MEHLISSA 2.0: Accelerating Full-body Molecular Communication Simulations

Lisa Y. Debus
Technische Universität Berlin
Berlin, Germany
debus@ccs-labs.org

Regine Wendt
Universität zu Lübeck
Lübeck, Germany
regine.wendt@uni-luebeck.de

Stefan Fischer
Universität zu Lübeck
Lübeck, Germany
stefan.fischer@uni-luebeck.de

Falko Dressler
Technische Universität Berlin
Berlin, Germany
dressler@ccs-labs.org

ABSTRACT

Personalized medicine increasingly relies on advanced simulations to support treatment planning. MEHLISSA is a simulation tool for in-body communication and disease modeling in the human circulatory system. Its previous implementation, based on the ns-3 framework, was computationally intensive and not suitable for large-scale biological simulations. In this work, we present MEHLISSA 2.0, a redesigned version with a streamlined simulation core. We demonstrate its applicability by simulating a typical large-scale molecular communication environment: CAR-T cell leukemia therapy based on established biological models. Benchmarking shows substantial performance improvements, particularly in long simulations with over 2x runtime reduction, which marks a significant step toward simulating realistic treatment scenarios.

CCS CONCEPTS

• **Networks** → **Network simulations**; • **Applied computing** → **Life and medical sciences**.

KEYWORDS

Internet of Bio-Nano-Things, Blood System, Network Simulation

ACM Reference Format:
Lisa Y. Debus, Regine Wendt, Stefan Fischer, and Falko Dressler. 2025. MEHLISSA 2.0: Accelerating Full-body Molecular Communication Simulations. In *The 12th Annual ACM International Conference on Nanoscale Computing and Communication (NANOCOM '25), October 23–25, 2025, Chengdu, China.* ACM, New York, NY, USA, 2 pages. https://doi.org/10.1145/3760544.3765642

1 INTRODUCTION

Modern medicine increasingly focuses on tailoring treatments and procedures to individual patients. To achieve this personalized medicine, clinicians collect heterogeneous data from patients to optimize treatments in an informed fashion. As an extension of collating single data points, there is significant potential in integrating personalized simulations in the design of treatment options [3].

We previously presented the medical holistic simulation architecture (MEHLISSA) [6] as a simulation tool for internet of bio-nano-things (IoBNT) applications like disease localization [4] and in-body THz communication [2]. While the simulator already provides great opportunities for the evaluation of different scenarios, its applicability to the realistic simulation of molecular communication (MC) in diseases and disease treatments is currently hampered by its runtime and memory complexity. If it is to be used for the evaluation of realistic scenarios, particularly, its runtime must be improved to be able to simulate the necessary number of particles.

In this work, we present a first step in this direction. We redesigned MEHLISSA and achieved a 2x runtime improvement. In the following, we describe the improved MEHLISSA 2.0 implementation and evaluate it in an example simulation of cancer treatment with chimeric antigen receptor (CAR)-T cells.

2 IMPLEMENTATION OF MEHLISSA 2.0

The original MEHLISSA application relies on the general-purpose event-based network simulator ns-3 to model the movement of MC particles through the human circulatory system (HCS). While ns-3 is very versatile and offers many options and extensions, these are not all necessary in MEHLISSA and unnecessarily increase its required computational resources. We therefore decided to remove MEHLISSA's dependency on ns-3 completely and instead implemented a much simpler simulation core.[1]

At the start of the simulation process, we create a `BloodCircuit` instance. It contains all `BloodVessel` and `Particle` objects. We pass the prepared `BloodCircuit` to an instance of the `Simulator` class on creation, which then starts the simulation process. The simulation loop moves forward in time according to the time step size set via the command line. In each step, the `Simulator` prompts the movement of the particles in every `BloodVessel` and their transition between connected vessels. The `Simulator` also coordinates several utility classes. Existing extensions of MEHLISSA or its predecessor BloodVoyagerS (BVS) can be adapted to work in MEHLISSA 2.0 by simply adapting the necessary calls to the new timer and position structures.

