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SOFIA UNIVERSITY -
MARKING MOMENTUM
FOR INNOVATION AND TECHNOLOGICAL TRANSFER

National Recovery and Resilience Plan
OF THE REPUBLIC OF BULGARIA

research group
Computer modelling

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COMPLEX SYSTEMS MODELLING

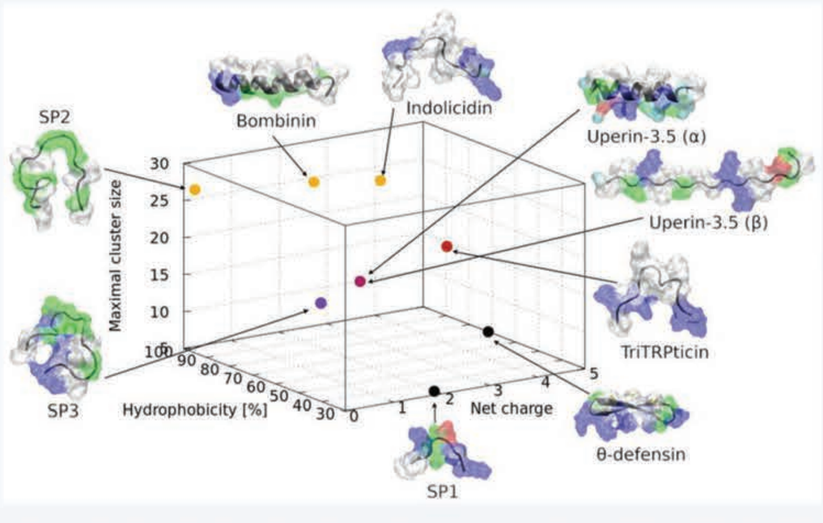
Simulations of complex systems in science are used to model and study various phenomena. Such simulations usually involve solving complex systems of differential equations using numerical methods, such as the finite difference method, finite element methods, Monte Carlo methods, etc. The goal is to understand the fundamental processes that govern the system's behavior and make predictions about its properties and future behavior. In silico studies belong to the most modern examples of scientific calculations, which, together with theoretical and experimental research, are today considered the third main pillar of modern science. On the one hand, they are based on specific theoretical models and are used to predict properties and processes based on detailed theoretical considerations. On the other hand, computer simulations can be used to test theoretical models, giving them an experimental character.

Modelling the Interactions of Antimicrobial Peptides (AMPs)

Antimicrobial peptides (AMPs) are short, naturally occurring amino acid sequences with broad-spectrum activity against bacteria, fungi, viruses, and even cancer cells. They typically exert their effects by disrupting microbial membranes, making them promising candidates for the development of novel antimicrobial therapies. Understanding their behavior in aqueous environments is therefore essential, particularly the role of aggregation in determining their stability, bioavailability, and therapeutic efficacy.

Peptide aggregation refers to the self-association of peptides into larger structures, ranging from soluble oligomers to insoluble amyloid-like assemblies. This process is influenced by multiple factors, including peptide concentration, temperature, pH, ionic strength, and the presence of other solutes.

We employed Molecular Dynamics (MD) simulations to investigate the aggregation propensity of several AMPs, including the amphibian peptides bombinin and uperin-3.5, the gastropod peptides SP1, SP2, and SP3, as well as the mammalian peptides indolicidin, θ-defensin, and tritrpticin. These peptides span a range of physicochemical properties, such as molecular weight, net charge, and hydrophobicity.



Our results show that the primary determinant of aggregation is the balance between hydrophobicity and hydrophilicity. Peptides with higher hydrophobic content tend to form larger clusters in solution, whereas increased net charge reduces clustering due to electrostatic repulsion. In contrast, molecular weight has a negligible effect on aggregation behavior, with minor exceptions observed for the smallest peptides, SP1 and θ-defensin.
Overall, these findings indicate that peptide aggregation is predominantly governed by amphipathicity, with electrostatic interactions acting as a secondary modulating factor.

Modelling the Interactions of Interferon γ C-terminus and Heparin-like Octasaccharides

We investigated the interaction between the C-terminal peptide of human interferon-γ (hIFNγ) and heparan sulphate (HS)-derived octasaccharides using an in silico approach. hIFNγ is a key immunomodulatory cytokine whose activity is regulated not only by receptor binding but also by interactions with glycosaminoglycans such as heparin and HS. These interactions, mediated by positively charged regions in the C-terminal domain, influence cytokine stability, distribution, and receptor affinity. Because experimental methods cannot precisely resolve sulfation patterns in HS oligosaccharides, the authors aim to computationally explore how different sulphate group arrangements affect binding affinity, with the broader goal of designing oligosaccharide-based inhibitors of hIFNγ.

