SEED-MEDIATED CONTROLLED GROWTH of RARE EARTH NANOCRYSTALS

By

Shihui Wen
School of Mathematical and Physical Sciences,
Faculty of Science

Supervisors:
Prof. Dayong Jin
Dr. Fan Wang

UNIVERSITY OF TECHNOLOGY SYDNEY

This thesis is presented for the degree of Doctor of Philosophy
September 2018

CERTIFICATE OF ORIGINAL AUTHORSHIP

I, Shihui Wen, declare that this thesis, submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the School of Mathematical and Physical Sciences, Faculty of Science at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise reference or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

Production Note:
Signature: Signature removed prior to publication.

Date: 03/09/2018

ACKNOWLEDGEMENTS

Firstly, I would like to extend my gratitude to my principal supervisor Prof. Dayong Jin who has always been motivating and supportive to me. What I learned and he trained is not only academic research skills but more important the Philosophy during my 3.5-year Ph.D candidature period. I enjoy these principles of success and employ them as the tool to explore the new knowledge and change my life. Definitely, they will benefit me all my life. Prof. Jin is not only the soul of our research team, but also the soul of many international collaborative research teams. I learnt a lot from his self-motivated and optimistic attitude to life, and aspiring, energetic and collaborative research style. His passion on the science research always impacts me to firmly believe what we do and will win at the end. I really appreciate his sincere help and thoughtful suggestions on my PhD program and my research career development. I also thank Jin for patiently teaching me on academic writing in a way that make my writings easily understandable by general audience.

I also would like to thank my co-supervisor Dr. Fan Wang for helping me in terms of the optical characterization and his professional advice on my research project. He gave me a lot of thoughtful comments on my publications.

Next, I would like to thank my colleagues, in particular, Dr. Deming Liu, Dr. Jiajia Zhou, Dr. Xiaoxue Xu, Dr. Gungun Lin, for significant contributions to my research projects and publications. I also thank Zhiguang Zhou, Chaohao Chen, Yongtao Liu, Chenshuo Ma, Hao He, Wei Ren, Chao Mi, Ming Guan, Yulong Sun, Yinghui Chen, Jiayan Liao, and other peers within our research group. I had a wonderful teamwork experience with them. Many colleagues at UTS, including Dr. Hien Dong, Dr. Olga Shimoni, Huan Wu, Yuan Liu, Baoming Wang, and others, gave me many valuable advices through my research projects. I also want to thank our international collaborators, Prof. Xiangyang Shi, Prof. Xiaogang Liu, Dr. Yi Du, and other members in their respective labs. Their expertise and contributions added great values to my research projects. I sincerely appreciate the generous help from all these nice people. Moreover, I want to thank Dr. Tom Lawson, who help me a lot during my joint research project at Macquarie University.

I acknowledge the financial support I received from University of Technology Sydney and Vice-Chancellor's Outstanding Achievement Scholarship to offer me many opportunities to expand my research experiences.

Finally, I would like to thank my lover, Du, who has been sacrificing so much to support me. She teaches me a lot about cooking, although I can only play some of her skills by myself now. For my beloved family, I thank my parents, Jiujun Wen and Chuanling Li, and my brother Jingke Wen, and other relatives, who have been economically and spiritually backing me up both over years.

Table of Contents

List of Publications

Published papers:

[1] **Shihui Wen**, Jiajia Zhou, Kezhi Zheng, Artur Bednarkiewicz, Xiaogang Liu, Dayong Jin, Advances in highly doped upconversion nanoparticles, ***Nature Communications*** (2018), **9**, 2415.

[2] Jiajia Zhou, **Shihui Wen**, Jiayan Liao, Christian Clarke, Sherif Abbas, Wei Ren, Chao Mi, Fan Wang, Dayong Jin, Activation of surface dark-layer to enhance upconversion in a thermal field, ***Nature Photonics*** (2018), **12**, 154-158.

[3] Fan Wang, **Shihui Wen**, Hao He, Baoming Wang, Zhiguang Zhou, Olga Shimoni, Dayong Jin, Microscopic inspection and tracking of single upconversion nanoparticles in living cells, ***Light: Science & Applications*** (2018), **7**, 18007.

[4] Wei Ren, **Shihui Wen**, Sherif Abdulkader Tawfik, Qian P Su, Gungun Lin, Lining A Ju, Michael J Ford, Harshad Ghodke, Antoine M van Oijen, Dayong Jin, Anisotropic functionalization of upconversion nanoparticles, ***Chemical Science*** (2018), **9**, 4352-4358.

