

# Nanozymes

Lizeng Gao,\* Hui Wei,\* Shaojun Dong,\* and Xiyun Yan\*

Nanozymes represent a new generation of artificial enzymes that provide a way to perform biological catalysis using nanomaterials. In 2007, Yan and co-workers discovered for the first time that ferromagnetic nanoparticles exhibited peroxidase-like activity,<sup>[1]</sup> which paved the way for the development of nanozymes. In 2013, Wei and Wang used the term “nanozymes” to define nanomaterials with enzyme-like properties as next generation artificial enzymes.<sup>[2]</sup> Owing to their unique features, including high activity, high stability, tunability of activity, multifunctionality, and low cost for scale-up, nanozymes have attracted great attention compared to enzymes, traditional enzyme mimics, and common nanomaterials.

In the past 16 years, nanozymes have become an emerging interdisciplinary field of nanotechnology, catalysis and biomedicine. To date, more than 420 laboratories from 42 countries have reported over 1200 types of nanozymes and published over 10 000 papers<sup>[3]</sup> (see **Figure 1**). Now, nanozymes can be rationally designed instead of being produced by trial-and-error. Excitingly, some nanozymes show comparable or even better catalytic performance compared to their nature counterparts. Consequently, nanozymes have shown great potential in the fields of functional nanomaterials, biomedicine, new energy, green synthesis, environmental treatment, etc. Nanozymes were selected in the Top Ten Emerging Technologies in Chemistry by the International Union of Pure and Applied Chemistry (IUPAC) in 2022.<sup>[4]</sup>

This special issue brings some of the most advanced progress in the field of nanozymes. There are 25 papers, including 9 *Reviews*, 4 *Perspectives*, and 12 *Research Articles*, with topics covering from rational design and modulation to mechanisms and potential applications. We believe that such a special issue will not only accelerate the development of the nanozyme field but also attract more researchers to explore the hidden talents of nanomaterials for broad applications.

Prof. Juewen Liu from University of Waterloo has contributed a perspective introducing the evolution of nanozyme definition and how to determine the activity (article number 2211041). Prof. Xingfa Gao from National Center for Nanoscience and Technology, Chinese Academy of Sciences (CAS), discusses the reaction mechanisms and kinetics of nanozymes, especially from the theoretical calculations (article number 2211151). In addition, unique features of nanozymes are summarized. For instance, Prof. Ning Gu and Prof. Yu Zhang from Southeast University summarize the progress of multi-enzyme-like features of nanozymes (article number 2211210). Interestingly, Prof. Lianbing Zhang from Northwestern Polytechnical University presents a manganese-based nanozyme with cold-adaptability to catalyze the reaction under low temperature (article number 2206421).

The engineering, improvement and optimization of catalytic performances regarding the activity and selectivity are important for the field of nanozymes, which connects the fundamental research and translational applications. Prof. Xinglu Huang from Nankai University presents a promising machine-learning assisted strategy for the rational design of new nanozymes (article number 2210848). Meanwhile, Prof. Xiaogang Qu from Changchun Institute of Applied Chemistry, CAS presents biosystem-inspired strategies for nanozymes design by leveraging the structure of active center of natural enzymes, simulating the behavior changes of natural enzymes in the catalytic process or mimicking the specific biological processes or living organisms (article number 2211147). Prof. Yuehe Lin from Washington State University present a strategy using phosphorus modulation to optimize iron single-atom nanozymes (article number 2209633). In addition, surface engineering is also an important route to improve the nanozyme performance. Prof. Sudipta Seal from University of Central Florida presents the fundamental surface chemistry processes and their implications in reducible metal oxide nanozymes (rNZs) (article number 2211261). Prof. Lizeng Gao from Institute of Biophysics, CAS presents a surface-ligand-engineered ruthenium nanozyme with high activity superior to horseradish peroxidase (article number 2300387). Prof. Paolo Scrimin and Prof. Fabrizio Mancin from University of Padova reveal that amines contribute to the stability of nanozymes (article number 2211624). Aptamer modification can also improve the performance of nanozymes, which is presented in a perspective by Prof. Itamar Willner from the Hebrew Uni-

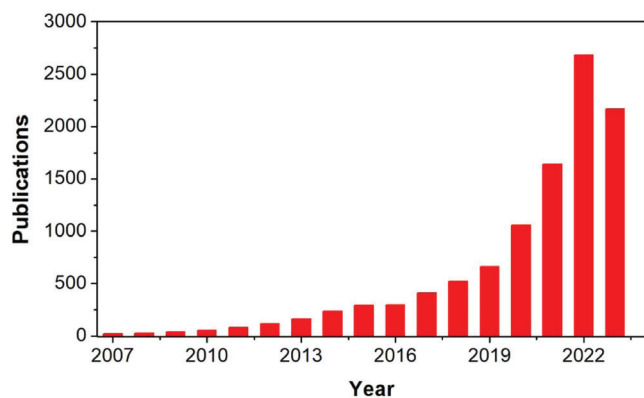
L. Gao, X. Yan  
CAS Engineering Laboratory for Nanozymes, Key Laboratory of Biomacromolecules  
Institute of Biophysics  
Chinese Academy of Sciences  
Beijing 100101, China  
E-mail: gaolizeng@ibp.ac.cn; yanxy@ibp.ac.cn

