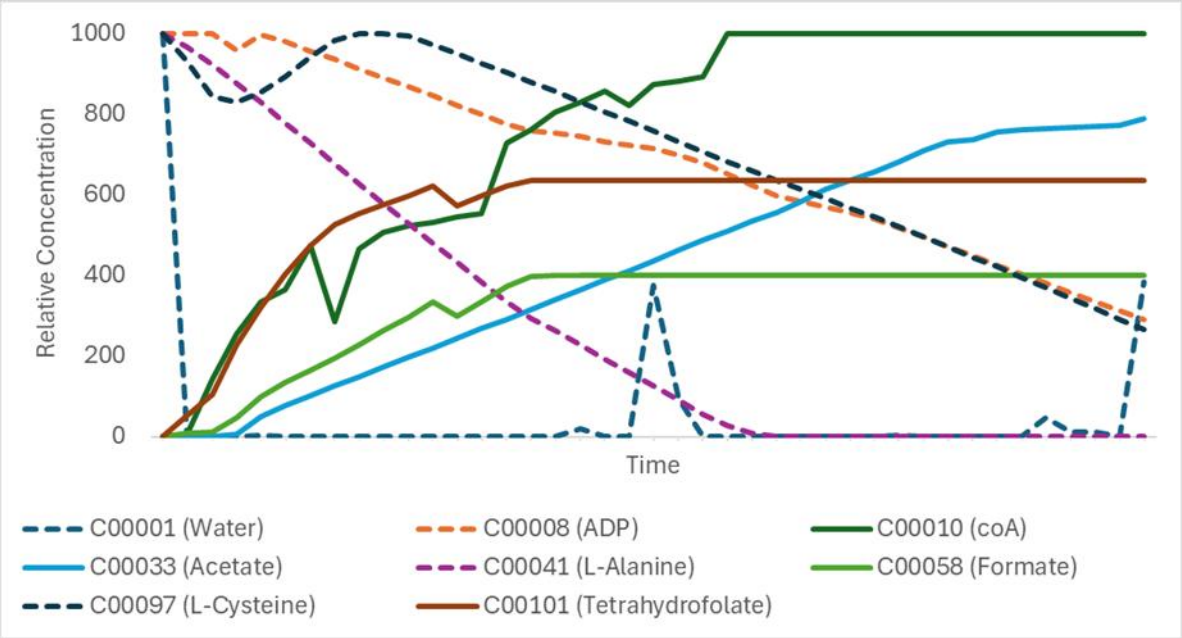

Figure 1: Selection of simulation results.

Conclusion

Here, we present an *ab initio* whole cell kinetic model of *Streptomyces murinus* CR-43, smuLA26; comprising of 1009 metabolites, 425 enzymes with corresponding transcriptions and translations and 1385 enzymatic reactions.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding Statement

This research did not receive any specific grant from funding agencies in the public, commercial or non-profit sectors.

Acknowledgement

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.

Data Availability Statement

Not applicable.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore, was exempt.

Informed Consent Statement
Informed consent was taken for this study.

Authors' Contributions
All authors contributed equally to this paper.

Supplementary Materials
Reaction descriptions and model can be download from https://bit.ly/smuLA26.

