SINGLE UPCONVERSION NANOPARTICLE OPTICAL CHARACTERIZATIONS FOR BIOPHOTONIC APPLICATIONS

By

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Certificate of Original Authorship

I, Zhiguang Zhou, declare that this thesis is submitted in fulfillment 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 literatures used are indicated in the thesis.

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

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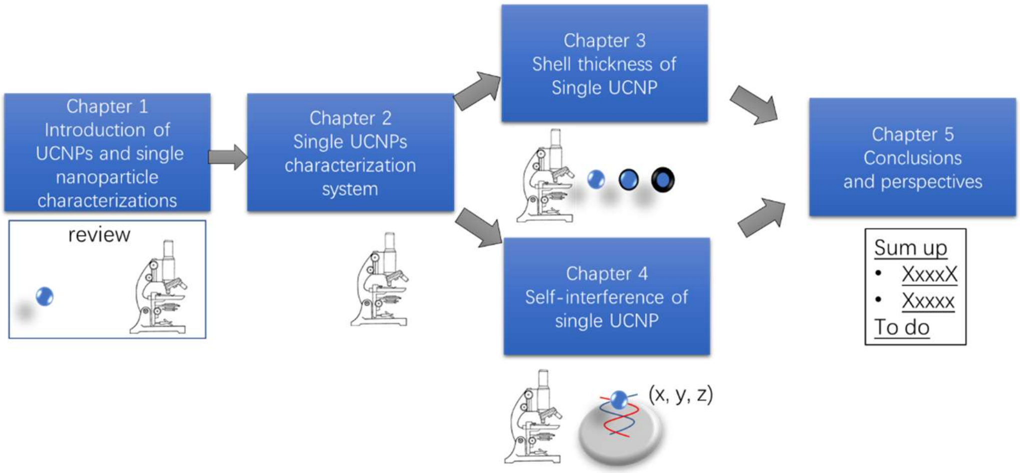
Format of Thesis

This thesis follows the conventional format of five chapters. The relationship between these chapters are shown in the flowchart below.



Chapter 1 is the introduction chapter and it has two sections. The first section introduces upconversion nanoparticles (UCNPs). It will introduce the upconversion luminescence mechanism, the material synthesis, the optical properties, and the current applications of UCNP. The second section is a literature review of the current progress in single nanoparticle characterization. It includes the significance and methods of single nanoparticle characterization as well as the specific characterizations and related applications it has already been applied to.

Chapter 2 provides detailed information of systems I developed for this thesis. The single nanoparticle optical characterization system (SNCS) will be introduced. Also, the operations of this system, such as preparation of samples and characterization methods, will be introduced. The applications of this system into cooperative works will also be shown in the last part of this chapter.

Chapter 3 and chapter 4 are the experimental chapters. In chapter 3, the single nanoparticle characterization methods will be applied to research the shell thickness of UCNP to get brighter particles. In chapter 4, the self-interference effects of UCNPs when placing on a mirror is researched and applied to get 3D super resolution position sensing.

Chapter 5 is the conclusions and perspectives of this thesis. The conclusions of this thesis will be summarized, and future works related with my thesis will be prospected.

List of Publications

Research Papers:

1. **Zhou Z**, Wang F, Liu Y, Yang X, Xi P, Xu Z, Kim S, Warkiani S, Jin D et al. *Partly destructive many-emitter self-interference in sub-diffraction limitation volume*. (About to submit)
2. Xu. X, **Zhou Z**, Liu Y, Wen S, Guo Z, , Gao L, Wang F, *Optimising passivation shell thickness of single upconversion nanoparticles using a time-resolved spectrometer.* APL Photonics. 2019, **4**(2): p. 026104.
3. Wang F, Wen S, He H, Wang B, **Zhou Z**, Shimoni O, et al. *Microscopic inspection and tracking of single upconversion nanoparticles in living cells*. Light: Science & Applications. 2018, **7**(4): p. 18007.
4. Guan M, **Zhou Z**, Mei L, Zheng H, Ren W, Wang L, et al. Direct cation exchange of surface ligand capped upconversion nanocrystals to produce strong luminescence. Chemical Communications. 2018, **54**(69): p. 9587-9590.
5. Liu Y, Lu Y, Yang X, Zheng X, Wen S, Wang F, Vidal X, Zhao J, Liu, D, **Zhou Z** et al. *Amplified stimulated emission in upconversion nanoparticles for super-resolution nanoscopy.* Nature. 2017, **543**(7644): p. 229.
6. Ma C, Xu X, Wang F, **Zhou Z**, Liu D, Zhao J, et al. *Optimal sensitizer concentration in single upconversion nanocrystals.* Nano Letters. 2017, **17**(5): p. 2858-64.
7. Ma C, Xu X, Wang F, **Zhou Z**, Wen S, Liu D, et al. *Probing the interior crystal quality in the development of more efficient and smaller upconversion nanoparticles.* The Journal of Physical Chemistry Letters. 2016, **7**(16): p. 3252-8.