[1]The code is available open source on GitHub at https://github.com/RegineWendt/MEHLISSA/tree/main/mehlissa2.0

NANOCOM '25, October 23–25, 2025, Chengdu, China

ACM ISBN 979-8-4007-2166-3/2025/10.
https://doi.org/10.1145/3760544.3765642

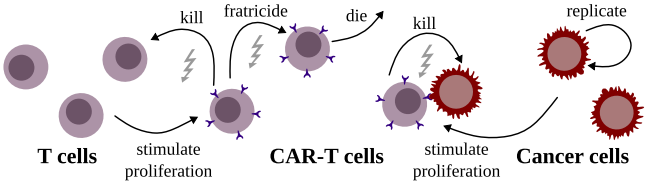

Figure 1: Particle interactions in the CAR-T cell treatment for leukemia based on Pérez-García et al. [5].

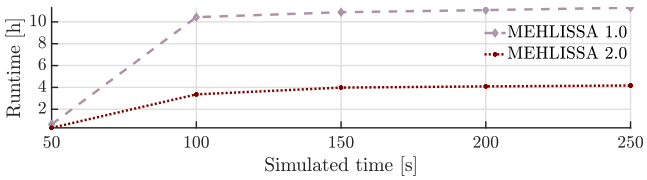

Figure 2: MEHLISSA 2.0 improves on the ns3-based MEHLISSA 1.0 with more than 2x runtime reduction.

3 EXAMPLE: CAR-T CELL TREATMENT

As an example, we implement the movement of particles in a chimeric antigen receptor (CAR)-T cell treatment for leukemia in MEHLISSA 2.0. CAR-T cells are a relatively new immunotherapy against cancer. The approach relies on modifying T cells into functionalized CAR-T cells that are specialized in attacking the tumorous T cells. At the moment, they are mainly used for the treatment of cancers based in the hematopoietic and lymphoid tissues [1]. Here, we aim to simulate the treatment of leukemia with CAR-T cells and implement the movement and interaction of CAR-T cells with leukemic cells and healthy T cells in the HCS.

We implemented classes to represent the CAR-T cells, leukemic T cells, and healthy T cells. Their interaction was implemented according to the mathematical model by Pérez-García et al. [5]. As shown in Figure 1, cancer cells replicate at a constant rate and are killed by CAR-T cells with a certain probability. At the same time, their interaction stimulates the proliferation of the CAR-T cells. With a lower probability, CAR-T cells can also be toxic towards the host immune system and kill off healthy T cells. Similarly, healthy T cells can also stimulate the proliferation of CAR-T cells. Additionally, CAR-T cells are killed by fratricide and die after a finite lifetime. The interaction probabilities and radii, as well as the replication rate, are set statically for each class.

At the start of the simulation, cancer cells and healthy T cells are positioned in a uniform distribution over the full HCS. MEHLISSA starts the simulation and allows a short period for the system to reach a steady state, before it injects CAR-T cells into the HCS via a `Bloodvessel` object. In the following simulation, all particles move through the HCS according to the blood flow in the vessels and interact with each other as described above.

4 EVALUATION

To evaluate the performance of MEHLISSA 1.0 and 2.0, we run the CAR-T cell treatment scenario in both. For a realistic treatment scenario, we would have to simulate in the range of 10^{11} cancer cells and T cells and up to 10^7 CAR-T cells. Simulating this many particles is not yet possible in MEHLISSA. In a scaled-down version of a realistic treatment scenario, we simulate $3 \cdot 10^5$ cancer cells and $3 \cdot 10^5$ healthy T cells moving through the HCS. 20 s after the start of the simulation $2 \cdot 10^2$ CAR-T cells are injected into the basilic vein. We set their interaction probability to be relatively low. In future work, we will evaluate fitting values for realistic treatment scenarios. We run a simulation of the CAR-T cell treatment for 50, 100, 150, 200, and 250 s in 1 s time steps. The scenario involves a high number of particles, which is the primary factor contributing to the runtime per simulated second in MEHLISSA.

