Designing multifunctional enzymatic devices for biosensing and chemical conversion

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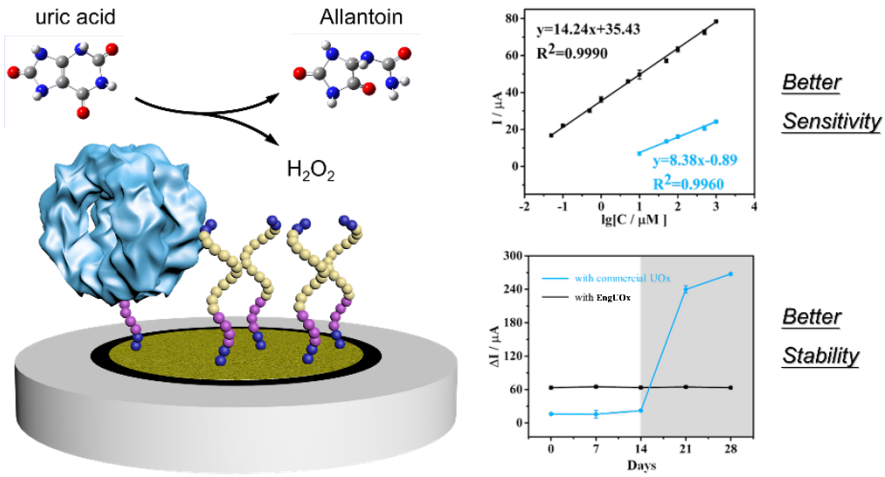
Summary

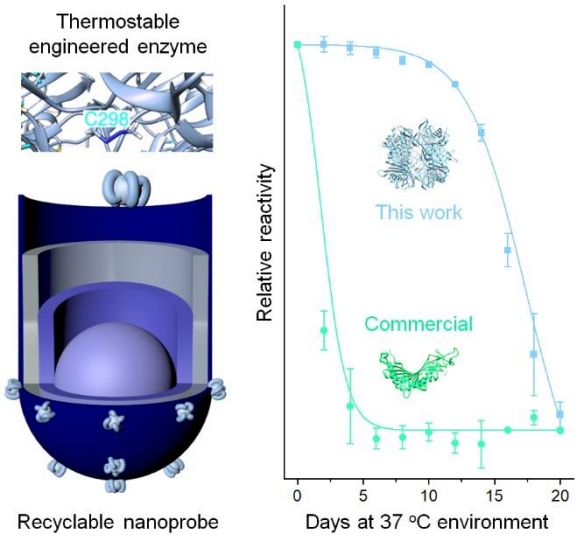
This thesis focuses on the **design of multifunctional enzymatic devices for biosensing and chemical conversion**, with a primary emphasis on improving the **performance** and **stability** of biosensors through enzyme engineering. Biosensors play a crucial role in modern diagnostics, allowing for rapid and accurate detection of biomarkers in the human body, which is essential for early disease diagnosis. In **Chapter 1,** we provided examples of enzymes used in the manufacture of different biosensors, with various readout signals. However, current biosensors face limitations in **sensitivity**, **selectivity**, and, most importantly, **stability**, which restricts their practical application and commercialization. To address these challenges, the thesis explores enzyme engineering as a solution to enhance the overall functionality of biosensors. Through rational design, the research demonstrates how engineered enzymes can improve biosensor performance across different signal readout systems: **electrochemical**, **optical**, and **photothermal.**

While electrochemical biosensors offer excellent sensitivity, their complex construction process can impact the activity of biomolecules.To address this challenge, we explored the use of thermostable enzymes in **Chapter 2** as a means of enhancing the stability of electrochemical biosensors. In this chapter, a **simple electrochemical biosensor** is developed using **engineered urate oxidase (UOx)** as the biorecognition element (Scheme 1). Compared to biosensors constructed with natural UOx, the engineered version shows significant improvements in both **stability** and **detection range**. The sensor operates by measuring changes in electrochemical signals generated during the UOx-catalyzed reaction. The improved stability of the engineered enzyme allows the sensor to function over a broader range of conditions, making it more practical for real-world diagnostic applications. This chapter demonstrates that by modifying enzymes at the molecular level, their inherent properties, such as stability and reactivity, can be significantly enhanced, opening up possibilities for more robust electrochemical biosensors in medical diagnostics.



