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PhD, PI, Professor

Shenzhen Institutes of Advanced Technology (SIAT)

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Education & Degrees

June 2018	Ph.D. in Biochemical engineering	East China University of Science and Technology
June 2012	B.E. in Bioengineering	Huazhong Agricultural University

Positions

July 2024 – Present	Adjunct professor	Shenzhen University of Advanced Technology
Dec 2023 – Present	Professor	SIAT, CAS
Feb 2023 – Dec 2023	Associate professor	SIAT, CAS
Feb 2018 – Dec 2022	Post doc	Chalmers University of Technology

Key Publications

- Reconstruction, simulation and analysis of enzyme-constrained metabolic models using GECKO
 Toolbox 3.0. *Nat Protoc* (2024) [ESI Highly Cited Paper, highlighted by <u>Nature Reviews</u>
 Genetics & Current Opinion]
- 2. Yeast has evolved to minimize protein resource cost for synthesizing amino acids. *PNAS* (2022)
- 3. In vitro turnover numbers do not reflect in vivo activities of yeast enzymes. *PNAS* (2021) [highlighted by <u>Current Opinion</u>, and recommended in <u>Faculty Opinions</u>]
- 4. Proteome constraints reveal targets for improving microbial fitness in nutrient-rich environments. *Mol Syst Biol* (2021)
- 5. Yeast optimizes metal utilization based on metabolic network and enzyme kinetics. *PNAS* (2021) [highlighted by <u>Current Opinion</u>, and picked up by <u>Mirage News</u>]
- 6. Energy metabolism controls phenotypes by protein efficiency and allocation. *PNAS* (2019) [recommended in <u>Faculty Opinions</u>, and picked up by <u>ScienceDaily</u> etc.]

Grants

2024.12 - 2027.11	National Key R&D Program of China	4 M CNY
2024.01 - 2026.12	Shenzhen Science and Technology Program	0.75 M CNY
2024.01 - 2026.12	Shenzhen Medical Research Fund	0.8 M CNY
2024.01 - 2026.12	Chinese Academy of Sciences Talents Program	X M CNY
2024.01 - 2026.12	National Talents Program	X M CNY
2023.12 - 2028.11	National Key R&D Program of China	1.2 M CNY

Editorial Experience

2024 – Present Advanced Biotechnology Youth editor

Peer Review Experience

Reviewer for scientific journals including Nature Communications, Trends in Biotechnology, PNAS, Cell Systems, Molecular Systems Biology, Analytical Chemistry, Computational and Structural Biotechnology Journal, Bioinformatics, Biotechnology and Bioengineering, Current Opinion in Systems Biology, Biotechnology Journal, ChemBioChem, FEMS Microbiology Letters, Advanced Biotechnology and Chinese Journal of Biotechnology.

Web of Science: https://www.webofscience.com/wos/author/record/2235260

Teaching Experience

- Mathematical modeling of energy metabolism. Lecture at Chalmers University of Technology.
 Sweden. Oct 10, 2022
- Constraint-based modeling of metabolism. Lecture at Shandong University. Virtual. Nov 10, 2021

Presentations

- Enzyme-constrained modeling. Conference of Industrial Biotechnology and Biomanufacturing of China. Tianjin, China. Nov 16, 2024 (Oral)
- Enzyme-constrained metabolic modeling. Symposium on Synthetic Biotechnology and Intelligent Biomanufacturing. Fuzhou, China. Aug 3, 2024 (Oral)
- Genome-scale modeling of metabolism with enzyme constraints. Sino-German MegaSyn Symposium 2024 by Dalian Institute of Chemical Physics of Chinese Academy of Sciences. Dalian, China. Jun 28, 2024 (Oral)
- Understanding metabolism by constraint-based models. The 207th Academic Seminar of the Institute
 of Synthetic Biology by Shenzhen Institutes of Advanced Technology of Chinese Academy of
 Sciences. Virtual. Jan 11, 2022 (Oral)
- Understanding metabolism by constraint-based models. International Forum for Young Scholars by Institute of Biological and Molecular Smart Manufacturing of ZJU-Hangzhou Global Scientific and Technological Innovation Center. Virtual. May 29, 2021 (Oral)
- Understanding metabolism by constraint-based models. International Forum for Young Scholars by School of Life Sciences of Nanjing University. Virtual. May 26, 2021 (Oral)
- Yeast optimizes metal utilization based on metabolic network and enzyme kinetics. International Forum for Young Scholars by School of Biotechnology of East China University of Science and Technology. Virtual. May 15, 2021 (Oral)
- Modeling energy metabolism with proteome constraints in *E. coli* and yeast. Annual Meeting of Novo Nordisk Foundation Center for Biosustainability. Lyngby, Denmark. Sept 4, 2019 (Poster)