([1-7] are closely related to my PhD program)

List of Acronyms

(in alphabetic order)

Abbreviations	**Full names**
2/3D	Two/three dimensions
AFM	Atomic Force Microscope
ALA	5-Aminolevulinic Acid
CCD	Charge-coupled device
CDs	Carbon Dots
CR	Cross Relaxation
CUC	Cooperative Upconversion
CW	Continuous Wave
demitter	distance change between emitter
DLS	Dynamic Light Scattering
EMU	Energy Migration Mediated Upconversion
ESA	Excited State Absorption
ETU	Energy Transfer Upconversion
FFT	Fast Fourier Transform
FOV	Field Of View
FRET	Fluorescence Resonance Energy Transfer
FWHM	Full Wavelength Half Maximum
IDI	Incomplete Destructive Interference

InM	Interference Microscopy
LUT	Look Up Table
MEANs	Mirror Enhanced Axial Narrowing Super resolution
MOF	Micro-structured Optical Fibers
ND	Neutral Density
NIR(IR)	Near Infrared (Infrared)
NIS	Nanoscale Interferometry Sensor
ODE	1-Octadecene
PA	Photon Avalanche
PALM	Photo-Activated Localization Microscopy
PDT	Photodynamic Therapy
PET	Positron Emission Tomography
PpIX	Protoporphyrin IX
PSA	Prostate Specific Antigen
PSF	Point Spread Function
QDs	Quantum Dots
RESOLFT	Reversible Saturable/Switchable Optical Linear Fluorescence Transition
RGB	Red Green Blue
SIM	Structured Illumination Microscopy
SLBL	Successive Layer-By-Layer

SNCS	Single Upconversion Nanoparticle Characterization System
SP	Short pass
SPAD	single-photon avalanche diode
SPECT	Single-Photon Emission Computed Tomography
STED	Stimulated Emission Depletion
STORM	Stochastic Optical Reconstruction Microscopy
TEM	Transmission Electron Microscopy
UCL	Upconversion Luminescence
UCNP(s)	Lanthanide-Doped Upconversion Nanoparticle(s)
ULISA	Upconversion-Linked Immunosorbent Assay

Abstract

Lanthanide elements-doped upconversion nanoparticles (UCNPs) are of great interest in both biophotonics and nanophotonics. These nanoparticles possess many advantages including low background noise level, low excitation energy, high photostability, tunable wavelength and lifetime, and high tissue penetration depth. However, the development of UCNPs has been hindered by a lack of quantitative analysis technology. Such technologies must have the ability to distinguish a single particle; and the sensitivity to detect the emission lifetime and spectrum of a single particle, both of which are challenging to achieve with the current optical measurement instrumentation.

In my PhD thesis, I will describe a novel single UCNPs characterization method, which offers a way to achieve highly precise, efficient, and quantitative measurements (Chapter 2). This technology will be applied in Chapter 3 to investigate the energy transfer process in the core shell UCNPs. The results revealed that the optimized shell thickness is 6.3 nm for fluorescence probe. In Chapter 4, I used this single particle characterization system to investigate the self-interference phenomenon of UCNPs on a mirror surface. Based on the observed intensity curves, I developed a nanosensor with the ability to detect axial position with 10 nm resolution. More importantly, I found an incomplete destructive interference (IDI) phenomenon, which may enable real-time super-resolution microscopy in the future. In Chapter 5, conclusions are drawn and the prospectives including single UCNP lasing, mirror enhanced super resolution, and interaction of multi-emitters in a UCNP are introduced.

Key words: upconversion nanoparticles, single nanoparticle characterization, confocal microscopy, core-shell structure, filter-based spectrometer, self-interference, distance sensing, real-time super resolution

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