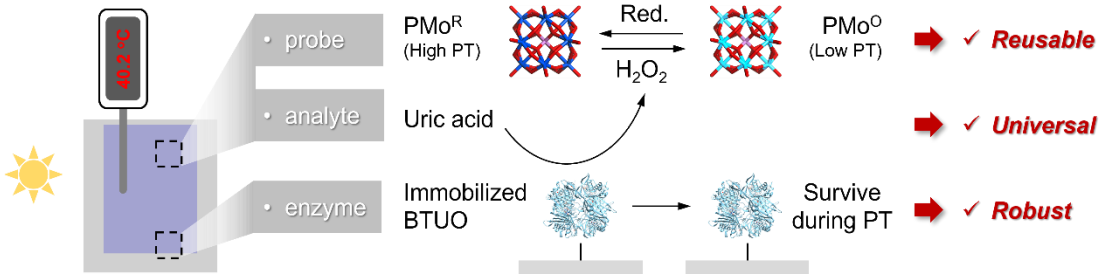
Scheme 1. Thermostable UOx enhanced the stability of the uric acid electrochemical biosensors to make this biosensor could be stored at room temperature for more than 2 weeks.

Following the successful design of devices that utilise thermally stable enzymes to enhance the stability of electrochemical enzyme-based sensors, we sought to apply this enzyme to other biosensors. We discovered that the issue of lack of recyclability of optical enzymatic biosensors could be addressed by employing our engineered enzyme. In **Chapter 3**, we introduce a **novel optical biosensor** that utilizes a redox-reversible probe combined with engineered UOx (Scheme 2). This biosensor uses **optical signals** (such as fluorescence or colorimetric changes) to detect the presence of target molecules. The main innovation in this chapter is the probe's **thermal stability** and **recyclability**. By using the engineered UOx, the biosensor becomes highly resistant to temperature fluctuations, maintaining its performance even in suboptimal conditions. Additionally, the sensor's probe can be recycled multiple times in the presence of redox agents, reducing waste and making the sensor more sustainable. This chapter illustrates how optical biosensors can benefit from enzyme engineering by providing more **sensitive**, **stable**, and **sustainable** solutions for real-time biomarker detection.



Scheme 2. Recyclable optical polyoxometalates as the optical agent for designing recyclable optical biosensors by using engineered UOx for uric acid detection.

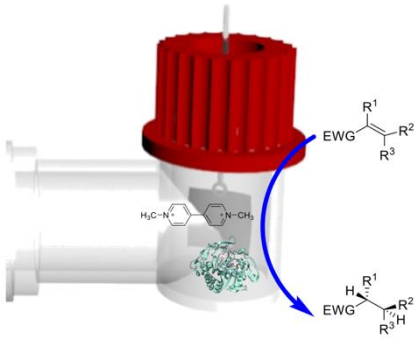
Furthermore, based on our experience in the design of household photothermal biosensors, we believe that if engineered enzymes can be applied to photothermal biosensors, there is the possibility of developing a simple, portable household device. In **Chapter 4**, a **recyclable photothermal biosensor** is developed, utilizing **engineered UOx** to detect **uric acid**. The biosensor uses **sunlight** as the excitation source and **temperature** as the readout signal, leveraging the photothermal effect of specially designed agents (Scheme 3). These agents respond to the hydrogen peroxide (H_2O_2) produced during the enzymatic reaction catalyzed by UOx. The innovative aspect of this sensor is its **recyclability**: the photothermal agents can be regenerated and reused, while the engineered UOx ensures the system's stability at elevated temperatures. This chapter highlights how photothermal biosensors, coupled with enzyme engineering, can offer a **non-invasive** and **cost-effective** solution for continuous monitoring of biomarkers such as uric acid, making them suitable for chronic disease management.



Scheme 3. Development of non-invasive and cost-effective photothermal biosensors by using engineered enzymes.

Meanwhile, our research indicates that electrochemical reactions can also assist in addressing the issue of cofactor cycling in biocatalytic processes. In **Chapter 5**, the

final experimental chapter, the thesis expands the application of enzymes beyond biosensing by constructing a **bioelectrocatalytic system**. This system uses enzymes in conjunction with **carbon cloth electrodes** and a **commercial mediator** to drive the **asymmetric hydrogenation of alkenes** (Scheme 4). The simplicity of the design—using unmodified and uncoated electrodes—reduces costs and simplifies the process, making it more accessible for industrial applications. The overall process enables efficient cofactor regeneration, a common challenge in biocatalytic redox reactions, through **electrochemical reactions**. This chapter underscores the versatility of enzymes, showing how they can facilitate not only biomarker detection but also complex chemical transformations in an industrial context.



