System Analysis Theory Applied for Development of Microalgae Processes and Photobioreactors in the Frame of Integral Biorefinery Concept

Alexander Dimitrov Kroumov*, **Maya Margaritova Zaharieva**, **Hristo Miladinov Najdenski**

Department of Infection Microbiology,
The Stephan Angeloff Institute of Microbiology
Bulgarian Academy of Sciences
26 Acad. G. Bonchev Str., 1000 Sofia, Bulgaria
E-mails: adkrumov@gmail.com, zaharieva26@yahoo.com, hnajdenski@abv.bg

**Corresponding author*

Received: July 03, 2024 **Accepted: December 12, 2024**

Published: December 31, 2024

Abstract: *Microalgae technology involves many steps of unit operations and is connected with global warming and pandemic problems because of the unique features of algal cells. Studying sophisticated systems cannot be without special mathematical tools and approaches that combine knowledge from many research areas. The system analysis theory applied in biotechnology with great success can be applied by principles of analogy to microalgae cultivation of cells in CO_2 fixation from flue gases in innovative closed photobioreactors (PBRs) where the products of biomass can have performed antimicrobial, anticancer, antiviral and other activities by challenging chemical agents. Recently, a multifunctional algology laboratory was created at the Stephan Angeloff Institute of Microbiology by applying knowledge in state of the art. The goal of this work was to summarize the 40 years of experience of the authors in this area and to show how this was realized by innovative engineering solutions for studying and developing the microalgae system. Special attention was paid to the development of hybrid, innovative PBRs with the aim of fully revealing the potential of microalgae strains not only for the complete absorption of CO_2 from flue gases but also for the synthesis of high-value products (HVP) with antimicrobial, antiviral and anticancer activity.*

Keywords: *Photobioreactors, System analysis, Biorefinery concept, Microalgae.*

Principles for the creation of a multifunctional algology laboratory

The authors applied all their knowledge about bioreactor design and its functioning in new applications where the light and processes of photosynthesis of microalgae are connected in photobioreactors space. The different scenarios and ideas of novel hybrid columns PBRs resulted in the building of more than 20 new constructions. They were scaled to create two zones: i) inoculums stage – inoculums preparation (small PBRs, in Fig. 1 above) and ii) production stage – obtaining biomass and valuable products on a larger scale (big PBRs, in Fig. 1 below).

The novel PBRs designs were created according to the knowledge database about hydrodynamics and control of fluid flow distribution in column bioreactor. The main idea when taking engineering solutions was to create a construction that allows obtaining optimal flashing light effect (FLE) which already is proven theoretically [20] and experimentally [11] to give several folds increasing of biomass concentration and it is responsible for revealing unsuspected capabilities of strains to synthesize valuable metabolites under stress from the light used and the trajectory of movement of the algae. Various unique PBR designs were created and tested in the production stage (Fig. 2).

Fig. 1 A multifunctional laboratory in real cultivation conditions of *Scenedesmus obliquus* strain bought from Czech Republic Culture Collection

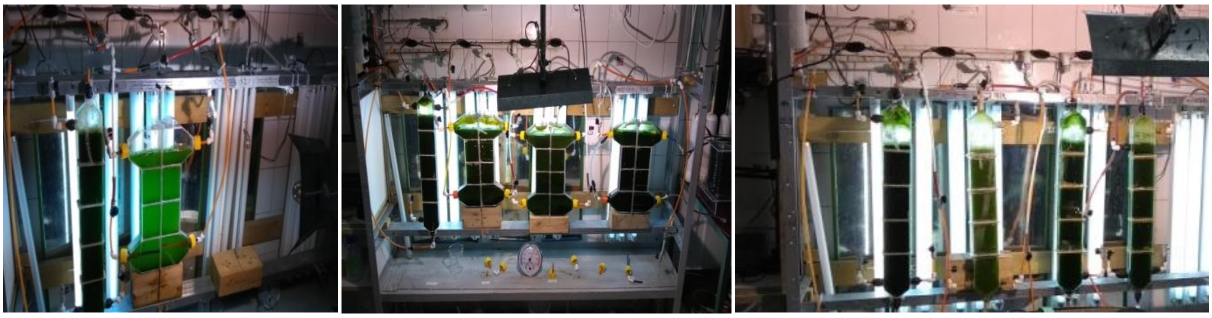

Fig. 2 Hybrid column-flat plate PBRs in working mode

Furthermore, by combining knowledge of hydrodynamics and cell shading at high cell densities, we created hybrid columnar and tubular designs. These new PBRs were also tested for different particle loadings and under the influence of light of different wavelengths – green, red and blue (not shown) (Fig. 3).

