DOCTORAL PROJECT PROPOSAL
DOCTORAL SCHOOL OF EXACT AND NATURAL SCIENCES
NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ
Contest 003, April 2021

Project title (in English)		
Acoustically-shaped light for improved ablative and imaging processes in tissues		
Project title (in Polish)		
Akustooptyczne kształtowanie wiązki światła w celu poprawy technik ablacyjnych i metod obrazowania tkanek		
Project submitter		
Dr hab. Ireneusz Grulkowski, prof. UMK …………………………………………………… degree/title, first and last name	**igrulkowski@fizyka.umk.pl** …………………………………………………………………………………… e-mail address	
	Insitute of Physics; Faculty of Physics, Astronomy and Informatics …………………………………………………………………………………… organizational unit	
Suggested supervisors and mentors		
1) main supervisor		
Dr hab. Ireneusz Grulkowski, prof. UMK …………………………………………………… degree/title, first and last name	**igrulkowski@fizyka.umk.pl** …………………………………………………………………………………… e-mail address	
	Institute of Physics; Faculty of Physics, Astronomy and Informatics, NCU …………………………………………………………………………………… organizational unit	
	field:	physics
2) auxiliary supervisor		
Dr. Marti Duocastella …………………………………………………… degree/title, first and last name	**marti.duocastella@ub.edu** …………………………………………………………………………………… e-mail address	
	Faculty of Physics, University of Barcelona …………………………………………………………………………………… organizational unit	
	field:	physics

1. PHD PROJECT DESCRIPTION (4000 characters max., including the aims and work plan)

Project title:

Acoustically-shaped light for improved ablative and imaging processes in tissues

1.1. Project goals:

- To improve the efficiency, penetration depth and spatial resolution of light-based methods for biomedical applications using combination of optics and acoustics (ultrasonics) technologies,
- To improve the delivery of light into tissues by using acoustically-shaped light, namely light which intensity distribution and propagation characteristics have been modified using ultrasound,
- To develop methodology for precise control of the focus position in tissues.

1.2. Outline

The use of optical techniques for biomedical applications is continuously expanding thanks to the unique features they offer, such as unsurpassed penetration depth, diffraction-limited resolution and possibility to operate with no physical contact. Depending on the nature of interaction of light with matter, the optical modalities can be used to either modify the structure / geometry of tissues or to perform visualization of tissues. Key examples of those technologies include **optical coherence tomography** (OCT) or **laser surgical procedures**, commonly used for the diagnostics and treatment of skin and eye conditions as relevant as skin cancer, macular degeneration or glaucoma.

Optical coherence tomography (OCT) is an imaging technique that detects back-reflected and back-scattered photons and enables non-contact and non-invasive three-dimensional (volumetric) visualization of tissue microstructure in vivo at high spatial and temporal resolution. Recent developments in light sources and wide-band electronics allowed for imaging beyond standard depth range values, which facilitated new clinical and non-biomedical applications of OCT technology. On the other hand, the advent of laser techniques offered an entirely new way of performing **ablation and treatment of tissue**. Indeed, the use of pulsed sources such as excimer or femtosecond lasers allowed the development of **novel types of surgeries that offer minimal invasiveness and unprecedented precision**. In all these methods, controlled light delivery into targeted areas is fundamental for optimal results. Failing to achieve so can cause a loss of contrast in the acquired images or even induce damage into the surrounding areas when performing laser surgery. However, existing approaches can lack the efficiency, ease of implementation or speed to provide the desired spatiotemporal control of light.

This collaborative project aims at addressing those issues by using novel acousto-optofluidic devices to shape the light. In particular, the main goal of this collaborative project is to improve the efficiency, penetration depth and spatial resolution of light-based methods for biomedical applications. Specifically, we aim to improve the delivery of light into tissues by using acoustically-shaped light, namely light which intensity distribution and propagation characteristics have been modified using ultrasound. As recently demonstrated by both Spanish and Polish partners, the unique interactions between light and sound leads to an unsurpassed control of light. In this project, **we will use this phenomenon to efficiently guide light deep into tissue, enabling two key features:**

(1) Acquisition of OCT images with enhanced signal-to-noise ratio and spatial resolution at depths not currently accessible with commercial systems;

(2) Local removal of tissue via laser ablation with improved efficiency, spatial resolution, and minimal heat dissipation effects.