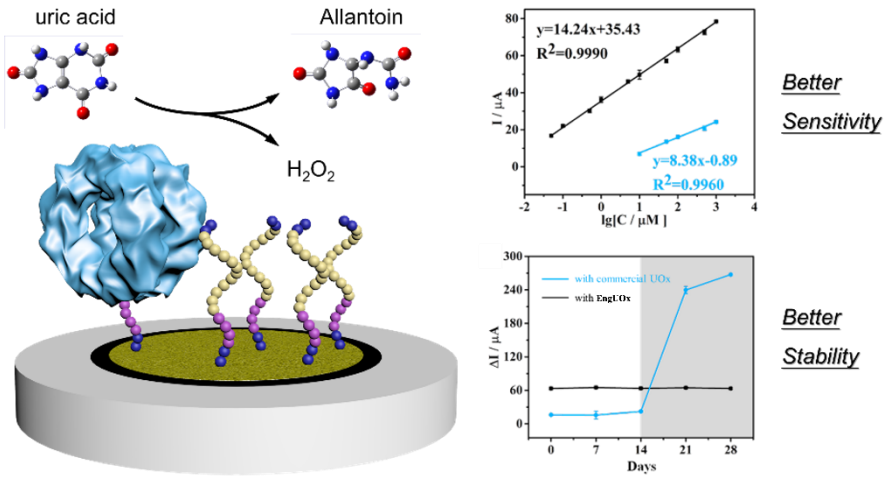
Scheme 4. Using methyl viologen as the mediator molecule to electrochemical regenerate co-factor within the bioelectrocatalysis.

The thesis concludes by emphasizing the significant advancements made using engineered enzymes in biosensor development. By improving stability, sensitivity, and recyclability, the biosensors designed in this research represent a step forward in both **medical diagnostics** and **chemical synthesis**. The use of enzyme engineering to tailor enzyme properties according to specific biosensor requirements is presented as a promising strategy for future innovations. The conclusion also outlines potential future research directions, including expanding the application of these biosensors to detect a wider range of biomarkers and further optimizing their stability for long-term use in diverse environmental conditions.

Samenvatting

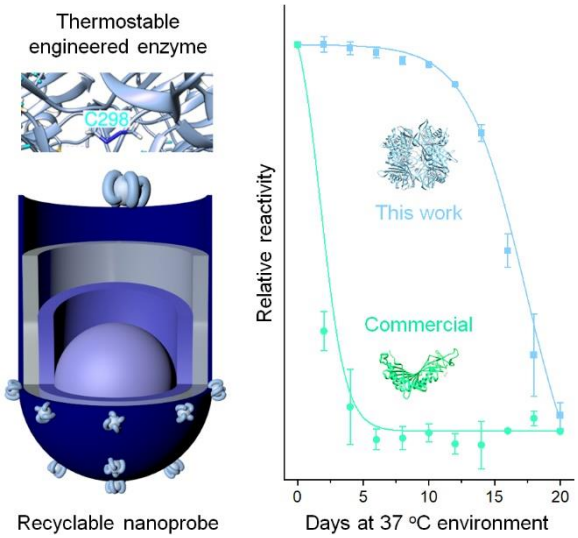
Dit proefschrift richt zich op **het ontwerp van multifunctionele enzymatische apparaten voor biosensing en chemische conversie**, met een primaire nadruk op het verbeteren van de prestaties en stabiliteit van biosensoren door middel van enzyme engineering. Biosensoren spelen een cruciale rol in de moderne diagnostiek, omdat ze een snelle en nauwkeurige detectie van biomarkers in het menselijk lichaam mogelijk maken, wat essentieel is voor een vroegtijdige diagnose van ziekten. In **Hoofdstuk 1** hebben we voorbeelden gegeven van enzymen die worden gebruikt bij de fabricage van verschillende biosensoren, met verschillende uitleessignalen. De huidige biosensoren hebben echter te maken met beperkingen in **gevoeligheid, selectiviteit** en, het belangrijkste, **stabiliteit**, waardoor hun praktische toepassing en commercialisatie beperkt is. Om deze uitdagingen aan te pakken, onderzoekt dit proefschrift enzymengineering als oplossing om de algehele functionaliteit van biosensoren te verbeteren. Door middel van rationeel ontwerp laat het onderzoek zien hoe gemanipuleerde enzymen de prestaties van biosensoren kunnen verbeteren in verschillende signaaluitleessystemen: **elektrochemisch, optisch** en **fotothermisch**.