The application of a special hybrid PBR with a bigger volume resulted in a patent [41] is shown in Fig. 4.

The authors checked all theoretical assumptions about innovative constructions of flat plate PBRs as well, column PBRs by developing a multifunctional laboratory in UNIOESTE-Toledo, Parana Brazil under the program "Science without Borders" under the Grant № 313737/2014-

4 with the CNPq Special Visiting Researcher Fellowship for Alexander Dimitrov Kroumov and Coordination for the Improvement of Higher Education Personnel (CAPES).

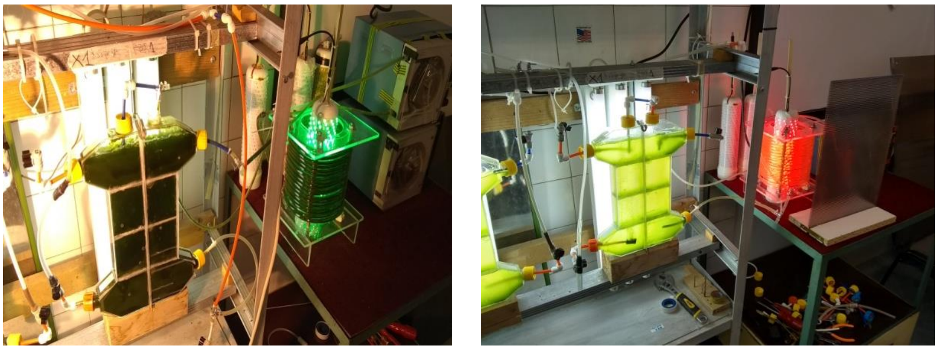

Fig. 3 Hybrid flat plate-tube PBRs with different light wavelengths

Fig. 4 A hybrid PBR including long tube and stirred thank reactor configuration [41]

Seven different microalgae species were isolated from Brazilian lakes, identified [36], and one of them *Poterioochromonas malhamensis* was used in real experiments to check the potential of chosen flat plate PBR with volume V_{pbr} = 10 L [11]. The flow distribution inside the PBR volume was calculated by using computational fluid dynamics software (Comsol Multiphysics 5.2). All details can be found in [11]. We are going only to mention that in the current paper, the controlled fluid flows in sectioned flat plat PBRs was possible to achieve biomass concentration of X = 16 g/L. The PBR without baffles succeeds to each about X = 4.5-5.0 g/L. Similar results with hybrid PBRs were achieved in the Bulgarian Lab although the scale of PBRs were different.

Modeling procedure

The milestone of every success in microalgae technology is the evaluation of the system in its complex form where PBR optimal construction gives the biggest weight to the techno-economical value of the overall system. Hence, investigating the PBR as a system is fundamental and we are going to describe step by step the procedure below whereby building the model of every subsystem of PBR is unavoidable.

Therefore, to successfully model the CO_2 utilization by algae and the production of high value products from their cells in the particular PBR design – many physical, chemical, biochemical, and photosynthetic parameters and processes must be considered and modelled [22, 35, 39]. In other words, to support the best conditions for a biological system concerning this particular species (CO_2, SO_2, and NO_2 from flue gas), engineering specifications must be done by considering flue gas composition interactions with microalgae behavior, and PBR design should be used to gives a particular life environment. All the knowledge of observable and measurable parameters about the system must be formalized in mathematical models. Planning of active experiments for optimal process development is obligatory. The revolutionary importance of the developed theory is to show clearly that methodology of "trial and error" is an empirical and slow approach.