References

1. Quinn GA, Banat AM, Abdelhameed AM, Banat IM. *Streptomyces* from traditional medicine: Sources of new innovations in antibiotic discovery. J Med Microbiol. 2020;69(8):1040-8.
2. Alam K, Mazumder A, Sikdar S, Zhao YM, Hao J, Song C, et al. *Streptomyces*: the biofactory of secondary metabolites. Front Microbiol. 2022;13:968053.
3. Devi S, Sharma M, Manhas RK. Purification and biological analysis of antimicrobial compound produced by an endophytic *Streptomyces* sp. Sci Rep. 2023;13(1):15248.
4. Singh N, Das D, Sherwani N, Singha A. *Streptomyces*: Sources of novel discoveries in antibiotic research to combat antimicrobial resistance. Virol Immunol J. 2025;9(1):1-8.
5. Dhillon B, Chakrabarti S. Draft genome sequence of *Streptomyces murinus* strain SPC1 with antimicrobial potential against fungal pathogens of palms. Microbiol Resour Announc. 2023;12(12):e00826-23.
6. Duan J, Hu X, Zhang S, Wang J, Chen F, Ibrahim E, et al. Pentamycin derived from *Streptomyces murinus* TCS22-109 as a promising biocontrol agent. Chem Biol Technol Agric. 2025;12(1):155.
7. Das V, Chatterjee NS, Pushpakaran PU, Lalitha KV, Joseph TC. Genomics and metabolomics profiling of mangrove-derived *Streptomyces murinus* THV12. Fermentation. 2023;9(6):576.
8. Vojnovic S, Aleksic I, Ilic-Tomic T, Stevanovic M, Nikodinovic-Runic J. *Bacillus* and *Streptomyces* spp. as hosts for enzyme production. Appl Microbiol Biotechnol. 2024;108(1):185.
9. Esnard J, Potter TL, Zuckerman BM. *Streptomyces* costaricanus sp. nov., isolated from nematode-suppressive soil. Int J Syst Bacteriol. 1995;45(4):775-79.
10. Tran A, Tang A, O'Loughlin CT, Balistreri A, Chang E, Coto Villa D, et al. C. elegans avoids toxin-producing *Streptomyces*. eLife. 2017;6:e23770.
11. Atasoy M, Scott WT, Regueira A, Mauricio-Iglesias M, Schaap PJ, Smidt H. Biobased short-chain fatty acid production. Biotechnol Adv. 2024;73:108363.
12. Khanijou JK, Kulyk H, Bergès C, Khoo LW, Ng P, Yeo HC, et al. Metabolomics and modelling approaches for systems metabolic engineering. Metab Eng Commun. 2022;15:e00209.
13. Gudmundsson S, Nogales J. Recent advances in model-assisted metabolic engineering. Curr Opin Syst Biol. 2021;28:100392.
14. Richelle A, David B, Demaegd D, Dewerchin M, Kinet R, Morreale A, et al. Metabolic modeling tools in biopharmaceutical industry. NPJ Syst Biol Appl. 2020;6(1):6.
15. Lee YQ, Choi YM, Park SY, Kim SK, Lee M, Kim D, et al. Genome-scale metabolic model-guided framework for live biotherapeutics. NPJ Syst Biol Appl. 2025;11(1):73.
16. Prabhu S, Kosir N, Kothare MV, Rangarajan S. Derivative-free data-driven discovery of kinetic models. Ind Eng Chem Res. 2025;64(5):2601-15.
17. Yeo KY, Arivazhagan M, Senthilkumar A, Saisudhanbabu T, Le MA, Wong B, et al. *Ab initio* whole-cell kinetic model of Yarrowia lipolytica. Medicon Med Sci. 2025;8(4):1-6.
18. Foster CJ, Wang L, Dinh HV, Suthers PF, Maranas CD. Building kinetic models for metabolic engineering. Curr Opin Biotechnol. 2021;67:35-41.
19. Lázaro J, Wongprommoon A, Júlvez J, Oliver SG. Enhancing genome-scale metabolic models with kinetic data. Bioinform Adv. 2025;5(1):vbaf166.
20. Okuda S, Yamada T, Hamajima M, Itoh M, Katayama T, Bork P, et al. KEGG Atlas mapping for metabolic pathways. Nucleic Acids Res. 2008;36(Web Server issue):W423-6.
21. Cho JL, Ling MH. Adaptation of whole-cell kinetic model UniKin1 to *E. coli*. EC Microbiol. 2021;17(2):254-60.