Hoewel elektrochemische biosensoren een uitstekende gevoeligheid bieden, kan hun complexe constructieproces de activiteit van biomoleculen beïnvloeden. Om deze uitdaging aan te gaan, hebben we in **Hoofdstuk 2** het gebruik van thermostabiele enzymen onderzocht als een manier om de stabiliteit van elektrochemische biosensoren te verbeteren. In dit hoofdstuk wordt **een eenvoudige elektrochemische biosensor** ontwikkeld met **gemanipuleerd uraatoxidase (UOx)** als biorecognitie-element (Schema 1). Vergeleken met biosensoren die gemaakt zijn met natuurlijk UOx, laat de gemanipuleerde versie significante verbeteringen zien in zowel **stabiliteit** als **detectiebereik**. De sensor werkt door het meten van veranderingen in elektrochemische signalen die gegenereerd worden tijdens de UOx-gekatalyseerde reactie. Door de verbeterde stabiliteit van het gemanipuleerde enzym kan de sensor in een breder scala van omstandigheden functioneren, waardoor het praktischer wordt voor diagnostische toepassingen in de echte wereld. Dit hoofdstuk laat zien dat door enzymen op moleculair niveau te modificeren, hun inherente eigenschappen, zoals stabiliteit en reactiviteit, aanzienlijk kunnen worden verbeterd, wat mogelijkheden biedt voor robuustere elektrochemische biosensoren in de medische diagnostiek.



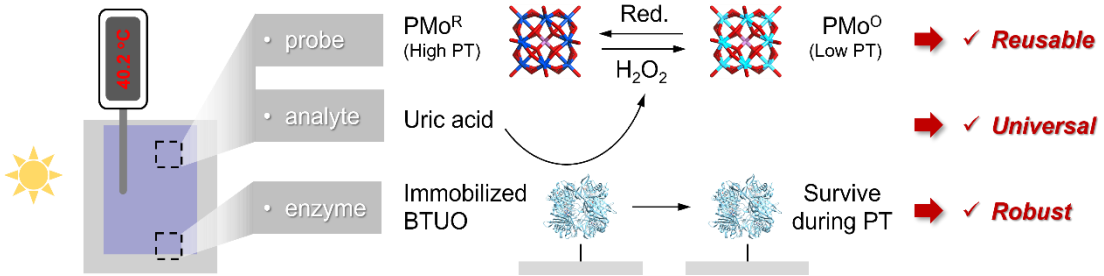
Schema 1. Thermostabiele UOx verbeterde de stabiliteit van de urinezuur elektrochemische biosensoren zodat deze biosensor meer dan 2 weken bij kamertemperatuur kon worden bewaard.

Na het succesvolle ontwerp van apparaten die thermisch stabiele enzymen gebruiken om de stabiliteit van elektrochemische, op enzymen gebaseerde sensoren te verbeteren, hebben we geprobeerd dit enzym toe te passen op andere biosensoren. We ontdekten dat het probleem van de gebrekkige recyclebaarheid van optische enzymatische biosensoren kon worden opgelost door ons ontwikkelde enzym te gebruiken. In **Hoofdstuk 3** introduceren we **een nieuwe optische biosensor** die gebruik maakt van een redox-omkeerbare sonde in combinatie met gemanipuleerd UOx (Schema 2). Deze biosensor gebruikt **optische signalen** (zoals fluorescentie of colorimetrische veranderingen) om de aanwezigheid van doelmoleculen te detecteren. De belangrijkste innovatie in dit hoofdstuk is de **thermische stabiliteit** en **recyclebaarheid** van de probe. Door gebruik te maken van het gemanipuleerde UOx is de biosensor zeer goed bestand tegen temperatuurschommelingen, waardoor hij zelfs in suboptimale omstandigheden goed blijft presteren. Bovendien kan de sonde van de sensor meerdere keren worden gerecycled in aanwezigheid van redoxmiddelen, waardoor minder afval ontstaat en de sensor duurzamer wordt. Dit hoofdstuk laat zien hoe optische biosensoren kunnen profiteren van enzymtechnologie door **gevoeligere**, **stabielere** en **duurzamere** oplossingen te bieden voor real-time detectie van biomarkers.