Supervision

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Zichao Wu 吴子超	Research assistant	2024-Present
Jingyu Yang 杨晶宇	PhD student (Guest)	2024-Present
Yilan Xie 谢怡兰	Master student (UCAS)	2024-Present
Jiazi Peng 彭佳姿	Master student (SUSTech)	2024 - Present
Yuhang Li 李渝航	Research assistant	2024 - Present
Yupeng Liao 廖渝鹏	Master student (Guest)	2024-Present
Yuanyuan Huang 黄媛媛	Research assistant	2024-Present
Yulong Deng 邓育珑	Research assistant	2024-Present
Longtao Li 李龙涛	Research assistant	2024-Present
Yu Huang 黄煜	Research assistant	2024-Present
Jiawei Huang 黄家蔚	Research assistant	2024-Present
Weihang Dong 董伟航	Master student (Guest)	2024-Present
Yongzhu Li 李永珠	Master student (UCAS)	2023 - Present
Siyu Han 韩思宇	Master student (Guest)	2023 - Present
Zhihao Liu 刘志豪	PhD student (Guest)	2023 - 2024
Jingyu Yang 杨晶宇	Research assistant	2023 - 2024

Full List of Publications

Google scholar: https://scholar.google.com/citations?hl=en&user=tArfdEcAAAAJ # equal contribution, * corresponding author