H. Wei  
Department of Biomedical Engineering  
College of Engineering and Applied Sciences  
Nanjing National Laboratory of Microstructures  
Jiangsu Key Laboratory of Artificial Functional Materials  
State Key Laboratory of Analytical Chemistry for Life Science  
School of Chemistry and Chemical Engineering  
Chemistry and Biomedicine Innovation Center (ChemBIC)  
Nanjing University  
Nanjing, Jiangsu 210023, China  
E-mail: weihui@nju.edu.cn

S. Dong  
State Key Laboratory of Electroanalytical Chemistry  
Changchun Institute of Applied Chemistry  
Chinese Academy of Sciences  
Changchun, jilin 130022, China  
E-mail: dongsj@ciac.ac.cn

 The ORCID identification number(s) for the author(s) of this article can be found under <https://doi.org/10.1002/adma.202305249>

DOI: 10.1002/adma.202305249



**Figure 1.** Number of articles versus year published in the field of nanozymes. The data are from Google Scholar on May 26, 2023.

versity of Jerusalem (article number 2210885). Defect engineering is also demonstrated to improve nanozyme performance by Prof. Yanli Zhao from Nanyang Technological University (article number 2206401). Importantly, Prof. J. Justin Gooding and Prof. Richard D. Tilley from University of New South Wales present a perspective about the approaches to improve the selectivity of nanozymes (article number 2211288), which may be helpful to further improve catalytic performance.

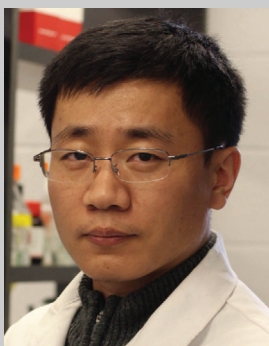
Several typical nanozymes are presented with specific applications. Prof. Erkang Wang and Prof. Jing Li from Changchun Institute of Applied Chemistry, CAS summarize the current advances on single-atom nanozymes and their biological applications (article number 2211724). Prof. Vincent M. Rotello from University of Massachusetts Amherst highlights the unique features of biorthogonal nanozymes in biomedical applications (article number 2300943). Prof. Xiue Jiang, who is also from Changchun Institute of Applied Chemistry, CAS, presents the progress on regulation of cellular metabolism using nanozymes to achieve therapeutic effects (article number 2301810). Specifically, Prof. Molly M. Stevens from Imperial College London presents the current understanding of nanozymes for disease diagnostics and biosensing applications and the unmet challenges (article number 2300184). Prof. Taeghwan Hyeon from Seoul National University presents the progress of ceria-based nanozymes as therapeutic antioxidants in biomedical field (article number 2210819).

Nanozymes with specific applications are also demonstrated in this special issue. Prof. James M. Tour from Rice University reports a coconut-derived oxidized activated charcoal (cOAC) nanozyme with superoxide dismutase (SOD)-like activity to treat traumatic brain injury (article number 2211239). Prof. Kelong Fan and Prof. Xiyun Yan from Institute of Biophysics, CAS report a peptide-templated nanozyme with responsibility to thrombin for remedying ischemic stroke (article number 2210144). Prof. Thomas Kent from Texas A&M University present a carbon nanozyme with H<sub>2</sub>S oxidation activity that can be used for the treatment of Down syndrome (article number 2211241). Prof. Omar K. Farha from Northwestern University reports a fibrous zirconium-based metal-organic framework (Zf-MOF) nanozyme aerogel to hydrolyze organophosphate toxins (article number 2300951). Prof. Liguang Xu from Jiangnan University reports a chiral MoSe<sub>2</sub> nanozyme for ultrasensitive monitoring of reactive oxygen species (ROS) in vivo (article number 2208037). Prof. Hyun Koo from University of Pennsylvania reports nanozyme-based robotics for targeted fungi eradication (article number 2300320). Prof. Minmin Liang from Beijing Institute of Technology reports an insect-inspired hierarchical nanozyme for antibacterial treatment (article number 2210455).

## Conflict of Interest

The authors declare no conflict of interest.