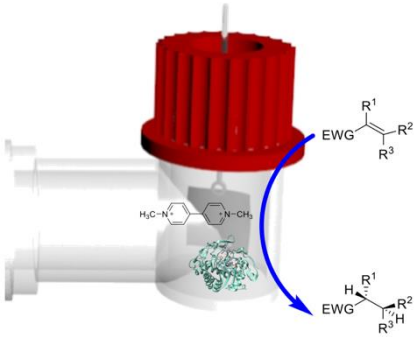
Schema 2. Recyclebare optische polyoxometalaten als optisch middel voor het ontwerpen van recyclebare optische biosensoren door gebruik te maken van geconstrueerde UOx voor urinezuurdetectie.

Gebaseerd op onze ervaring in het ontwerpen van fotothermische biosensoren voor huishoudelijk gebruik, geloven we bovendien dat als gemanipuleerde enzymen kunnen worden toegepast op fotothermische biosensoren, er de mogelijkheid is om een eenvoudig, draagbaar huishoudelijk apparaat te ontwikkelen. In **Hoofdstuk 4** wordt **een recyclebare fotothermische biosensor** ontwikkeld die gebruik maakt van **gemanipuleerd UOx** om **urinezuur** te detecteren. De biosensor gebruikt **zonlicht** als excitatiebron en temperatuur als afleessignaal en maakt gebruik van het fotothermische effect van speciaal ontworpen agentia (Schema 3). Deze agentia reageren op de waterstofperoxide (H_2O_2) die wordt geproduceerd tijdens de enzymatische reactie die door UOx wordt gekatalyseerd. Het innovatieve aspect van deze sensor is de **recyclebaarheid** ervan: de fotothermische agentia kunnen geregenereerd en hergebruikt worden, terwijl de ontwikkelde UOx de stabiliteit van het systeem bij hoge temperaturen garandeert. Dit hoofdstuk laat zien hoe fotothermische biosensoren, in combinatie met enzymengineering, een **niet-invasieve** en **kosteneffectieve** oplossing kunnen bieden voor continue monitoring van biomarkers zoals urinezuur, waardoor ze geschikt zijn voor het beheer van chronische ziekten.



Schema 3. Ontwikkeling van niet-invasieve en kosteneffectieve fotothermische biosensoren met behulp van gemanipuleerde enzymen.

Ondertussen geeft ons onderzoek aan dat elektrochemische reacties ook kunnen helpen bij het aanpakken van het probleem van cofactorcycli in biokatalytische processen. In **Hoofdstuk 5**, het laatste experimentele hoofdstuk, breidt het proefschrift de toepassing van enzymen uit tot meer dan alleen biosensing door **een bio-elektrokatalytisch systeem** te bouwen. Dit systeem gebruikt enzymen in combinatie met **koolstofdoekelektroden** en **een commerciële mediator** om de **asymmetrische hydrogenering van alkenen** aan te sturen (Schema 4). De eenvoud van het ontwerp - het gebruik van ongewijzigde en ongecoate elektroden - verlaagt de kosten en vereenvoudigt het proces, waardoor het toegankelijker wordt voor industriële toepassingen. Het totale proces maakt efficiënte cofactorregeneratie mogelijk, een veelvoorkomende uitdaging in biokatalytische redoxreacties, door middel van **elektrochemische reacties**. Dit hoofdstuk onderstreept de veelzijdigheid van enzymen en laat zien hoe ze niet alleen biomarkerdetectie maar ook complexe chemische transformaties in een industriële context kunnen vergemakkelijken.



Schema 4. Het gebruik van methylviolet als de mediatormolecule om co-factor elektrochemisch te regenereren binnen de bio-elektrokatalyse.

Het proefschrift eindigt met het benadrukken van de significante vooruitgang die geboekt is bij het gebruik van gemanipuleerde enzymen in de ontwikkeling van biosensoren. Door de stabiliteit, gevoeligheid en recyclebaarheid te verbeteren, betekenen de in dit onderzoek ontworpen biosensoren een stap voorwaarts in zowel **medische diagnostiek** als **chemische synthese**. Het gebruik van enzymengineering om enzymeigenschappen aan te passen aan specifieke biosensorvereisten wordt gepresenteerd als een veelbelovende strategie voor toekomstige innovaties. De conclusie schetst ook mogelijke toekomstige onderzoeksrichtingen, waaronder het uitbreiden van de toepassing van deze biosensoren om een breder scala aan biomarkers te detecteren en het verder optimaliseren van hun stabiliteit voor langdurig gebruik in diverse omgevingscondities.