The start of the procedure should be the analysis of a crucially important step such as medium optimization. An example will be CO_2 utilization from industrial waste gas such as flue gas. A robust algorithm of medium optimization for culturing algae was developed [7, 8] and was used with great success when performing real experiments in laboratories of the USA [7], Bulgaria [40] and Brazil [11, 36]. The algorithm is considered as a base of the elemental composition of microalgae, and carbon dioxide as a non-organic source of carbon. The mathematical procedure used linear programming to calculate the values of the chemical elements in the medium. The program is coded in MAPLE15® software of symbolic mathematics. It has to be noticed, that the algorithm allows calculating macro- and micro-elements when the medium composition change. It means the objective function in the search can be built for different purposes like biomass maximization or overproduction of desired metabolites. Therefore, a loop procedure is needed to search for and to obtain an optimal chemically defined medium. This is extremely important for process development on a big scale. For example, the purification of industrial gases from CO_2 first passed a step of absorption, for example in water. Then, water chemistry should be studied and how it will be linked with the microalgae metabolism. It means that connections between aqueous ions of the flue gas such as CO_2, O_2, SO_x, NO_x, HCL, and microalgae growth must be understood and modeled [23]. Studying water chemistry requires knowledge about the thermodynamic properties of chemical components and their possible interactions. In the USA laboratories, we have used MINEQL+4.6 software as a tool for evaluating chemical equilibrium aqueous speciation of gases, solid phase saturation states, and precipitation-dissolution. It helped us to find the best modification of the M-8 medium and apply it on the industrial scale.

Further, guided by the system analysis theory [35] we analyzed PBR as a system in the frame of integral biorefinery concept [20, 35]. The main stages of system analysis theory [17, 18] applied to the development of the PBR phenomenological model can be presented as follows:

- Determination of the PBR as a system and its modeling procedure;
- Decomposition of the PBR system in sub-systems and studying them separately;
- Building and development of the models of the sub-systems;
- Synthesis of system development in complex models of sub-systems and their relationships;
- For practical application, the complex PBR phenomenological model is simplified;
- Simulations with the model and obtaining its best design;
- Experimental verification of the developed complex models in every level and sub-systems;
- Solving PBR scale-up problems.

In order to be successful in the process development of this complex system, it must be decomposed into sub-systems. Further, the sub-systems must be studied and modeled and the final results of the combination of all this knowledge is to build a complex model with which PBR optimal geometry can be achieved. Here, we will explain briefly the strategy. The whole theory about the PBR modeling can be found elsewhere [11].

The first hierarchic level of knowledge

This is a key point to the overall understanding, description, development, and control of the system behavior. In this step, two fundamental strategies and considerations must be distinguished:

- The development of "pure" kinetics on CO_2 from air; algae tolerance to gas supplied with 15% CO_2 which means performing experiments where no limitation and other effects of hydrodynamics and mass-transfer take place [26];
- The development of "real" microalgae growth kinetics on CO_2 from industrial waste gas, for example, flue gas (15% CO_2 and 6% O_2, and SO_2 up to 2000 ppm);
- Microalgae's high tolerance to flue gas components (especially to a high content of SO_x, NO_x), it means real microalgal growth kinetics is when experiments are performed in a real PBR design.

Water chemistry of dissolved flue gas components

Flue gas contains high concentrations of CO_2 (up to 15%) and many other impurities which dissociations in the liquid phase will definitely change the medium pH. Hence, pH monitoring and control is a key state parameter and has to be considered in PBR modeling. In this case especially helpful to predict water chemistry was to use software which had data on thermodynamic properties of chemical components such as MINEQL+5.0 software (Chemical Speciation Modeling Software) or Hydra plug-in from MEDUSA (Make Equilibrium Diagrams Using Sophisticated Algorithms) [31].

Mass balances of CO_2 species in water

An overview of flue gas speciation and chemical equilibria in the water can be found elsewhere [35]. The features of processes of photosynthesis in microalgae cells are very well investigated and described as a function of pH and CO_2 speciation [4]. Combining this knowledge in models of specific growth rate (SGR) allows microalgae cultivation process to be optimized and controlled.

Mass balances of SO_2 species in water

Mass balances describing the concentrations of SO_2 species in water help to build a robust pH model of the autotrophic cultivation of microalgae on flue gas [23].

Modeling pH

Hence, this key parameter can be used robustly for process monitoring and control. In microalgae cultivation high supply of CO_2 in the liquid phase lowers pH. On the other hand, during the algae growth, the utilization of total carbon from the cells available as CO_2 (aq), HCO_3^- and CO_3^{2-} ions resulted as an increase of the pH value. It is important to notice that during microalgae culturing usually optimal photosynthesis conditions are in pH range between 6 and 10, wherein the bicarbonate species dominates [4]. Therefore, pH parameter can be used as a control technique so called "pH-stat" where other key state parameters are kept in optimal values (temperature, light irradiation, etc.).

