Univerza v Mariboru

# FRAMEWORK PROGRAMME OF EARLY STAGE RESEARCHER TRAINING[1]

## 1. BASIC DATA

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| Mentor's name and surname | **Matjaž Hriberšek** | Mentor's register number at ARIS (SICRIS)**:** | **11167** |
| Mentor's e-mail: | matjaz.hribersek@um.si | Mentor's tel. no.: | +386 2 2207772 |
| Research programme (RP) leader's name and surname: | Matjaž Hriberšek | RP leader's register number at ARIS (SICRIS): | 11167 |
| Title of research programme: | Research in Power, Process, and Environmental Engineering | RP's Register number at ARIS (SICRIS): | P2-0196 |
| Research organisation (RO) of University of Maribor, where training shall be conducted: | Faculty of Mechanical Engineering | RO Register number at ARIS (SICRIS): | 0795 |
| Research field according to ARIS classification: | Procesno strojništvo 2.13.00 | Research field according to Ortelius classification (EURAXESS) | 15.22 Process engineering |

## 2. DEFINITION OF RESEARCH PROBLEM AND GOALS OF DOCTORAL RESEARCH[2]

Starting point of research task of the early stage researcher and its position in the research programme, where the mentor is included, work hypothesis, research goals and foreseen result with emphasis on an original contribution to science:

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| Starting point of the research task<br><br>In silico development of device and formulation specific lyophilization process can significantly accelarate technological transfer and improve throughput in processing of biopharmaceuticals. This is achieved by implementing high accuracy model based numerical simulations, based on vendor /open source CFD with in-house formulation/equipment specific CFD sub-models as well as |

*[1] Term early stage researcher (ESR) is written in male form and used as neutral for women and men.*

*[2] Research and study programme of training have to harmonise with contents of the research programme, where the mentor is a member.*

standalone computational models. The computational framework serves as a basis for development of digital models, which present an excellent basis for in silico determination of the formulation/device specific design space, with main focus on the primary drying stage as the most critical process stage. They can also provide a risk-free digital laboratory for process testing purposes and predictive analytics.

The research problem and goals
The research problem the candidate will address deals with development of advanced digital lyophilization models for implementation in 3D-CFD digital models of lyophilization devices with vials. Depending on the desired computational response time, different levels of digital model complexity will be developed. The development of computational vial type/stopper type specific pressure drop models of water runs will be performed in silico and validated on a lab scale, to be later used in the development of formulation specific mass transfer resistance models and CFD based digital models of the lyophilization device. The formulation specific experimental runs with recorded formulation temperature kinetics will be used in dedicated in-house computational axysymmetric 3D lyophilization model for determination of formulation specific lyophilization model parameters. The current limitation of the established models lie in the fact, that the resistance models do not distinguish between the resistance of the formulation, the resistance of the vial/stopper combination and the resistance of the lyophilizer internal geometry, which limits the transferrability of the formulation model across different vial/stopper/device cases. In the proposed research, the in-house developed 3D vial/stopper lyophilization model will be implemented and extended by incorporating the axysymmetric vial lyophilization model. This will lead to highly accurate pressure distribution computational results obtained from the coupled 3D-CFD vial lyophilization model, that will be allow to derive dedicated mass resistance models, that will take into account the formulation properties only. Finally, decoupled digital submodels will be developed, that are formulation, vial, stopper and device geometry specific and can be transferred across devices as well as scales without the need for further adjustment of digital model parameters. With the performed computational runs and experimental validation tests an extensive database will be developed, which will present a strong starting point for development of dedicated machine learning based models, presenting the second goal of the candidate's doctoral studies. They will form the backbone of AI decision models, which have the potential to significantly improve the control of the lyophilization process. Here, the focus will be on development of primary drying time determination based on AI assessment of the ramping phase of the primary drying phase, which can significantly reduce the overall drying times and as a consequence energy consumption of the process.

Foreseen results
The first original contribution to science will be the development of dedicated mass transfer resistance model, that accounts for the mass transfer resistance of the drying formulation excluding the vial/stopper properties, which is extremely difficult to achieve in physical experiment. The second original contribution will be an advanced digital twin of lyophilization capable of process control based on combination of machine learning models and mechanistic CFD based lyophilization models.

Position of the early stage researcher
The candidate will join the Research group for power, process and environmental engineering (https://cris.cobiss.net/ecris/si/sl/group/2079). The research team is primarily concerned with the problem of fluid flow, heat and mass transfer and uses this knowledge to solve engineering problems. The areas covered are process engineering, combustion, environmental protection, turbomachinery, combustion engines, thermal machines, cooling and drying technology, thermodynamics, etc. The research team consists of 18 members, three of whom are young researchers.

