prof. dr hab. inż. Leszek R. Jaroszewicz,
corresponding member of
the Polish Academy of Sciences
Institute of Technical Physics
Military University of Technology
jarosz@wat.edu.pl

24th September, 2024 r.

REVIEW

of the doctoral thesis of Aleha Sudakou, M.Sc.
subtitled: "Depth-resolved assessment of tisssue oxygen saturation using time-domain near infrared spectroscopy"

The subject of this review is the aforementioned doctoral thesis of Aleh Sudakou, M.Sc., whose Promoter is Prof. dr hab. inż. Adam Liebert, Corresponding Member of the Polish Academy of Sciences. The review was meticulously prepared based on the letter SN/416/6.1/2023 dated 12.07.2024 (date of receipt 26.07.2024) from the Deputy Director of the Institute of Biocybernetics and Biomedical Engineering of the Polish Academy of Sciences (IBIB PAN) on the appointment me by the Scientific Council of IBIB PAN of a reviewer.

According to the current regulations, the *Law on Higher Education and Science* of 20 July 2018 (Journal of Laws of 2023, item 742, as amended), the role of the reviewer is to determine whether the applicant for a doctoral degree has the required scientific output (requirement of Art. 186) and whether the doctoral dissertation presents the candidate's general theoretical knowledge in the discipline as well as the ability to conduct scientific work independently (requirement of Art. 187 paragraph 1) and, above all, whether the subject of the doctoral dissertation is a truly original and innovative solution to a scientific problem (requirement of Art. 187 paragraph 2).

The dissertation submitted for review is an English-language discussion of five high-scoring scientific publications co-authored by the doctoral student. The doctoral student is the first co-author of these papers, and his significant contributions to these publications have been identified in separate statements confirmed by the supervisor.

Having studied the dissertation, I do not doubt the following facts:

1. the doctoral dissertation initiated in the discipline of biomedical engineering in the field of engineering and technology science falls entirely within the discipline of biomedical engineering;
2. the dissertation is theoretical (based on numerical studies) and experimental. The stated aim of the dissertation on page 5, consistent with its theme, has five clearly formulated objectives: *wavelength selection, performance metrics, system characterization, new phantom, and new method* - verifiable based on the submitted dissertation;
3. the support of the dissertation by **four** publications, from the years 2019-2023, related to the topic of the dissertation, located in the **JCR database with a total IF value of 14.115**, in which the **Doctoral Student is the first co-author**, is the basis for stating the fulfillment of the statutory requirement of Art. 186 concerning the Doctoral Student's scientific output, as well

as the requirement of Art. 187 paragraph 2 regarding the inclusion in the dissertation of a truly original solution to a scientific problem;

4. also, the issue of conducting a proper analysis of sources, including world literature (the doctoral student, in addition to the items cited in the above works, provides 47 in their discussion), the state of knowledge and applications in industry does not raise any objections. Undoubtedly, the author has sufficient knowledge in this area, and the conclusions from the review of sources oriented towards the problem solved were formulated clearly and convincingly.

In proceeding with a detailed review of the dissertation, I state that English is not my mother tongue; hence, I cannot assess the linguistic correctness in detail. However, because the dissertation is based on four extensive articles published in the *Biomedical Optics Express* published by the professional society **Optica**, founded as the **Optical Society of America** in 1916, the language issue cannot be objectionable.

In evaluating this work, I conclude that improving the resolution of non-invasive optical methods for imaging the human body is currently a key challenge for the practical application of these methods. One of these methods is near-infrared spectroscopy NIRS, where the properties of the light wavelength used allow sufficiently deep penetration of the object under study. However, the main problem of this method is the separation of helpful information from the different layers into which the radiation penetrates and the lack of a real benchmark for the results obtained, i.e., the existence of standardization and the efficiency of the method used. These two challenges are addressed in the reviewed paper, in which the doctoral student focuses on assessing oxygenation (StO_2) of the cerebral cortex. It should be emphasized that this is not a limitation but more of a validation of the applied solution, which can be successfully applied in other studies, e.g., studies of muscles or kidneys. The doctoral student does not build a new stand for his research but uses the stand built at the IBIB PAN, which is unique worldwide, for time-domain NIRS measurements. Additionally, his work is based on an advanced Monte Carlo (MC) code developed in IBIB PAN for modelling light propagation in tissues.