Complete biokinetics model of the algal population

The first hierarchic level of knowledge combines all models on the population level as follows:

- Modeling the most important kinetic parameter-light intensity effect on the SGR;
- Modeling SGR as a function of other main state parameters;
- Modeling water chemistry of dissolved flue gas components and involving it in a kinetic model of microalgae growth on the population level;
- Modeling of photoautotrophic SGR as function of CO_2 concentration;

- Modeling product formation (O_2 evolution) and inhibition of SGR;
- Modeling mixotrophic SGR.

Scale-down procedure

When the overall kinetic model of SGR is built, the researcher may simulate different scenarios of optimal process functioning. It must be noticed that the deformation of complete photobioreactor model parameters as function of a scale reflects in a decrease of overall process productivity. A step-by-step procedure of bioreactor scale-up and scale-down was discussed in details by the authors [9, 27, 34, 37]. Increasing the scale of the system (especially PBR volume) decreases the system productivity and in some cases may reach critical values. In the past, the scale-up problems were solved empirically where the bioreactor/photobioreactor volume was increased gradually and analyzed, modeled and designed which is very costly and time consuming. The approach based on a theory of similarity was widely used, but it was not enough to guarantee robust results. The modern schemes of scale-up [14] procedures are based exclusively on a modeling approach, for example computational fluid dynamics (CFD) where all active lab and pilot plant experiments are based on simulations results. We are using such information from these levels and CFD software to achieve optimal design of flat plate PBRs [11] and hybrid flat plate-column PBRs, as well as in Brazilian and Bulgarian Labs.

The second hierarchic level (PBR performance)

In this hierarchic level macro processes are arranged in sub-systems where mass-transfer, hydrodynamics and light availability in PBRs are analyzed and modeled. Especially important as a tool is an application of CFD mathematics [28]. On its base, the researcher is able to simulate many complex hydrodynamic conditions and coupling them with microalgae kinetics to create new most advanced PBRs. Many other works were developed by applying CFD simulations in order to achieve improved light illumination conditions for different PBR geometries, and consequently higher PBR biomass productivity, and reduced costs for energy [1, 2, 10, 13, 42]. These results have shown that the only way to overcome the drawbacks in the field of closed PBR development and microalgae process optimization is through complex modeling and simulation. By using catalogs of kinetic models representing different microalgae physiology phenomena and matching their requirements with key engineering state parameters (mass transfer, light availability, flow distribution, etc.). The current state-of-art about microalgae cell requirements for light availability and its specific influence (light source, wavelength and intensity, light/dark cycles, FLE) on their growth and metabolism can be found elsewhere [12, 38]. It is important to notice that any new technique involving image analysis to study the internal in vessel light distribution must be under consideration [15, 16] in order to improve the search for optimal PBR design and further to help solving its scale-up problem. Of course, the application of any method has to be cost effective.

The third hierarchic level (complete PBR model)

The third hierarchic level (for example, the complete PBR model) is the final step in system modeling procedure. We were focused on the development of complete PBR mathematical model. Validation of this level has to be done based on real experiments in the pilot plant, if the PBR is easily scalable. Many research groups investigated the relationship between microalgae kinetics and flow distribution in PBRs [24, 29, 30] in order to improve PBR performance. Computer simulations with the complex PBR mathematical model were demonstrated by advanced research groups [25]. Description of the hydrodynamics and mass-transfer processes in the liquid phase may change as a function of PBR design and fluid distribution which is studied by CFD method. Hence, the development of complex

PBR phenomenological model depends on our knowledge about the system (in this case, PBR system) and available information preserved in models about the subsystems and their relationships. To find the optimal microalgae process in real PBR design, the scale-up procedure has to be converted to the conditional optimization procedure where the complex PBR model and chosen objective function (OF) determine the success. The key stage of PBR scale-up is to determine the OF and the limits of chosen control parameters of the overall microalgae process.

Therefore, the microalgae cultivation methodology for CO_2 sequestration includes mathematical evaluation of all the unit operations and downstream processing involved in the scheme by completing a life cycle assessment (LCA) of CO_2 sequestration. Hence, the system analysis and techno-economic analysis [3, 6, 32] of the “Algae Production Scheme and Technology” must be a subject. Further, the proper optimization technique must be applied to optimize the functioning of the whole scheme which evaluates its financial effectiveness and final products including high value products (HVP).

The basis of the integral biorefinery concept

The use of mathematical tools for process optimization and control is crucial to develop competing technology. Hence, the great potential of microalgae for the production of energy is foremost associated with the minimization of production costs of biomass and high value products from it for given operational conditions and equipment. To accomplish such a strategy, integral use of all microalgae products must be realized as follows: lipids, proteins and carbohydrates; added-value co-products; high value products with antimicrobial, antiviral, anticancer and other effects [21, 22, 40].