The project will be implemented at the cooperating research groups at the Nicolaus Copernicus University (Bio-Optics & Optical Engineering Lab, BOEL) and the University of Barcelona.

1.3. Work plan

The specific aims given by both work packages will be achieved using the following methodology:

(1) Optimization of imaging/ablative processes using acoustically-shaped light with phantom tissue samples

The core technology of the project is the use of an optofluidic system that uses sound to shape the light. In this system, acoustic waves are generated in a fluid-filled cavity by means of piezoelectric actuators. The integration of such a system into traditional optical architectures results in an unsurpassed control of light. However, the application of acoustically-shaped light in biomedicine and for ablation/monitoring of soft tissue remains in its infancy. To fill this void and mature the use of beam shaping technologies for biomedical applications, the first part of the project will seek the optimization of acoustically-shaped light in OCT and laser ablative processes. In particular, we will perform a systematic study of the main technological parameters that influence light delivery-depth into soft materials for imaging and laser processing applications, respectively. This will be carried out using phantom samples consisting of an elastomer doped with different concentrations of high refractive index (reflective / scattering) particles. Underlying these experimental tasks, basic diffraction modeling of acoustically-shaped light propagation in scattering media will be conducted by both partners to help inform the experimental development and verification.

(2) Development of imaging and laser surgical systems based on shaped light for the monitoring and processing of ex-vivo tissue samples

The second part of the project will focus on the monitoring and processing of biological tissue samples. In particular, porcine corneal and epidermal samples will be used for the realization of parametric studies aimed at the quantification of the ablation efficiency and the imaging depth possibilities offered by acoustically-shaped light. Based on these results, empirical relations between the driving conditions of the optofluidic system and the gain in efficiency/penetration depth will be reported to find the optimal light delivery conditions in real-world samples. OCT images of tissue before and after laser treatment will be performed. This will be used to assess the potential benefits of integrating, in a single platform, laser surgery with in-situ, high-resolution monitoring.

1.4. Literature

[1] I. Grulkowski, S. Manzanera, L. Cwikliński, F. Sobczuk, K. Karnowski, P. Artal, Swept source OCT and tunable lens technology for comprehensive imaging and biometry of the whole eye, Optica 5 (2018), 52-59.
[2] S. Kang, M. Duocastella, C.B. Arnold, Variable optical elements for fast focus control, Nature Photon. 14(9), 533-542 (2020).
[3] A. Zunino, S. Surdo, M. Duocastella, Dynamic Multifocus Laser Writing with Acousto-Optofluidics, Adv. Mat. Technol. 4(12), 1900623 (2019).

1.5. Required initial knowledge and skills of the PhD candidate

- MSc in one from the following disciplines: physics, engineering, informatics or related field,
- Basic computer skills, programing skills (e.g. Labview, C/C++, Matlab or Python),
- Good communications skills,
- Ability to communicate in English,
- Not required but welcome: Experience in optics confirmed with co-authored scientific articles, conference presentations, internships on related subjects.

1.6. Expected development of the PhD candidate's knowledge and skills

Core skills:

- Integrated training in biomedical photonics, data acquisition and data processing,
- Optical engineering methods and tools for design and optimization of advanced optical systems,
- Experience in development of advanced optical imaging modalities (microscopy, tomography etc.),
- Knowledge on laser physics,

Transferrable (soft) skills:

- Analytical thinking,
- Good laboratory practices,
- Project management,
- Science communication for different audiences (incl. oral and poster presentations),
- Scientific writing,
- Team work & international cooperation.

2. INFORMATION ON ACADEMIC ACHIEVEMENTS BY SUGGESTED PROJECT SUPERVISORS

A. Suggested supervisor	Dr hab. Ireneusz Grulkowski, prof. UMK …………………………………………………………………………… degree/title, first and last name

a. Grants obtained in the last 5 years

1. Characterization of ocular biomechanics in vivo in age-related eye diseases using novel optical modality (OPUS; # 2018/31/B/NZ5/02156), 2019-2022, National Science Center, Principal Investigator (923 000 PLN)
2. Lenticular and vitreal light scattering and refraction for tomorrow's eye diagnostics (TEAM; # POIR.04.04.00-00-5C9B/17-00), 2018-2022, Foundation for Polish Science, Principal Investigator (3 975 005 PLN)
3. Evaluation of novel diagnostic approaches for early detection of opacifications in cataractous eyes (HARMONIA; # 2017/26/M/NZ5/00849), 2018-2021, National Science Center, Principal Investigator (485 500 PLN)
4. Advanced BiomEdical OPTICAL Imaging and Data Analysis BE-OPTICAL (Marie Skłodowska-Curie Innovative Training Network;# H2020-MSCA-ITN-2015-ETN), 2016-2019, Supervisor of an Early Stage Researcher
5. Ultrahigh-speed modulation of light beam aberrations for performance improvement of the imaging systems (SONATA-BIS; # 2014/14/E/ST7/00637), 2015-2019, National Science Center, Principal Investigator (1 200 000 PLN)