[5] Chaohao Chen, Fan Wang, **Shihui Wen**, Qian Peter Su, Mike CL Wu, Yongtao Liu, Baoming Wang, Du Li, Xuchen Shan, Mehran Kianinia, Igor Aharonovich, Milos Toth, Shaun P Jackson, Peng Xi, Dayong Jin, Multi-photon near-infrared emission saturation nanoscopy using upconversion nanoparticles, ***Nature Communications*** (2018), **9**, 3290.

[6] Wei Ren, Yingzhu Zhou, **Shihui Wen**, Hao He, Gungun Lin, Deming Liu, Dayong Jin, DNA-mediated Anisotropic Silica Coating of Upconversion Nanoparticles, ***Chemical Communications*** (2018), **54**, 7183-7186.

[7] Yinghui Chen, Hien T. T. Duong, **Shihui Wen**, Chao Mi, Yingzhu Zhou, Olga Shimoni, Stella M. Valenzuela, Dayong Jin, Exonuclease III-Assisted Upconversion Resonance Energy Transfer in a Wash-Free Suspension DNA Assay, ***Analytical Chemistry*** (2018) **90**, 663-668.

[8] Yujia Liu, Yiqing Lu, Xusan Yang, Xianlin Zheng, **Shihui Wen**, Fan Wang, Xavier Vidal, Jiangbo Zhao, Deming Liu, Zhiguang Zhou, Chenshuo Ma, Jiajia Zhou, James A. Piper, Peng Xi, Dayong Jin, Amplified stimulated emission in upconversion nanoparticles for super-resolution nanoscopy, ***Nature*** (2017) **543**, 229-233.

[9] Hao He, Christopher B Howard, Yinghui Chen, **Shihui Wen**, Gungun Lin, Jiajia Zhou, Kristofer J Thurecht, Dayong Jin, Bispecific antibody-functionalized upconversion nanoprobe, ***Analytical Chemistry*** (2018) **90**, 3024-3029.

[10] Deming Liu, Xiaoxue Xu, Yi Du, Xian Qin, Yuhai Zhang, Chenshuo Ma, **Shihui Wen**, Wei Ren, Ewa M. Goldys, James A. Piper, Shixue Dou, Xiaogang Liu, Dayong Jin, Three-dimensional controlled growth of monodisperse sub-50 nm heterogeneous nanocrystals, ***Nature Communications*** (2016) **7**, 10254.

[11] Du Li, **Shihui Wen**, Wenjie Sun, Jiulong Zhang, Dayong Jin, Chen Peng, Mingwu Shen, and Xiangyang Shi, One-Step Loading of Gold and Gd_2O_3 Nanoparticles within PEGylated Polyethylenimine for Dual Mode Computed Tomography/Magnetic Resonance Imaging of Tumors, ***ACS Applied Bio Materials*** (2018) **1**, 221-225.

[12] Chenshuo Ma, Xiaoxue Xu, Fan Wang, Zhiguang Zhou, **Shihui Wen**, Deming Liu, Jinghua Fang, Candace I. Lang, Dayong Jin, Probing the Interior Crystal Quality in the Development of More Efficient and Smaller Upconversion Nanoparticles, ***The Journal of Physical Chemistry Letters*** (2016) **7**, 3252-3258.

[13] Liang Wang, Long Ren, D Mitchell, G Casillas-Garcia, Wei Ren, C Ma, XX Xu, **Shihui Wen**, F Wang, J Zhou, Xun Xu, Weichang Hao, Shi Xue Dou, Yi Du, Enhanced energy transfer in heterogeneous nanocrystals for near infrared upconversion photocurrent generation, ***Nanoscale*** (2017) **9**, 18661-18667.

[14] Hien Duong, Yinghui Chen, Sherif Abdulkader Tawfik, **Shihui Wen**, Maryam Parviz, Mike J Ford, Olga Shimoni, Dayong Jin, Systematic Investigation of Functional Ligands for Colloidal Stable Upconversion Nanoparticles, ***RSC Advances*** (2018) **8**, 4842-4849.

[15] Yue Cong, Bingyang Shi, Yiqing Lu, **Shihui Wen**, Roger Chung, Dayong Jin, One-step conjugation of glycyrrhetinic acid to cationic polymers for high-performance gene delivery to cultured liver cell, ***Scientific reports*** (2016) **6**, 21891.