22. Kwan ZJ, Teo W, Lum AK, Ng SM, Ling MH. *Ab initio* whole-cell kinetic model of Stutzerimonas balearica. Acta Sci Microbiol. 2024;7(2):28-31.
23. Maiyappan S, Sim SS, Ramesh G, Low L, Matarage ML, Ling MH. *Ab initio* whole-cell kinetic models of Bacillus subtilis. J Clin Immunol Microbiol. 2025;6(2):1-6.
24. Sim BJH, Tan NTF, Ling MHT. Multilevel metabolic modelling using ODEs. In: Ranganathan S, Cannataro M, Khan AM, editors. Encycl Bioinform Comput Biol. 2nd Ed. Oxford: Elsevier. 2025;491-8.
25. Müller-Hill B. The lac operon: a short history of a genetic paradigm. Berlin: Springer. 1996.
26. Churchward G, Bremer H, Young R. Transcription in bacteria at different DNA concentrations. J Bacteriol. 1982;150(2):572-81.
27. Gray WJ, Midgley JE. Control of RNA synthesis in bacteria. Biochem J. 1971;122(2):161-9.
28. Kubitschek HE. Cell volume increase in *Escherichia coli*. J Bacteriol. 1990;172(1):94-101.
29. Hu P, Janga SC, Babu M, Díaz-Mejía JJ, Butland G, Yang W, et al. Global functional atlas of *E. coli*. PLoS Biol. 2009;7(4):e96.
30. So LH, Ghosh A, Zong C, Sepúlveda LA, Segev R, Golding I. Transcriptional time series in *E. coli*. Nat Genet. 2011;43(6):554-560.
31. Schwanhäusser B, Busse D, Li N, Dittmar G, Schuchhardt J, Wolf J, et al. Corrigendum: Gene expression control. Nature. 2013;495(7439):126-7.
32. Maurizi MR. Proteases and protein degradation in *E. coli*. Experientia. 1992;48(2):178-201.
33. Murthy MV, Balan D, Kamarudin NJ, Wang VC, Tan XT, Ramesh A, et al. UniKin1: A universal whole-cell kinetic model. Acta Sci Microbiol. 2020;3(10):4-8.
34. Bar-Even A, Noor E, Savir Y, Liebermeister W, Davidi D, Tawfik DS, et al. Moderately efficient enzyme. Biochemistry. 2011;50(21):4402-10.
35. Ling MH. AdvanceSyn toolkit. MOJ Proteomics Bioinform. 2020;9(4):83-86.
36. Yong B. Comparison of Runge-Kutta and homotopy analysis methods. J Phys Conf Ser. 2019;1317:012020.
37. Ling MH. COPADS IV ODE solvers. Adv Comput Sci Int J. 2016;5(3):5-11.
38. Saisudhanbabu T, Yeo KY, Arivazhagan M, Senthilkumar A, Le MA, Wong TB, et al. Whole-cell kinetic model of *Limos lactobacillus* fermentum. EC Clin Med Case Rep. 2025;8(4):1-4.
39. Arivazhagan M, Senthilkumar A, Yeo KY, Saisudhanbabu T, Le MA, Wong TB, et al. Whole-cell kinetic model of *Bifidobacterium bifidum*. Acta Sci Nutr Health. 2025;9(1):42-5.
40. Senthilkumar A, Madhunisha A, Yeo KY, Saisudhanbabu T, Le MA, Wong TB, et al. Whole-cell kinetic model of *Lactobacillus acidophilus*. J Clin Immunol Microbiol. 2025;6(1):1-5.
41. Wong TB, Le MA, Arivazhagan M, Senthilkumar A, Yeo KY, Saisudhanbabu T, et al. Whole-cell kinetic models of *E. coli*. Scholastic Med Sci. 2025;3(2):1-4.
42. Ambel WB, Tan LP, Toh D, Thirunavukarasu D, Natarajan K, Ling MH. UniKin2: A pan-reactome kinetic model. Int J Res Med Clin Sci. 2025;3(2):77-80.
43. Ahn-Horst TA, Mille LS, Sun G, Morrison JH, Covert MW. Expanded whole-cell model of *E. coli*. NPJ Syst Biol Appl. 2022;8(1):30.
44. Chagas MS, Trindade Dos Santos M, Argollo de Menezes M, da Silva FAB. Boolean gene regulatory network of *Pseudomonas aeruginosa*. Front Microbiol. 2023;14:1274740.
45. Hao T, Song Z, Zhang M, Zhang L, Yang J, Li J, Sun J. Metabolic-protein interaction network of Eriocheir sinensis. Genes (Basel). 2024;15(4):410.

About the journal

ATHENAEUM SCIENTIFIC PUBLISHERS

Journal of Clinical Immunology and Microbiology is an international, peer-reviewed, open-access journal published by Athenaeum Scientific Publishers. The journal publishes original research articles, case reports, editorials, reviews, and commentaries relevant to its scope. It aims to disseminate high-quality scholarly work that contributes to research, clinical practice, and academic knowledge in the field.

All submissions are evaluated through a structured peer-review process in accordance with established editorial and ethical standards. Manuscripts are submitted and processed through the journal's online submission system.

Manuscript submission: **https://athenaeumpub.com/submit-manuscript/**