List of Publications

Part of this thesis:

Chapter 1: Designing multifunctional enzymatic devices for biosensing. *Manuscript in preparation*.

Chapter 2: Z. Wei, T. Knaus, Y. Liu, Z. Zhai, A. F. G. Gargano, G. Rothenberg, N. Yan and F. G. Mutti*, A high-performance electrochemical biosensor using an engineered urate oxidase. *Chem. Commun.,* **2023**, 59, 8071. DOI: 10.1039/D3CC01869E

Chapter 3: Y. Liu, Z. Wei, M. Damian, X. Zhu, T. Knaus, H. Zhang*, F. G. Mutti* and F. F. Loeffler*, Recyclable and robust optical nanoprobes with engineered enzymes for sustainable serodiagnostics. *Adv. Mater.,* **2023**, 35, 2306615. DOI: 10.1002/adma.202306615

Chapter 4: Z. Wei, M. Damian, Y. Liu*, P. Peters, T. Knaus, Z. Ma, F.F. Loeffler* and F.G. Mutti*, Robust and reusable solar-powered photothermal assay based on engineered enzymes. *Submitted.*

Chapter 5: Z. Wei, T. Knaus, M. Damian, Y. Liu, C. S. Santana, N. Yan, G. Rothenberg* and F. G. Mutti*, Bio-electrocatalytic alkene reduction using ene - reductases with methyl viologen as electron mediator. *ChemBioChem,* **2024,** e202400458. DOI: 10.1002/cbic.202400458

Other publications:

1. Y. Liu, X. Zhu, Z. Wei, F. Wei, L.Li, L. Ma, F. Li*, and J. Zhou*, Customized photothermal therapy of subcutaneous orthotopic cancer by multichannel luminescent nanocomposites. *Adv. Mater.* **2021**, 33, 2008615. DOI: 10.1002/adma.202008615

2. Z. Wei, T. Cao, L. Li, X. Zhu, J. Zhou*, and Y. Liu*, Dual-channel lanthanide-doped nanoprobe for reliable multi-signal ratiometric detection of H_2S in whole blood. *Chem. Commun.,* **2022**, 58, 9642. DOI: 10.1039/d2cc03360g

3. Y. Liu, X. Zhu, Z. Wei, K. Wu, J. Zhang, F. G. Mutti, H. Zhang*, F. F. Loeffler*, and J. Zhou*. Multi-channel lanthanide nanocomposites for customized synergistic

treatment of orthotopic multi-tumor cases. *Angew. Chem. Int. Ed.* **2023**, 62, 202303570. DOI: 10.1002/ange.202303570

4. Y. Liu*, Z. Wei, F. G. Mutti, H. Zhang, and F. F. Loeffler*. Redox-responsive inorganic fluorescent nanoprobes for serodiagnosis and bioimaging. *Coordin. Chem. Rev.,* **2024**, 509, 215817. DOI: 10.1016/j.ccr.2024.215817

5. Y. Liu, Z. Wei, J. Zhang, Y. Xu, J. Zhou, Z. Ma, F. G. Mutti, H. Zhang*, X. Zhu*, and F. F. Loeffler*. Customized enhancement of thermal sensitivity of tumors at different subcutaneous depths by multichannel lanthanide nanocomposites. *Adv. Mater.,* **2024**, 36, 2402981. DOI: 10.1002/adma.202402981

6. Y. Liu, T. Knaus, Z. Wei, J. Zhang, M. Damian, S. Ronneberger, X. Zhu, P. H. Seeberger, H. Zhang,*F. G. Mutti,* and F. F. Loeffler*. Confined flash printing and synthesis of stable perovskite nanofilms under ambient conditions. *Adv. Mater.,* **2024**, 2409592. DOI: 10.1002/adma.202409592

7. Y. Liu*, and Z. Wei*, Multichannel Lanthanide-Doped Nanoprobes for Serodiagnosis and Therapy. *Chem. Rec.,* **2024**, e202400100. DOI:10.1002/tcr.202400100

Contributions to this thesis

Chapter 1
Introduction to enzymatic devices for biosensing

Z. Wei	Developed the hypotheses, surveyed the literature, and wrote the manuscript.
Y. Liu	Background knowledge supported of optical, and photothermal biosensors and surveyed the literature.
F. Mutti	Reviewed the manuscript and made suggestions for improvements.
G. Rothenberg	Reviewed the manuscript and made suggestions for improvements.