([1] - [10] are closely related to my PhD program)

Conferences:

[1] **Shihui Wen**, Deming Liu, Wei Ren, Chenshuo Ma, Bingyang Shi, Xiaoxue Xu, Dayong Jin, Developing multifunctional heterogeneous upconversion nanocrystals for multimodality bioimaging and biomedicine, 6th International Nanomedicine Conference, July 6-8, 2015.

[2] **Shihui Wen**, Deming Liu, Wei Ren, Chenshuo Ma, Xiaoxue Xu, Dayong Jin, Seed Mediated One-pot Growth of Multifunctional Heterogeneous Upconversion Nanocrystals, ICONN 2016, February 7-11, 2016.

[3] **Shihui Wen**, Du Li, Deming Liu, Xiaoxue Xu, Yi Du, David R. G. Mitchell, Bingyang Shi, Xiangyang Shi, Dayong Jin, Seed mediated one-pot growth of versatile heterogeneous upconversion nanocrystals for multimodal bioimaging, SPIE BioPhotonics Australasia, October 17-20, 2016, pp. 1001315-1001315-7.

[4] **Shihui Wen**, Du Li, Deming Liu, Dayong Jin, Seed Mediated One-pot Growth of Multifunctional Heterogeneous Upconversion Nanocrystals, Phosphor Safari 2016, 28 Nov - 1 Dec, 2016.

[5] **Shihui Wen**, Du Li, Deming Liu, Dayong Jin, Develop Multi-Functional Contrast Agent for Deep Tissue In Vivo Bioimaging, 2017 MRS Spring Meeting & Exhibit, April 17-21, 2017.

ABSTRACT

With relatively large surface areas and tunable composition and morphology, nanoparticles possess unexpected properties comparing with their bulk counterparts. Controlled synthesis and fine-tuning of their composition, morphology, and surface properties are the fundamental cornerstones in nanoscience and nanotechnology towards optimized overall performance of a variety of nanoparticles discovered today.

Upconversion nanoparticles (UCNPs) are a new family of luminescent nanomaterials attracting a large amount of research interests, because these materials are capable of converting two or more lower-energy photons into one high energy photon. To date, a wide range of applications have been developed, including fluorescent microscopy, nanoscale thermometry, photodynamic therapy, optogenetics, security inks, photovoltaic converters, and 3-dimensional volumetric displays.

This thesis focuses on exploring materials science to establish new methods for fine-tuning the size, shape and composition of lanthanide doped UCNPs, and study their optical properties, in particular to integrate multiple functionalities. I demonstrate the seed-mediated controlled growth approach is very promising for on-demand production of a library of multifunctional nanocrystals. This wet-chemical approach offers high precision in controlled synthesis of homogeneous and heterogeneous nanocrystals with desirable size, shape and deposition of dopants. The outcomes of this thesis not only include a series of knowledge discovered for controlled growth of lanthanide doped nanomaterials, but also lead to a range of new applications demonstrated, such as super-resolution nanoscopy imaging, single-particle tracking, and multimodal bioimaging.

This thesis begins with a comprehensive review of the size-/shape-dependent properties and the controlled wet-chemical synthesis of nanomaterials, especially for the recently developed UCNPs, forming the introduction Chapter 1. This chapter has been further enhanced by a review article surveying the role of controlled growth and their new advances in producing highly doped UCNPs enabling new applications (published in *Nature Communications* 2018). In Chapter 2, I provide the full details of materials and methods employed in this thesis. And the following four chapters summarize the core results from 666 synthesis experiments to produce a range of homogeneous (Chapter 3), heterogeneous (Chapter 5) and single directional grown barcoded nanocrystals at arbitrary sizes (Chapter 6), as well as

a comprehensive characterization and investigation of crystal growth mechanisms (Chapter 4) that underpins these synthesis techniques.

In Chapter 3, I demonstrate the seed-mediated growth method for fabricating homogeneous nanocrystals doped with different concentrations of activator ions. While typically due to the large synthesis-to-synthesis variation, conventional methods only result in different sizes of UCNPs during different synthesis, my facile seed-mediated method achieves precise control in size (one nanometer resolution) to yield a series of monodisperse UCNPs at the same size, which enables the quantitative optical characterizations. This forms the foundation for a range of single nanocrystal measurements and evaluations of their optical properties towards a series of novel applications in nanoscopy. This work has resulted in three co-authored publications, the low-power stimulated emission depletion (STED) nanoscopy (published in *Nature* 2017), the near-infrared emission saturation (NIRES) super-resolution nanoscopy (published in *Nature Communications* 2018), and microscopic inspection and tracking of single nanocrystals in living cells (published in *Light: Science & Applications* 2018).