I consider the five objectives to be the core elements of the doctoral student's original contribution:

Regarding objectives 1 – *wavelength selection*. He developed a method for choosing the emission spectra region corresponding to the smallest uncertainty in the determined concentrations of chromophores, considering the characteristics of the NIRS systems. The method estimates expected uncertainties in the determined parameter due to photon noise. The above, published as *Biomed. Opt. Express*, **10**, 4621-4635 (2019), with 10 citations, shows that the minimum standard deviation of estimated COO concentration changes with the brain layer equal to 0.40 μM covered by scalp and skull is for in wavelength range 725 – 913 nm. However, for a realistic responsibility spectrum of the used system, the wavelength is moved to a range of 688-875 nm with a minimum above standard deviation equal to 0.47 μM.

Regarding objective 2 – *performance metrics.* He developed a method for quantitatively comparing different measures and providing different tests for evaluating performance and overall ranking. As he has shown in *Biomed. Opt. Express*, **11**, 4348-4365 (2020), with 15 citations, these tests can assist in developing and assessing new data analysis methods and in the standardization efforts in the NIRS community.

Regarding objective 3 – *system characterization.* The proof of this objective is contained in the work *Biomed. Opt. Express*, **12**, 6629-6650 (2021), with 18 citations, where PhD candidate has provided a detailed description and validation of the multi-wavelength time-domain NIRS system using the state-of-art performance assessment method. It should be underlined that he used the results obtained as proof of objectives 1 and 2.

Regarding objective 4 – *a new phantom.* He has developed a new phantom that allowed for the first time to independently simulate dynamic changes in StO_2 in two layers. As he has shown in *Biomed. Opt. Express*, **14**, 3506-3531 (2023), with 11 citations, the built phantom might help in the international ongoing effort towards standardization of the performance assessment of NIRS devices and overcoming the contamination from the superficial layer. I can confirm the PhD student's statement that one of the main remaining challenges regarding this phantom is a reference measure that would provide the true value of StO_2.

Regarding objective 5 – *a new method.* This objective's proof relates to the phantom described above and is based on the description included in the previously cited publication (*Biomed. Opt. Express*, **14**, 3506-3531 (2023), with 11 citations). The described new method improved the accuracy in the determination of optical properties and, hence, in the determined StO_2 in two layers using measurements on the top of the superficial layer, for the dynamic StO_2 from 100% to 0%, validating for the first time the depth-resolved StO_2 measurement.

It is difficult to question the validity of the research extensively described in four publications in a renowned journal such as *Biomedical Optics Express*, totalling 77 pages, but I have two substantive comments regarding the introduction to these papers:

1. due to using the INRS system at IBIB PAN as a base, it seems expedient to present it in the introduction. Its description in the publication *Biomed. Opt. Express*, **12**, 6629-6650 (2021), is unreadable - see a reprint of publication page 6631 Fig. 1;

2. the above comment also applies to the developed phantom, which can be found on page 3512 in the publication *Biomed. Opt. Express*, **14**, 3506-35631 (2023), as Fig. 1. I think its description in the introduction would be more helpful.

Discussion notes:

- in this work, the PhD student deals with optical methods, essentially near-infrared spectroscopy, using spectral characteristics. I am interested in the Doctoral student's position on the influence, or lack thereof, of the polarisation of the used optical beam on the quality of the images obtained;

- what is the difference between the time-resolved near-infrared spectroscopy technique described in proofing objective 1 [*Biomed. Opt. Express*, **10**, 4621-4635 (2019)] and the time-domain near-infrared spectroscopy technique applied in the NIRS system developed in IBIB and used in three other publications;

- what type of optical fibre is used in INRS developed in IBIB PAN?

In conclusion, I hereby state that the submitted dissertation satisfies the requirements of Articles 186 and 187 of the *Law on Higher Education and Science* of 20 July 2018. (Journal of Laws of 2023, item 742, as amended), both as regards the required scientific output, the Doctoral Student's presentation of general theoretical knowledge in the discipline of biomedical engineering, and the ability to conduct scientific work independently and, above all, as an original solution to a scientific problem. In the latter respect, the most relevant from the point of view of the current

regulations, I conclude that the thesis represents an outstanding scientific achievement: a documented practical solution to an engineering and technical problem relevant to biomedicine. I conclude that it is an exemplary course of 'adaptive' scientific research that additionally fulfils the requirements of IBIB PAN regarding the distinction of the work. Thus, I apply for **the distinction of the present dissertation** and request that it be accepted as a doctoral dissertation and admitted to public defense.