The implementation of the presented PBRs helped us to obtain the biomass of two algal strains and to test their antibacterial activity on food-borne pathogens. Zaharieva et al. [40] cultured a strain of the species *Tetradesmus* (former *Scenedesmus*) *obliquus* in small-scale PBRs under different light conditions (inner green or red light and outer white light) and compared the pharmacological activity of dichloromethane extracts in relation to their chemical composition. The results revealed that a combination of internal and external LED light is very efficient for the production of carotenoids and fatty acids which possess well known antioxidant and antibacterial activities. A higher biomass concentration (6.95 g/L) was achieved when green internal LED light was applied. The use of internal red light led to a cell density of 5.87 g/L. The production of biopigments was 5 and 5.5 mg/gdw at green and red LED, respectively, which is a promising achievement in the state of the art for *Tetradesmus* spp. The extracts obtained from both PBRs potentiated the activity of clinically applied antibiotics such as ciprofloxacin, penicillin and enrofloxacin, did not show cytotoxicity on normal mice fibroblasts and are suitable candidates for food additives in the poultry industry [19, 40]. Rusinova-Videva et al. [33] cultured the same *Tetradesmus obliquus* strains in flat PBRs and achieved an absolute dry weight of 2.8 g/L. A methanol extract of the biomass exhibited a moderate antibacterial activity against the pathogenic bacterial strain *Staphylococcus aureus* but further investigations are needed to test its application in combination treatment [33]. Brachkova et al. [5] cultured *Chlorella vulgaris* strain in small-scale PBRs with internal white or blue light and external white light and found out that the microalgal cells cultured under blue internal light are characterized by approximately six-fold higher content of carotenoids (9.39 mg/g dry weight) than those maintained under internal white light (1.48 mg/g dry weight).

Conclusions

With this work, we demonstrate the successful application of system analysis theory for process development, optimal PBRs design, and scale-up. The development of a novel complex PBR phenomenological model and a light illumination model linked with algal physiology were the solid base to achieve optimal microalgae cultivation trajectory in PBRs under the frame of integral biorefinery concept where the crucial role for technology effectiveness was maximization and isolation of HVP from algal biomass in the multistep optimization procedure. To successfully solve the task of PBRs scale up problems multidisciplinary team must be formed by sharing the modern advanced methods of analysis and mathematical tools.

Acknowledgements

The initiation of this work was under the Algae project with Prof. Czarena Crofchek at Biosystems and Agricultural Engineering Department, University of Kentucky, Lexington, USA, 212 C. E. Barnhart Building, KY 40546-0276. The authors are grateful to the Bulgarian National Science Fund for partial financial support under the Grants ДФНИ-Е01/0001 (2011); КП-06-Н37/12 (2019) and КП-06-Н53/2 (2021), as well as to the National Counsel of Technological and Scientific Development (CNPq) program "Science without Borders" under the Grant 313737/2014-2 with the Special Visiting Researcher Fellowship for Alexander Kroumov and Coordination for the Improvement of Higher Education Personnel (CAPES).