In Chapter 4, I systematically investigate the mechanisms and a range of potential determining factors to identify the key to the controlled growth. I discover that the reaction mix, after the core being synthesized, plays an important role in reducing the time for the successive epitaxial growth of shells in the seed-mediated growth method. I successfully fabricate the integrated heterogeneous core@shell nanocrystals with high performance in luminescence intensity. While typically due to the low stability of sub-10-nm nanocrystals in the reaction mix, it is hard to use sub-10-nm nanocrystals as the seed using conventional methods. Here using my method, I demonstrate the sub-10-nm nanocrystals as the seeds for epitaxial growth of the inert shells to yield the ultra-small core@shell nanocrystals. These bright and ultra-small core@shell UCNPs will pave the way for nanomedicine applications. This work has resulted in one first-authored research paper under submission.

In Chapter 5, I employ the heterogeneous seed-mediated growth approach to fabricate the core@shell@shell sandwich nanostructure with various sensitizer and activator doping concentrations but at the same size. These highly controlled samples enable the systematic characterizations to identify the optimum doping concentrations of both sensitizers and activators from a large dynamic range, which guarantees the same amount of active photon conversion layer between an inert core template and an inert layer of shell that isolates the surface quenchers. This allows us to directly compare and identify the optimum combination of sensitizers (Yb^{3+}) and emitters (Tm^{3+}) as a new guideline to synthesize a range of bright and small single UCNPs, particularly optimized for different excitation conditions. With the optimized doping concentration, I have also fabricated the small and bright core@shell nanocrystals with the size comparable to that of antibodies (~ 15 nm). This work has resulted in my second first-author research work under submission.

In Chapter 6, I challenge to control the growth direction using the seed-mediated growth method. I first systematically investigate the roles of the surfactant molecule oleic acid and oleate on different facets. Through fine-tuning of the amount of surfactant molecules and the concentration of the shell precursor, I have achieved the absolute one-direction growth of UCNPs nanorods by the layer-by-layer deposition of precursor on the desired crystal facet. On-demand deposition of arbitrary kind of precursors along the longitudinal direction has resulted in a series of nanorods in the length range from 24 nm to 242 nm. Combining the heterogeneous growth approach, I demonstrate multifunctional contrast agents for multimodal bioimaging, with each functionalization being maximized and logically assembled within a single barcoded nanorod. This suggests future heterogeneous nanocrystals with integrated functions can be realized by the programmable growth of multifunctional barcode crystals with tunable size, composition, and properties. This work has resulted in a co-authored paper (published in *Nature Communications* 2016) and my third first-author research work under submission.

The conclusion and future scope part, Chapter 7, summarizes the key achievements presented in this thesis, which is around the new facile approach of the seed-mediated growth for fine-tuning the size, shape and composition of UCNPs. I have also included discussions on the potentials of using this method and knowledge developed here for UCNPs doped with other ions, and the fabrication of high-quality on-demand hybrid nanocrystals to unlock a new horizon of nanomaterials science. This, in turn, will promise a huge potential in enabling new nanotechnologies, such as super-resolution imaging, multimodal bioimaging, optogenetics, nanothermometry, photovoltaics, and laser refrigeration.

Key Words: upconversion nanocrystals, seed-mediated growth, epitaxial growth, heterogeneous structure, rare earth, lanthanides, multimode bioimaging, barcode.

List of Acronyms (in alphabetic order)

CT	Computed Tomography
EDS	Energy-Dispersive X-ray Spectroscopy
FWHM	Full-Width at Half-Maximum
MR	Magnetic Resonance
NIR	Near Infrared
NIRES	Near-Infrared Emission Saturation
OA	Oleic acid
OA^-	Oleate anions
OAH	Oleic acid molecular
ODE	1-octadecene
OM	Oleylamine
PDT	Photodynamic Therapy
PET	Positron Emission Tomographic
PTT	Photothermal Therapy
QDs	Quantum dots
RE	Rare Earth elements
SPECT	Single Photon Emission Computed Tomography
SPR	Surface Plasmon Resonance
STED	Stimulated Emission Depletion
STEM	Scanning Transition Electron Microscopy
TEM	Transition Electron Microscopy
TFA	Trifluoroacetate
THF	Tetrahydrofuran
UCNPs	Upconversion Nanoparticles
UV	Ultraviolet
XPS	X-ray Photoelectron Spectroscopy
XRD	X-ray Powder Diffraction