Chapter 2
Engineered enzymes for improving the stability of electrochemical biosensors

Z. Wei	Conceived the idea, designed and built the biosensors surveyed the literature, and wrote the manuscript.
T. Knaus	Engineered enzyme knowledge supported and enzyme purification.
Y. Liu	Background knowledge supported and surveyed the literature.
Z. Zhai	Chromatography-mass spectrometry characterization supported and measurement methods design.
A. F. G. Gargano	Chromatography-mass spectrometry characterization supported and measurement methods design.
F. Mutti	Reviewed the manuscript and made suggestions for improvements.
N. Yan	Reviewed the manuscript and made suggestions for improvements.
G. Rothenberg	Reviewed the manuscript and made suggestions for improvements.

Chapter 3

Recyclable and robust optical nanoprobes with engineered enzymes for sustainable serodiagnostics

Z. Wei	Designed the methodology, established the model for the study, performed the experiments, and wrote the manuscript.
Y. Liu	Conceived the project, analyzed the data, designed the methodology, established the model for study, performed the experiments, and wrote the manuscript.
T. Knaus	Engineered enzyme knowledge supported and enzyme purification.
X. Zhu	UCNP nanomaterials knowledge supported and constructed disease models.
M. Damian	Engineered enzyme knowledge supported and enzyme purification.
F. Mutti	Reviewed the manuscript and made suggestions for improvements.
H. Zhang	Reviewed the manuscript and made suggestions for improvements.
F. F. Loeffler	Reviewed the manuscript and made suggestions for improvements.

Chapter 4

Robust and reusable solar-powered photothermal assay based on engineered enzymes

Z. Wei	Designed the methodology, established the model for study, prepared the probes, and wrote the manuscript.
Y. Liu	Conceived the project, established the Android application, analyzed the data, and wrote the manuscript.
M. Damian	Engineered enzyme knowledge supported and enzyme purification.
P. Peters	Enzyme purification.
T. Knaus	Engineered enzyme knowledge supported and enzyme purification.

Z. Ma	Reviewed the manuscript and made suggestions for improvements.
F. F. Loeffler	Reviewed the manuscript and made suggestions for improvements.
F. Mutti	Reviewed the manuscript and made suggestions for improvements.

Chapter 5

Bio-electrocatalytic alkene reduction using ene-reductases with methyl viologen as electron mediator

Z. Wei	Designed the methodology, performed the experiments, and wrote the manuscript.
T. Knaus	Engineered enzyme knowledge supported and enzyme purification.
M. Damian	Engineered enzyme knowledge supported and enzyme purification.
Y. Liu	Data analysis and writing the manuscript.
C. S. Santana	Electrochemistry knowledge supported and data analysis.
N. Yan	Reviewed the manuscript and made suggestions for improvements.
G. Rothenberg	Reviewed the manuscript and made suggestions for improvements.
F. Mutti	Reviewed the manuscript and made suggestions for improvements.

Acknowledgment

The day I wrote those letters was typical of an autumn day in the Netherlands. The sky was overcast, but there was no rain, and the ground was covered with fallen leaves. I have just had a conversation with **Prof. Francesco. G. Mutti**, my supportive supervisor. This discussion is similar to the initial meeting we had four years ago. I distinctly recall the day I received the reply email indicating that he wished to discuss my CSC scholarship application with me. I must admit that my English is not sufficiently advanced to enable me to fully comprehend the discussions held at that time. However, I do recall that Francesco subsequently sent me a meeting summary. By the time four years had elapsed, I had already participated in numerous meetings and interviews with a variety of professors. I have yet to encounter another professor who could provide a meeting summary to a student in such a prompt and efficient manner. During the four years of study and research, I was able to obtain feedback in a timely manner when I requested assistance. He consistently provided detailed reviews of my manuscripts, posters, and presentations, even correcting minor spelling and abbreviation issues in the reference section. His expertise in the field of enzymes and biocatalysis has consistently offered valuable insights that have helped me overcome experimental challenges. Words cannot express the gratitude I have for his guidance and support over the past four years. The experience of those four years will forever be a valuable part of my professional history. Thank you, Francesco!