References

1. Barboza-Rodríguez R., R. M. Rodríguez-Jasso, G. Rosero-Chasoy, M. L. R. Aguado, et al. (2024). Photobioreactor Configurations in Cultivating Microalgae Biomass for Biorefinery, Bioresource Technology, 394, 130208.
2. Belohlav V., T. Jirout, E. Uggetti, R. Díez-Montero, et al. (2024). Computational Fluid Dynamics Coupled to Biokinetic Models: Numerical Methodology for Microalgae Cultivation Optimization, Process Safety and Environmental Protection, 181, 367-376.
3. Bennion E. P., D. M. Ginosar, J. Moses, F. Agblevor, et al. (2015). Lifecycle Assessment of Microalgae to Biofuel: Comparison of Thermochemical Processing Pathways, Applied Energy, 154, 1062-1071.
4. Borowitzka M. A. (1988). Algal Growth Media and Sources of Algal Cultures, Microalga Biotechnology, Borowitzka, M. A. and L. J. Borowitzka (Eds).
5. Brachkova A., M. M. Zaharieva, Y. Ilieva, M. Kaleva, et al. (2022). Complex Engineering Approach in a Process Development Algology Laboratory, Annual of Sofia University "St. Kliment Ohridski", Book 4: Scientific Sessions of the Faculty of Biology, Sofia, Bulgaria, St. Kliment Ohridski University Press, 107, 44-49.
6. Chauton M. S., K. I. Reitan, N. H. Norsker, R. Tveterås, et al. (2015). A Techno-economic Analysis of Industrial Production of Marine Microalgae as a Source of EPA and DHA-rich Raw Material for Aquafeed: Research Challenges and Possibilities, Aquaculture, 436, 95-103.
7. Crofcheck C. L., M. Montross, K. Cassidy, A. Kroumov, et al. (2010). Medium Optimization for CO_2 Mitigation from Flue Gas, In Annual Institute of Biological Engineering Meeting in Cambridge, Cambridge, UK.
8. Crofcheck C. L., M. Monstross, E. Xinyi, A. P. Shea, et al. (2012). Influence of Media Composition on the Growth Rate of *Chlorella vulgaris* and *Scenedesmus acutus* Utilized for CO_2 Mitigation, In 2012 Dallas, Texas, July 29 - August 1, 2012, American Society of Agricultural and Biological Engineers.
9. Garcia-Ochoa F., E. Gomez (2009). Bioreactor Scale-up and Oxygen Transfer Rate in Microbial Processes: An Overview, Biotechnology Advances, 27(2), 153-176.

10. Gómez-Pérez C. A., J. Espinosa, L. M. Ruiz, A. J. B. Van Boxtel (2015). CFD Simulation for Reduced Energy Costs in Tubular Photobioreactors Using Wall Turbulence Promoters, Algal Research, 12, 1-9.
11. Hinterholz C. L., D. E. G. Trigueros, A. N. Módenes, C. E. Borbaet, et al. (2019). Computational Fluid Dynamics Applied for the Improvement of a Flat-plate Photobioreactor towards High-density Microalgae Cultures, Biochemical Engineering Journal, 151, 107257.
12. Hu J. Y., T. Sato (2017). A Photobioreactor for Microalgae Cultivation with Internal Illumination Considering Flashing Light Effect and Optimized Light-source Arrangement, Energy Conversion and Management, 133, 558-565.
13. Inostroza C., Š. Papáček, J. M. Fernández-Sevilla, F. G. Acién (2023). Optimization of Thin-layer Photobioreactors for the Production of Microalgae by Integrating Fluid-dynamic and Photosynthesis Rate Aspects, Journal of Applied Phycology, 35(5), 2111-2123.
14. Jin M., Y. Xu, J. Chen, X. Wei, et al. (2024). A Comprehensive Universal Model Framework of Microalgae Growth Dynamics for Photobioreactor Scaling-up Design and Optimization, Energy Conversion and Management, 299, 117832.
15. Jung S. K., S. B. Lee (2003). Image Analysis of Light Distribution in a Photobioreactor, Biotechnology and Bioengineering, 84(3), 394-397.
16. Jung S. K., S. B. Lee (2006). *In situ* Monitoring of Cell Concentration in a Photobioreactor Using Image Analysis: Comparison of Uniform Light Distribution Model and Artificial Neural Networks, Biotechnology Progress, 22(5), 1443-1450.
17. Kaffarov V., A. Vinarov, L. Gordeev (1979). Modelling Biochemical Reactors, Forrest Industry, Moscow. (in Russian)
18. Kaffarov V., A. Vinarov, L. Gordeev (1985). Modelling and System Analysis of Biochemical Industrial Production, Forrest Industry, Moscow. (in Russian)
19. Kim T. C., M. M. Zaharieva, Y. Ilieva, A. Brachkova, et al. (2022). Innovative Approach for CO_2 Fixation in New Photobioreactor Design as a Perspective Framework for Microalgal Green Factories, Annual of Sofia University "St. Kliment Ohridski", Book 4: Scientific Sessions of the Faculty of Biology, Sofia, Bulgaria, St. Kliment Ohridski University Press, 107, 5-18.
20. Kroumov A. D., A. N. Módenes, D. E. G. Trigueros, F. R. Espinoza-Quiñones, et al. (2016). A Systems Approach for CO_2 Fixation from Flue Gas by Microalgae – Theory Review, Process Biochemistry, 51(11), 1817-1832.
21. Kroumov A. D., F. B. Scheufele, D. E. G. Trigueros, A. N. Modenes, et al. (2017). Modeling and Technoeconomic Analysis of Algae for Bioenergy and Coproducts, Algal Green Chemistry, 201-241.
22. Kroumov A. D., F. B. Scheufele, M. M. Zaharieva, D. Zheleva-Dimitrova, et al. (2022). Optimal Biomass Production by Cyanobacteria, Mathematical Evaluation, and Improvements in the Light of Biorefinery Concept, Ecophysiology and Biochemistry of Cyanobacteria, 401-429.
23. Kroumov A. D., G. V. Gacheva, I. I. Iliev, S. D. Alexandrov, et al. (2013). Analysis of Sf/V Ratio of Photobioreactors Linked with Algal Physiology, Genetics and Plant Physiology, 3(1-2), 55-64.
24. Merchuk J. C., F. Camacho, E. Molina-Grima (2007). Photobioreactor Design and Fluid Dynamics, Chemical & Biochemical Engineering Quarterly, 21(4), 345-355.
25. Nauha E. K., V. Alopaeus (2013). Modeling Method for Combining Fluid Dynamics and Algal Growth in a Bubble Column Photobioreactor, Chemical Engineering Journal, 229, 559-568.