- o Peer-reviewed research articles
 - 1. Han S., Wu K., Wang Y.*, Li F.*, **Chen Y.***, 2024. Auxotrophy-based curation improves the consensus genome-scale metabolic model of yeast. *Synth Syst Biotechnol* 9, 861–870.
 - 2. Chen Y.#, Gustafsson J.#, Tafur Rangel A.#, Anton M., Domenzain I., Kittikunapong C., Li F., Yuan L., Nielsen J., Kerkhoven E.J.*, 2024. Reconstruction, simulation and analysis of enzyme-constrained metabolic models using GECKO Toolbox 3.0. *Nat Protoc* 19, 629–667.
 - 3. Li F.#*, Chen Y.#, Anton M.#, Nielsen J.*, 2023. GotEnzymes: an extensive database of enzyme parameter predictions. *Nucleic Acids Res* 51, D583–D586.
 - 4. **Chen Y.**, Nielsen J.*, 2022. Yeast has evolved to minimize protein resource cost for synthesizing amino acids. *Proc Natl Acad Sci U S A* 119, e2114622119.
 - 5. **Chen Y.**, Nielsen J.*, 2021. In vitro turnover numbers do not reflect in vivo activities of yeast enzymes. *Proc Natl Acad Sci U S A* 118, e2108391118.
 - Chen Y.#, van Pelt-KleinJan E.#, van Olst B., Douwenga S., Boeren S., Bachmann H., Molenaar D., Nielsen J.*, Teusink B.*, 2021. Proteome constraints reveal targets for improving microbial fitness in nutrient-rich environments. *Mol Syst Biol* 17, e10093.
 - 7. **Chen Yu**, Li F., Mao J., Chen Yun, Nielsen J.*, 2021. Yeast optimizes metal utilization based on metabolic network and enzyme kinetics. *Proc Natl Acad Sci U S A* 118, e2020154118.
 - 8. Chen Y., Sun Y., Liu Z., Dong F., Li Y., Wang Y.*, 2020. Genome-scale modeling for *Bacillus coagulans* to understand the metabolic characteristics. *Biotechnol Bioeng* 117, 3545–3558.
 - 9. **Chen Y.**, Nielsen J.*, 2019. Energy metabolism controls phenotypes by protein efficiency and allocation. *Proc Natl Acad Sci U S A* 116, 17592–17597.
 - 10. **Chen Y.**, Wang Y.*, Nielsen J.*, 2017. Systematic inference of functional phosphorylation events in yeast metabolism. *Bioinformatics* 33, 1995–2001.
 - 11. Chen Y., Dong F., Wang Y.*, 2016. Systematic development and optimization of chemically defined medium supporting high cell density growth of *Bacillus coagulans*. *Appl Microbiol Biotechnol* 100, 8121–8134.
 - 12. Chen R.#, Chen X.#, Chen Y., Yang J., Chen W.*, Zhou Y.J.*, Zhang L.*, 2025. De novo biosynthesis of plant lignans by synthetic yeast consortia. *Nat Chem Biol* 1–10.
 - 13. Chen X.*, Li F., Li X., Otto M., **Chen Y.**, Siewers V.*, 2025. Model-assisted CRISPRi/a library screening reveals central carbon metabolic targets for enhanced recombinant protein production in yeast. *Metab Eng* 88, 1–13.
 - 14. Qin N.#, Li L.#, Wan X., Ji X., Chen Yu, Li C., Liu P., Zhang Y., Yang W., Jiang J., Xia J., Shi S., Tan T., Nielsen J.*, Chen Yun*, Liu Z.*, 2024. Increased CO2 fixation enables high carbon-yield production of 3-hydroxypropionic acid in yeast. *Nat Commun* 15, 1591.
 - 15. Zhang Y., Su M., Chen Y., Wang Z., Nielsen J., Liu Z.*, 2023. Engineering yeast mitochondrial metabolism for 3-hydroxypropionate production. *Biotechnology for Biofuels and Bioproducts* 16, 64.
 - 16. Qin N., Li L., Ji X., Pereira R., **Chen Yu**, Yin S., Li C., Wan X., Qiu D., Jiang J., Luo H., Zhang Yueping, Dong G., Zhang Yiming, Shi S., Jessen H.J., Xia J., Chen Yun, Larsson C., Tan T., Liu Z.*, Nielsen J.*, 2023. Flux regulation through glycolysis and respiration is balanced by inositol pyrophosphates in yeast. *Cell* 186, 748-763.e15.

- 17. Cao X., Yu W., **Chen Y.**, Yang S., Zhao Z.K., Nielsen J., Luan H., Zhou Y.J.*, 2023. Engineering yeast for high-level production of diterpenoid sclareol. *Metab Eng* 75, 19–28.
- 18. Li F.#, Yuan L.#, Lu H., Li G., Chen Y., Engqvist M.K.M., Kerkhoven E.J.*, Nielsen J., 2022. Deep learning-based kcat prediction enables improved enzyme-constrained model reconstruction. *Nat Catal* 5, 662–672.
- 19. Li F., Chen Y.#, Qi Q., Wang Y.#, Yuan L.#, Huang M., Elsemman I.E., Feizi A.*, Kerkhoven E.J., Nielsen J.*, 2022. Improving recombinant protein production by yeast through genome-scale modeling using proteome constraints. *Nat Commun* 13, 2969.
- 20. Xia J., Sánchez B.J., Chen Y., Campbell K., Kasvandik S., Nielsen J.*, 2022. Proteome allocations change linearly with the specific growth rate of *Saccharomyces cerevisiae* under glucose limitation. *Nat Commun* 13, 2819.
- Chen R., Gao J., Yu W., Chen X., Zhai X., Chen Y., Zhang L.*, Zhou Y.J.*, 2022.
 Engineering cofactor supply and recycling to drive phenolic acid biosynthesis in yeast. *Nat Chem Biol* 18, 520–529.
- 22. Lu H.#, Li F.#, Yuan L.#, Domenzain I., Yu R., Wang H., Li G., **Chen Y.**, Ji B., Kerkhoven E.J., Nielsen J.*, 2021. Yeast metabolic innovations emerged via expanded metabolic network and gene positive selection. *Mol Syst Biol* 17, e10427.
- 23. Qin J., Krivoruchko A., Ji B., **Chen Y.**, Kristensen M., Özdemir E., Keasling J.D., Jensen M.K., Nielsen J.*, 2021. Engineering yeast metabolism for the discovery and production of polyamines and polyamine analogues. *Nat Catal* 4, 498–509.
- 24. Zhang J.#, Petersen S.D.#, Radivojevic T., Ramirez A., Pérez-Manríquez A., Abeliuk E., Sánchez B.J., Costello Z., **Chen Y.**, Fero M.J., Martin H.G., Nielsen J., Keasling J.D., Jensen M.K.*, 2020. Combining mechanistic and machine learning models for predictive engineering and optimization of tryptophan metabolism. *Nat Commun* 11, 4880.
- 25. Liu Q., Yu T., Li X., Chen Yu, Campbell K., Nielsen J., Chen Yun*, 2019. Rewiring carbon metabolism in yeast for high level production of aromatic chemicals. *Nat Commun* 10, 4976.
- 26. Lv X., Yu B., Tian X., Chen Y., Wang Z., Zhuang Y., Wang Y.*, 2016. Effect of pH, glucoamylase, pullulanase and invertase addition on the degradation of residual sugar in Llactic acid fermentation by *Bacillus coagulans* HL-5 with corn flour hydrolysate. *J Taiwan Inst Chem Eng* 61, 124–131.