I would like to express my gratitude to another of my supervisors, **Prof. Gadi Rothenberg**, with whom I had the opportunity to work as a student as a result of a series of fortuitous circumstances. I remember him saying that I was the first student to be accepted into his research group without having an interview with him. However, this did not affect the way he treated me. I was already afforded the same access as other students, able to knock on his door at any time to ask questions on both academic and general matters. Furthermore, I also extended invitations to group trips and group dinners, and I received my annual Christmas gift. I gained valuable insights from him, including how to create a compelling report, how to draft a strong CV and even some communication skills. I have also benefited from these experiences in my personal life, and I am a better person than I was four years ago. I am confident that these skills will prove to be a valuable asset in my future career. Thank you, Gadi!

另一位我想感谢的导师是晏宁教授，正是在晏老师和 Francesco 的推动下，我才能开始这个项目，并且有机会来到荷兰阿姆斯特丹大学学习。虽然开始阶段因为疫情的原因，使得我跟晏老师在 Uva 见面得机会并不多，但是晏老师时刻都在关心着我的研究和生活动向。同时，他也会因材施教，根据我的目标，总

是给出合理得建议和适时的鞭策。这让我在工作-学习间的平衡上受益匪浅。虽然，在我博士研究的最后阶段，晏老师已经不能来到 Uva 进行面对面的指导，但是他还是能跨越时差的阻碍，对我的研究问题进行远程指导，这使我对电化学的研究有了更深入的理解。这些工作和学习上的减缓了我在异国他乡的思乡之情，感谢晏老师！

I would also like to express my gratitude to **Prof. Ning Yan**, my co-supervisor. I am grateful to Ning and Francesco for enabling me to commence this program and pursue my studies at the University of Amsterdam. Despite the limited opportunity to meet with Ning at Uva at the outset due to the epidemic, Ning consistently demonstrated concern for my research and personal well-being. Additionally, he consistently provided well-considered counsel and timely motivation, aligning his guidance with my aspirations and objectives. This has assisted me in achieving a healthy work-life balance. Despite being unable to attend Uva for the final stage of my PhD research, Ning was able to provide remote tutorials on my research questions across time zones, which enabled me to gain a deeper understanding of electrochemistry research. Thank you, Ning!

I would like to thank the professors on the committee, **Prof. Dr. Arian van Asten, Prof. Dr. Bas de Bruin, Prof. Dr. Stanley Brul, Prof. Dr. Hong Zhang** from the University of Amsterdam, and **Dr. Caroline E. Paul** from the Delft University of Technology. I would like to thank you for taking the time to read my thesis, and I would be very grateful if you could provide me with your suggestions and participate in my defense.

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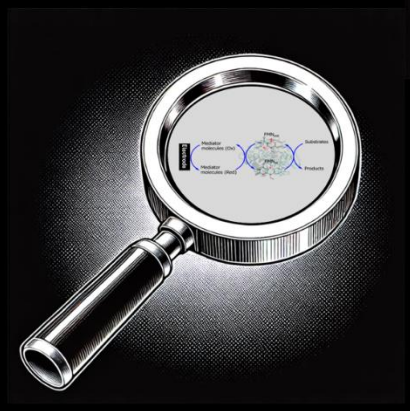
Zheng Wei was born in Beijing, China in 1995. He graduated from Capital Normal University with a BSc degree and was ready to become a high school chemistry teacher. However, he decided to continue his studies in chemistry and started his Master's journey at Capital Normal University. He was under the supervision of Prof. Zhanfang Ma to learn how to design and construct electrochemical biosensors for early cancer diagnosis. During this period, he published 5 peer-reviewed papers and obtained 2 patents. He received his MSc in Physical Chemistry in 2020.

Zheng moved to Amsterdam in November 2020 and started his PhD research at the University of Amsterdam under the supervision of Prof. Gadi Rothenberg, Prof. Ning Yan, and Prof. Francesco Mutti. His main research topic is the use of engineered enzymes for the design of biosensing devices. He has also done some research on the use of electrochemical methods to assist cofactor regeneration in biocatalytic reactions. During his PhD, he published 10 papers and prepared a patent application for sustainable biosensing devices.



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