26. Nedbal L., M. Trtílek, J. Červený, O. Komárek, et al. (2008). A Photobioreactor System for Precision Cultivation of Photoautotrophic Microorganisms and for High-content Analysis of Suspension Dynamics, Biotechnology and Bioengineering, 100(5), 902-910.
27. Neubauer P., S. Junne (2010). Scale-down Simulators for Metabolic Analysis of Large-scale Bioprocesses, Current Opinion in Biotechnology, 21(1), 114-121.
28. Pires J. C. M., M. C. M. Alvim-Ferraz, F. G. Martins (2017). Photobioreactor Design for Microalgae Production through Computational Fluid Dynamics: A Review, Renewable and Sustainable Energy Reviews, 79, 248-254.
29. Pottier L., J. Pruvost, J. Deremetz, J. F. Cornet, et al. (2005). A Fully Predictive Model for One-dimensional Light Attenuation by *Chlamydomonas reinhardtii* in a Torus Photobioreactor, Biotechnology and Bioengineering, 91(5), 569-582.
30. Pruvost J., J. Legrand, P. Legentilhomme, A. Muller-Feuga (2002). Simulation of Microalgae Growth in Limiting Light Conditions: Flow Effect, AIChE Journal, 48(5), 1109-1120.
31. Puigdomenech I. (2004). HYDRA (Hydrochemical Equilibrium-constant Database) and MEDUSA (Make Equilibrium Diagrams Using Sophisticated Algorithms) (18Feb2004 ed., pp. Inorganic Chemistry Software), Estocolmo: Royal Institute of Technology.
32. Rezvani S., N. R. Moheimani, P. A. Bahri (2016). Techno-economic Assessment of CO_2 Bio-fixation Using Microalgae in Connection with Three Different State-of-the-art Power Plants, Computers & Chemical Engineering, 84, 290-301.
33. Rusinova-Videva S., A. Adamov, A. Brachkova, M. M. Zaharieva, et al. (2022). Multifunctional Algology Lab for CO2 Fixation by *Scenedesmus obliquus* with Potential for Synthesis of High-value Products, Annual of Sofia University "St. Kliment Ohridski", Book 4: Scientific Sessions of the Faculty of Biology, Sofia, Bulgaria, St. Kliment Ohridski University Press, 107, 35-43.
34. Sastre R. R., Z. Csögör, I. Perner-Nochta, P. Fleck-Schneider, et al. (2007). Scale-down of Microalgae Cultivations in Tubular Photo-bioreactors – A Conceptual Approach, Journal of Biotechnology, 132(2), 127-133.
35. Scheufele F. B., C. L. Hinterholz, M. M. Zaharieva, H. M. Najdenski, et al. (2019). Complex Mathematical Analysis of Photobioreactor System, Engineering in Life Sciences, 19(12), 844-859.
36. Schuelter A. R., A. D. Kroumov, C. L. Hinterholz, A. Fiorini, et al. (2019). Isolation and Identification of New Microalgae Strains with Antibacterial Activity on Food-borne Pathogens. Engineering Approach to Optimize Synthesis of Desired Metabolites, Biochemical Engineering Journal, 144, 28-39.
37. Sweere A. P. J., K. C. A. Luyben, N. W. F. Kossen (1987). Regime Analysis and Scale-down: Tools to Investigate the Performance of Bioreactors, Enzyme and Microbial Technology, 9(7), 386-398.
38. Wang S. K., A. R. Stiles, C. Guo, C. Z. Liu (2014). Microalgae Cultivation in Photobioreactors: An Overview of Light Characteristics, Engineering in Life Sciences, 14(6), 550-559.
39. Wu X., J. C. Merchuk (2001). A Model Integrating Fluid Dynamics in Photosynthesis and Photoinhibition Processes, Chemical Engineering Science, 56(11), 3527-3538.
40. Zaharieva M. M., D. Zheleva-Dimitrova, S. Rusinova-Videva, Y. Ilieva, et al. (2022). Antimicrobial and Antioxidant Potential of *Scenedesmus obliquus* Microalgae in the Context of Integral Biorefinery Concept, Molecules, 27(2), 519.
41. Zaharieva M. M., H. Najdenski, A. Kroumov, H. Shachpazov, et al. (2023). Construction of a Complex Photobioreator for Microalgae Biomass Capturing CO_2 from Flue Gases, Patent Office of the Republic of Bulgaria, 4703U1, C 12 M 1/100, Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, 30.