Peer-reviewed reviews

- Li L., Nielsen J.*, Chen Y.*, 2025. Personalized gut microbial community modeling by leveraging genome-scale metabolic models and metagenomics. *Curr Opin Biotechnol* 91, 103248.
- 2. **Chen Y.**#*, Gustafsson J.#, Yang J., Nielsen J., Kerkhoven E.J.*, 2024. Single-cell omics analysis with genome-scale metabolic modeling. *Curr Opin Biotechnol* 86, 103078.
- 3. **Chen Y.**, Li F., Nielsen J.*, 2022. Genome-scale modeling of yeast metabolism: retrospectives and perspectives. *FEMS Yeast Res* 22, foac003.
- 4. **Chen Y.**, Nielsen J.*, 2021. Mathematical modeling of proteome constraints within metabolism. *Curr Opin Syst Biol* 25, 50–56.
- Chen Y., Nielsen J.*, 2016. Flux control through protein phosphorylation in yeast. FEMS Yeast Res 16, fow096.
- 6. Shi S., Chen Y., Nielsen J.*, 2025. Metabolic Engineering of Yeast. Annu Rev Biophys.

- 7. Mao J.#, Zhang H.#, **Chen Yu**, Wei L., Liu J., Nielsen J.*, Chen Yun*, Xu N.*, 2024. Relieving metabolic burden to improve robustness and bioproduction by industrial microorganisms. *Biotechnol Adv* 74, 108401.
- 8. Li F.*, Chen Y., Gustafsson J., Wang H., Wang Y., Zhang C., Xing X., 2023. Genome-scale metabolic models applied for human health and biopharmaceutical engineering. *Quant Biol* 11, 363–375.

Commentaries

1. **Chen Y.***, Li F., 2024. Metabolomes evolve faster than metabolic network structures. *Proc Natl Acad Sci U S A* 121, e2400519121.

o Book chapters

- 1. **Chen Y.**, Nielsen J., Kerkhoven E.J., 2021. Proteome Constraints in Genome-Scale Models, in: Nielsen, J., Stephanopoulos, G., Lee, S.Y. (Eds.), Metabolic Engineering: Concepts and Applications. John Wiley & Sons, Ltd, pp. 137–152.
- 2. **Chen Y.**, Li G., Nielsen J., 2019. Genome-Scale Metabolic Modeling from Yeast to Human Cell Models of Complex Diseases: Latest Advances and Challenges, in: Oliver, S.G., Castrillo, J.I. (Eds.), Yeast Systems Biology: Methods and Protocols, Methods in Molecular Biology. Springer, New York, NY, pp. 329–345.
- 3. Lu H., Chen Y., Nielsen J., Kerkhoven E.J., 2021. Kinetic Models of Metabolism, in: Nielsen, J., Stephanopoulos, G., Lee, S.Y. (Eds.), Metabolic Engineering: Concepts and Applications. John Wiley & Sons, Ltd, pp. 153–170.

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