- [1] L. Gao, J. Zhuang, L. Nie, J. Zhang, Y. Zhang, N. Gu, T. Wang, J. Feng, D. Yang, S. Perrett, X. Yan, *Nat. Nanotechnol.* **2007**, *2*, 577.
- [2] a) H. Wei, E. Wang, *Chem. Soc. Rev.* **2013**, *42*, 6060; b) J. Wu, X. Wang, Q. Wang, Z. Lou, S. Li, Y. Zhu, L. Qin, H. Wei, *Chem. Soc. Rev.* **2019**, *48*, 1004; c) H. Wei, L. Gao, K. Fan, J. Liu, J. He, X. Qu, S. Dong, E. Wang, X. Yan, *Nano Today* **2021**, *40*, 101269; d) Y. Huang, J. Ren, X. Qu, *Chem. Soc. Rev.* **2019**, *119*, 4357.
- [3] K. Fan, L. Gao, H. Wei, B. Jiang, D. Wang, R. Zhang, J. He, X. Meng, Z. Wang, H. Fan, T. Wen, D. Duan, L. Chen, W. Jiang, Y. Lu, B. Jiang, Y. Wei, W. Li, Y. Yuan, H. Dong, L. Zhang, C. Hong, Z. Zhang, M. Cheng, X. Geng, T. Hou, Y. Hou, J. Li, G. Tang, Y. Zhao, et al., *Prog. Chem.* **2023**, *35*, 1.
- [4] IUPAC Announces the 2022 Top Ten Emerging Technologies in Chemistry, <https://iupac.org/iupac-2022-top-ten/> (accessed: October 2022).



**Lizeng Gao** is a professor at Institute of Biophysics, Chinese Academy of Sciences (CAS). He received his B.S. and M.S. degree from Jilin University and Ph.D. degree from Institute of Biophysics, CAS. He joined CAS Engineering Laboratory for Nanozymes at Institute of Biophysics, CAS in 2019. His research focuses on discovering intrinsic biological activities of nanomaterials (nanozymes) and developing biomimetic strategies for catalytic biomedical applications including antibacterial, antitumor, etc. He received the IADR Innovation in Oral Care Award in 2015.



**Hui Wei** is a Professor at Nanjing University and a Fellow of the Royal Society of Chemistry. He received his B.S. degree from Nanjing University (advisor: Professor Xinghua Xia) and Ph.D. degree from Changchun Institute of Applied Chemistry, Chinese Academy of Sciences (advisor: Professor Erkang Wang). He then joined Professors Yi Lu's and Shuming Nie's groups for two postdoctoral trainings before he started his independent career at Nanjing University. His research interests are focused on the design and synthesis of functional nanomaterials (such as nanozymes) and the development of new methodologies for analytical and biomedical applications.



**Shaojun Dong** is a professor of chemistry at Changchun Institute of Applied Chemistry, Chinese Academy of Sciences. She has been a member of the Academy of Sciences of the Developing World since 1999. She has been on the editorial and advisory boards of six international journals: *Chemical Communications*, *Biosensors & Bioelectronics*, *Electrochemistry Communications*, *Sensors*, *Bioelectrochemistry*, and *Talanta*. Her research interests concentrate on electrochemistry with interdisciplinary fields, such as chemically modified electrodes, nanomaterials and nanotechnology, bioelectrochemistry, spectroelectrochemistry, and biofuel cells. Recently, she presented the idea for single-atom structure-mimetic nanozymes and also described the glucose-oxidase-like catalytic mechanism of noble-metal nanozymes. To date, she has published much more than 1000 papers in international SCI journals and 16 books/monographs cited over 62 000 times with an *H*-index over 120. She has been selected as a global "Highly Cited Researcher" 8 times over 19 years (2002–2019) by ISI Web of Science.



**Xiyun Yan** is a professor at the Institute of Biophysics, CAS. In 2015, she was elected as the new president of Asian Biophysics Association and Academician of Chinese Academy of Sciences. Her research interests include studying tumor biology, finding novel targets, and developing new methods for tumor diagnosis and therapy. In 2007, she and her research group discovered that iron oxide nanoparticles possess peroxidase-like activity, which provided the first evidence of nanozymes. Subsequently, she used nanozymes as enzyme mimics to create new methods for tumor diagnosis and nanozymestrip for rapid local detection of infectious diseases such as the Ebola virus. In 2022, she, along with her colleagues, formulated an ISO Standard for Nanozyme activity measurement, which has been launched (ISO/TS 5094) and a China National Standard for Nanozyme vocabulary, which is now in the final stage of approval. She was recognized as a highly cited researcher by Clarivate in 2022, publishing 219 papers with an *H*-index in Scopus of 57 ranking in the top 1% for field and year in cross-field. Meanwhile, she was also included in Elsevier's "World's Top 2% Scientists" of 2022.