Interferometric imaging of the whole eye using active optical elements (IUVENTUS PLUS; # IP2014 014073), 2013-2015, Ministry of Science and Higher Education, Principal Investigator (300 000 PLN)

b. H-index value

according to Google Scholar	22
according to Scopus	18

c. Number of quotations

according to Google Scholar	2242
according to Scopus	1463
d. Value of Field Weighted Citation Impact in the last 5 years (by SciVal)	1.56

e. List of four major academic papers published or accepted for publication in the last 4 years

1) D. Ruminski, J. Sebag, R. Duarte Toledo, A. Jiménez-Villar, J. K. Nowak, S. Manzanera, P. Artal, I. Grulkowski, Volumetric Optical Imaging and Quantitative Analysis of Age-Related Changes in Anterior Human Vitreous, Invest. Ophthalmol. Vis. Sci. 62(4), 31 (2021)

2) I. Grulkowski, S. Manzanera, L. Cwikliński, F. Sobczuk, K. Karnowski, P. Artal, Swept source OCT and tunable lens technology for comprehensive imaging and biometry of the whole eye, Optica 5 (2018), 52-59.

3) A. Rodríguez-Aramendía, F. Díaz-Doutón, J. Fernández-Trullàs, P. Falgueras, L. González, J. Pujol, I. Grulkowski, J. L. Güell, Whole anterior segment and retinal swept source OCT for comprehensive ocular

screening, Biomed. Opt. Express 12(3), 1263-1278 (2021)
4) I. Grulkowski, Anterior Segment OCT, in: Handbook of Visual Optics Vol. II: Instrumentation and Vision Correction, P. Artal (ed.), CRC Press Taylor & Francis Group, Boca Raton (2017).
f. List of promoted doctoral students: their titles, last names, titles of doctoral dissertations, names of universities, year and field of graduation
N/A (2 PhD students finish their study in 2021, 2 other PhD students in progress)
g. Description of previous (and potential) scientific cooperation with other academic centers in the last 5 years (1 page)
The Bio-Optics & Optical Engineering Lab at the Institute of Physics possesses extensive collaboration network in Poland and abroad. Currently, all project are realized in cooperation with external groups. The list of previous (current) cooperation links is given below: • Laboratorio de Óptica; Universidad de Murcia, Murcia (Spain) – Prof. Pablo Artal • VMR Institute for Vitreous Macula and Retina, Huntington Beach, CA (USA) – Prof. Jerry Sebag, MD • University of Barcelona, Barcelona (Spain) – Dr. Marti Duocastella • Information Optics Group, University of Warsaw – Prof. Ryszard Buczyński • Instituto de Óptica "Daza de Valdés"; Consejo Superior de Investigaciones Científicas, Madrid (Spain) – Prof. Susana Marcos • Physical Optics and Biophotonics Group; Department of Physical Chemistry of Biological Systems; Institute of Physical Chemistry; Polish Academy of Sciences, Warsaw (Poland) – Prof. Maciej Wojtkowski & Dr. Karol Karnowski • Department of Physics; Warsaw University of Technology, Warsaw (Poland) – Dr. Krzysztof Świtkowski • Department of Optics and Photonics; Faculty of Fundamental Problems of Technology; Wrocław University of Technology, Wrocław (Poland) – Prof. Henryk Kasprzak • Department of Optometry; Faculty of Medicine; Collegium Medicum, Nicolaus Copernicus University, Toruń (Poland) – Prof. Bartłomiej Kałużny, MD • Department of Pediatric Gastroenterology and Metabolic Diseases; Poznań University of Medical Sciences, Poznań (Poland) – Jan K. Nowak, MD, PhD and Prof. Jarosław Walkowiak, MD This enables to provide a trained student with a necessary support from other research centers.