We summarize the simulation runtimes for MEHLISSA 1.0 and 2.0 for the evaluated scenarios in Figure 2. While the simulation of 50 s already shows an improvement from 0.6 h to 0.3 h runtime, it becomes more pronounced for longer simulations. For the simulation of 250 s, MEHLISSA 2.0 only runs 4.1 h and is 2.5 times as fast as MEHLISSA 1.0 with 11.3 h. Since only the simulation loop with some supporting utility functions and no major particle movement functionalities were changed, the behavior of the two simulators remains comparable even at the different runtimes. This shows that the overhead of ns-3 was substantial in longer simulations.

5 CONCLUSION

The achieved runtime improvements formulate a step towards the goal of simulating real-world medical treatment scenarios. While the presented version of MEHLISSA does not allow a full-scale simulation of a CAR-T cell treatment in its current state, it already allows a faster evaluation of the interaction of cells in the HCS. In future work, we will parallelize MEHLISSA and improve its memory management to enable longer simulation times with more particles.

ACKNOWLEDGMENTS

This work was funded by the German Federal Ministry of Research, Technology and Space (BMFTR) in project IoBNT under grant number 16KIS1986K and by the German Research Foundation (DFG) in project NaBoCom under grant number DR 639/21-2.

REFERENCES

[1] Gunjan Dagar, Ashna Gupta, Tariq Masoodi, Sabah Nisar, Maysaloun Merhi, Sheema Hashem, Ravi Chauhan, Manisha Dagar, Sameer Mirza, Puneet Bagga, Rakesh Kumar, Ammira S. Al-Shabeeb Akil, Muzafar A. Macha, Mohammad Haris, Shahab Uddin, Mayank Singh, and Ajaz A. Bhat. 2023. Harnessing the Potential of CAR-T Cell Therapy: Progress, Challenges, and Future Directions in Hematological and Solid Tumor Treatments. *Journal of Translational Medicine* 21, 1 (7 2023). https://doi.org/10.1186/s12967-023-04292-3

[2] Laurenz Ebner, Jorge Torres Gómez, Saswati Pal, Doğanalp Ergenç, Regine Wendt, Stefan Fischer, and Falko Dressler. 2024. BVS-Net: A Networking Tool for Studying THz-based Intra-body Communication Links. In *ACM NANOCOM 2024, WiP Workshop*. ACM, Milan, Italy, 132–133. https://doi.org/10.1145/3686015.3691639

[3] Evangelia Katsoulakis, Qi Wang, Huanmei Wu, Leili Shahriyari, Richard Fletcher, Jinwei Liu, Luke Achenie, Hongfang Liu, Pamela Jackson, Ying Xiao, Tanveer Syeda-Mahmood, Richard Tuli, and Jun Deng. 2024. Digital Twins for Health: a Scoping Review. *npj Digital Medicine* 7 (March 2024). https://doi.org/10.1038/s41746-024-01073-0

[4] Saswati Pal, Jorge Torres Gómez, Regine Wendt, Stefan Fischer, and Falko Dressler. 2024. Age of Information-based Abnormality Detection with Decay in the Human Circulatory System. *IEEE Transactions on Molecular, Biological and Multi-Scale Communications* 10, 3 (Sept. 2024), 487–492. https://doi.org/10.1109/TMBMC.2024.3426951

[5] Víctor M. Pérez-García, Odelaisy León-Triana, María Rosa, and Antonio Pérez-Martínez. 2021. CAR T Cells for T-Cell Leukemias: Insights from Mathematical Models. *Communications in Nonlinear Science and Numerical Simulation* 96 (May 2021). https://doi.org/10.1016/j.cnsns.2020.105684

[6] Regine Wendt and Stefan Fischer. 2020. MEHLISSA: A Medical Holistic Simulation Architecture for Nanonetworks in Humans. In *ACM NANOCOM 2020*. ACM. https://doi.org/10.1145/3411295.3411305