References:
RAMŠAK, Matjaž, HRIBERŠEK, Matjaž. Vial wall effect on freeze-drying speed. Journal of pharmaceutical sciences. May 2024, vol. 113, iss. 5, str. 1275-1284, ilustr. ISSN 1520-6017, DOI: 10.1016/j.xphs.2023.12.005. [COBISS.SI-ID 192744451]

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KAMENIK, Blaž, HRIBERŠEK, Matjaž, ZADRAVEC, Matej. Determination of pressure resistance of a partially stoppered vial by using a coupled CFD-0D model of lyophilization. European journal of pharmaceutics and biopharmaceutics. [Print ed.]. Jun. 2022, vol. 175, str. 53-64, ilustr. ISSN 0939-6411. DOI: 10.1016/j.ejpb.2022.04.010. [COBISS.SI-ID 108191491]
RAVNIK, Jure, RAMŠAK, Matjaž, ZADRAVEC, Matej, KAMENIK, Blaž, HRIBERŠEK, Matjaž. Experimental and stochastic analysis of lyophilisation. European journal of pharmaceutics and biopharmaceutics. [Print ed.]. Feb. 2021, vol. 159, str. 108-122, ilustr. ISSN 0939-6411. DOI: 10.1016/j.ejpb.2020.12.011. [COBISS.SI-ID 45939459]
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RAVNIK, Jure, JOVANOVAC, J., TRUPEJ, Aleksander, VIŠTICA, N., HRIBERŠEK, Matjaž. A sigmoid regression and artificial neural network models for day-ahead natural gas usage forecasting. Cleaner and responsible consumption. [Online ed.]. Dec. 2021, vol. 3, str. 1-13. ISSN 2666-7843. DOI: 10.1016/j.clrc.2021.100040. [COBISS.SI-ID 84192771]
HRIBERŠEK, Matjaž, RAVNIK, Jure, RAMŠAK, Matjaž, ZADRAVEC, Matej, ILJAŽ, Jurij, KAMENIK, Blaž. Lyophilization model development for the use in technology transfer : contract no. BIO3/2019, LEK d.d. : final report. Maribor: Fakulteta za strojništvo, Katedra za energetsko, procesno in okoljsko inženirstvo (KEPOI), 2020. 1 zv. (loč. pag.), ilustr. [COBISS.SI-ID 22996502]

## 3. STUDY PROGRAMME

Foreseen study programme, to which early stage researcher shall be enrolled in academic year 2025/2026:

The doctoral school study programme, 3. cycle, DOCTORAL SCHOOL OF THE FACULTY OF MECHANICAL ENGINEERING

Year 2025/2026: 1.year; Individual research work 1 and 2, Elective subjects
Year 2026/2027: 2.year; Individual research work 3 and 4, Elective subjects
Year 2027/2028: 3. year; Individual research work 5 and 6;
Doctoral dissertation writing; Defense of doctoral dissertation.

## 4. DESCRIPTION OF WORK AND TASKS

Implementing projects of scientific research.
Taking part in the design of research programmes.
Cooperating with research sponsors.
Drawing up research and other reports.

Monitoring and coordinating research work according to the grant agreement.
Ensuring safety and health at work.
Organising and instructing employees and students on using personal safety equipment and other safety measures.
Performing other tasks at the behest of the superiors.
Participating in ad-hoc and permanent committees of university or faculty bodies.
Acting on behalf of colleagues and superiors during their absence (upon authorisation).
Participating in annual and other inventories.
Performing other related tasks delegated by superiors.

## 5. REQUESTED LEVEL OF EDUCATION

VII/2. tariff group

## 6. REQUESTED FIELD OF EDUCATION

Technical, Natural sciences

## 7. KLASIUS SRV

Seventh level: Second cycle of higher and similar education/Second cycle of higher and similar education

## 8. KLASIUS P

145 – Education of teachers of individual subjects
4 - Natural science, mathematics and computing
5 - Engineering, manufacturing and construction

## 9. REQUESTED KNOWLEDGE

Computer skills: MS Windows, Word, Excel, Internet, CFD (Ansys, OpenFOAM), e-mail, e-commerce

## 10. REQUESTED SPECIAL REQUIREMENTS

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## 11. REQUESTED LANGUAGES

Active knowledge of one world language

## 12. REQUESTED WORK EXPERIENCE

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## 13. FORESEEN POSTDOCTORAL TRAINING

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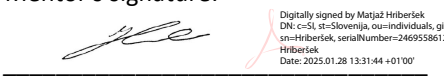
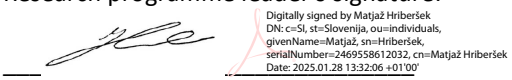
Mentor's signature:




Research programme leader's signature:




Name and surname of Dean or authorised person[3]:
red. prof. dr. Matej Vesenjak

Signature of dean or authorised person:


Place and date:

Maribor 28. 01. 2025

Stamp:

[3] The training program is signed by the dean of the member where the ESR's employment and training will take place.