B. Suggested Co-supervisor	Dr Marti Duocastella ……………………………………………………………………… degree/title, first and last name
a. Grants obtained in the last 5 years	
1. Ultrasonic endoscopes for DEEP light focusing (ERC CONSOLIDATOR GRANT # 101002460) 2021-2026, European Research Council, Principal Investigator (1 862 462 €) 2. OrganVision, Technology for real-time visualizing and modelling of fundamental process in living organoids towards new insights into organ-specific health, disease, and recovery (FET OPEN # 964800), 2021-2025, European Comission, Principal Investigator (Total award amount: 3,7 M€ - 533 000 € to Universitat de Barcelona) 3. 'Verso una nuova biologia con un microscopio 3D a milioni di fotogrammi al secondo' (Compagnia di San Paolo, ROL 24704), 2020-2022, Principal investigator (153 000 €) 4. 'Sistema ultra-veloce per il tracciamento 3d di oggetti nanometrici' (Compagnia di San Paolo, ID	

2015.AAI4112.U4919), 2015-2017, Pincipal investigator (186 000 €)	
b. H-index value	
according to Google Scholar	25
according to Scopus	21
c. Number of quotations	
according to Google Scholar	2762
according to Scopus	1920
d. Value of Field Weighted Citation Impact in the last 5 years (by SciVal)	-

e. List of four major academic papers published or accepted for publication in the last 4 years

1) M. Duocastella, G. Sancataldo, P. Saggau, P. Ramoino, P. Bianchini, A. Diaspro, Fast Inertia-Free Volumetric Light-Sheet Microscope, ACS Photonics 4(7), 1797-1804 (2017)

2) S. Surdo, M. Duocastella, Fast Acoustic Light Sculpting for On-Demand Maskless Lithography, Advanced Science 6(14), 1900304 (2019).

3) S. Kang, M. Duocastella, C.B. Arnold, Variable optical elements for fast focus control, Nature Photon. 14(9), 533-542 (2020).

4) A. Zunino, S. Surdo, M. Duocastella, Dynamic Multifocus Laser Writing with Acousto-Optofluidics, Adv. Mat. Technol. 4(12), 1900623 (2019).

f. List of promoted doctoral students: their titles, last names, titles of doctoral dissertations, names of universities, year and field of graduation

1. PhD student, Simonluca Piazza, “Advanced optical systems for fabrication and imaging”, Università degli studi di Genova, 2018, biomedical engineering
2. PhD student, Giuseppe Sancataldo, “Fast and deep imaging of 3D biological systems”, Università degli studi di Genova, 2017, biomedical engineering
3. PhD student, Alessandro Zunino: thesis defense expected on December 2021

g. Description of previous (and potential) scientific cooperation with other academic centers in the last 5 years (1 page)

1. Prof. Peter Saggau, Acousto-optic systems, Baylor College of Medicine, Houston, USA
2. Prof. Craig B. Arnold, TAG lenses, Princeton University, Princeton, USA
3. Prof. Paolo Decuzzi, Light-based methods for nanomedicine, Istituto Italiano di Tecnologia, Genoa, Italy
4. Prof. Alberto Diaspro, Fast volumetric microscopy, Istituto Italiano di Tecnologia, Genoa, Italy
5. Prof. Ireneusz Grulkowski, Acousto-optic imaging, Nicolaus Copernicus University, Torun, Poland

4. DECLARATION OF Availability and Access to TECHNICAL/EXPERIMENTAL/FINANCIAL RESOURCES NECESSARY AND SUFFICIENT TO COMPLETE THE PROJECT

I declare that our research team has sufficient infrastructure to implement the proposed project. The BOELab has access to well-equipped laboratories with necessary equipment. Every year, the group invests resources to update its equipment. Additionally, we are able to provide trainee with sufficient supplementary materials to conduct the studies.

5. DECLARATION CONCERNING THE AUTHORSHP OF THE PROJECT IDEA

I declare that the author of the idea for the doctoral project is:

………Ireneusz Grulkowski and Marti Duocastella……………………………………………………………………………………………

6. DECLARATION CONCERNING THE POSSIBILITY OF PUBLISHING THE CONTENT OF THE PROJECT

I declare that the description of the project submitted do the contest from point 1. can be published on the website of Doctoral School of Exact and Natural Sciences, Nicolaus Copernicus University in Toruń.

08.05.2022.

place, date

signature of project submitter