42. Zhang Q. H., X. Wu, S. Z. Xue, Z. H. Wang, et al. (2013). Hydrodynamic Characteristics and Microalgae Cultivation in a Novel Flat-plate Photobioreactor, Biotechnology Progress, 29(1), 127-134.

Assoc. Prof. Alexander Dimitrov Kroumov, Dr. Chem. Eng., Ph.D.
E-mail: adkrumov@gmail.com

Alexander Kroumov graduated with M.Sc. Degree at the Institute of Chemical Engineering, Sofia, Bulgaria (1979). His Ph.D. in Technical Sciences (1987) he obtained from Department of Cybernetics of Chemical-Technology Processes, D. I. Mendeleev Institute of Chemical Technology, Moscow, Russia, with a Ph.D. thesis entitled "Development of Mathematical Models and Software for Scale-up of Tower Bioreactors". After being a senior scientist at the University of Lexington, USA, he worked seven years as a Professor in Chemical Engineering at UNIOESTE – Toledo and the State University of Maringá, Paraná, Brazil. He is a co-founder of the Biotechnology Center at UNIOESTE – Toledo. His student and scientific collaborator was accepted as the best Ph.D. student of all time at UNICAMP – Sao Paulo, Department of Chemical Engineering. A. Kroumov's scientific interests are in the field of green technologies, bioprocess development, bioreactors/photobioreactors design and scale up. He has multidisciplinary and international experience by executing many projects in Brazil and USA. He has published over 90 articles and patents (impact factor of his publications over 80, *h*-index 24 and 1194 citations in Scopus).

Assoc. Prof. Maya M. Zaharieva, Ph.D.
E-mail: zaharieva26@gmail.com

Assoc. Prof. Maya M. Zaharieva defended her Ph.D. thesis in oncopharmacology in 2008 at the Medical University of Sofia, Bulgaria. In 2008-2010 she worked as a Humboldt Fellow at the German Cancer Research Centre (Heidelberg, Germany). Since 2012 she has been working at the Department of Infectious Microbiology, The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, where she established the scientific laboratory "Cytotoxicity and Signal Transduction" in the frame of the Program "Equipment Subsidies" of the Alexander von Humboldt Foundation. Her scientific interests are focused on the pharmacology of compounds produced by microalgae, bacteria, fungi and plants, and antimicrobial resistance. She has published 46 articles (over 800 citations in Scopus, *h*-index 17) and participated in over 30 scientific projects.

doi: 10.7546/ijba.2024.28.4.001037

Academician Prof. Hristo Miladinov Najdenski, DVM, D.Sc.
E-mail: hnajdenski@abv.bg

Academician Prof. Hristo Miladinov Najdenski graduated from the Veterinary Faculty at Trakia University (Stara Zagora) and obtained his Doctor of Veterinary Medicine Sciences (D.Sc.) in specialty Microbiology. He has been a Director of The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences in the period 2012-2019. His scientific interests are in the field of zoonotic bacteria, virulence factors, bacterial-host relationships, infectious immunology, molecular biology, ecology of pathogenic bacteria, new antibacterial agents, and antimicrobial resistance. He has multidisciplinary and international achievements by executing many projects in Europe and Bulgaria. He has more than 170 internationally and worldwide recognized publications (143 documents in Scopus, *h*-index 27, 2516 citations).