To achieve this, we generated 35 distinct octasaccharide sequences containing one acetyl and seven sulphate groups and simulated their interactions with the hIFNγ C-terminal peptide. Molecular dynamics (MD) simulations were performed for multiple initial configurations, followed by binding free energy calculations using MM-GBSA and entropy estimation via quasi-harmonic approximation (QHA). Binding is consistently driven by favorable enthalpic contributions, while entropy typically opposes binding due to reduced conformational freedom upon complex formation.

The analysis identified several high-affinity octasaccharides and revealed some subtle preferences in sulfation patterns. In particular, a single sulfate group at position 2 is favored over two, and if position 5 is sulfated, the binding is enhanced. However, the high overall sulfation level limited the strength of these trends, and methodological limitations (especially in entropy estimation) reduced our ability to distinguish closely related sequences. Despite these challenges, the study demonstrates that computational screening can efficiently narrow down candidate oligosaccharides for experimental validation, reducing the search space significantly and providing a rational basis for designing hIFNγ inhibitors.

Publications

The results were reported in three papers:

- P. Petkov, E. Lilkova, C. Nedeva, L. Litov, and N. Ilieva, "In Silico Analysis of the Interaction of Human Interferon γ C-terminal peptide and Heparan Sulphate Derived Octasaccharides", Comptes rendus de l'Académie Bulgare des Sciences, , vol. 78, no. 3, pp. 348–355, 2025, DOI: 10.7546/CRABS.2025.03.04.
- E. Lilkova, P. Petkov, E. Krachmarova, N. Ilieva, and L. Litov, "Modelling the Interaction of the hIFNγ C-Terminal Peptide and HS-Derived Octasaccharides", Georgiev et al. (eds.), Advanced Computing in Industrial Mathematics, Studies in Computational Intelligence Vol. 522, 133–142, 2025, Springer , DOI: 10.1007/978-3-031-76782-1_11.
- P. Petkov, R. Marinova, L. Litov, P. Sirakova, E. Lilkova, K. Kamburova, E. Krachmarova, S. Taneva, F. Allemand, A. Mouhand, A. Thureau, N. Sibille, N. Ilieva, "Neutral peptides allow aggregation of cationic peptides in antimicrobial secretory fluids". Biochemical and Biophysical Research Communications, 778, 152294, 2025 DOI: 10.1016/j.bbrc.2025.152294.

Modeling gaseous particle detectors

Simulation of physical processes in gaseous detectors for ionizing radiation is a cornerstone of detector R&D and optimization, and is particularly important in the search for eco-friendly alternatives to currently used gases, especially Freon-based mixtures in detectors such as Resistive Plate Chambers (RPCs). These simulations are typically performed using the dedicated toolkit GARFIELD++.

In some detectors, the electric charge generated by electron avalanche development in the active gas volume can become sufficiently large to distort the local electric field, thereby affecting subsequent avalanche evolution. This phenomenon, known as a *space-charge effect*, is critical for accurate modeling of detectors with resistive electrodes, such as RPCs and the recently proposed Resistive Cylindrical Chambers (RCCs).

In this work, **we develop a high-performance simulation framework for gaseous detectors** with resistive electrodes by integrating advanced computational tools and exploiting high-performance computing (HPC) resources. A key component of the framework is the use of **parallel computations in GARFIELD++, enabling efficient large-scale avalanche simulations** and electron transport modeling. Through parallel execution (including multi-threading and distributed workloads), GARFIELD++ can address the computational demands of microscopic detector response simulations.

The framework couples GARFIELD++ with PETSc for solving large-scale electrostatic partial differential equations (PDEs), and with FEniCSx / DOLFINx as a flexible finite-element interface. This tightly integrated HPC-oriented workflow ensures consistency between field calculations and microscopic charge transport while maintaining scalability.

This approach enables precise avalanche simulations and detailed modeling of space-charge effects, which are essential for RPCs and RCCs. While the framework is applicable to a wide range of detector geometries, we present a case study based on an RCC geometry, chosen due to the limited existing literature and its complex electric field configuration.

Development and Optimization.

The newly developed simulation framework has been validated using a detailed Resistive Cylindrical Chamber (RCC) case study. Performance studies revealed that a parallel execution model based on full data replication across MPI processes is limited by memory (RAM) constraints, particularly for large-scale simulations within the GARFIELD++ environment.

To address this limitation, a significant optimization has been implemented. Large data structures associated with the electrostatic field maps have been migrated from local C++ containers replicated on each MPI process to a dedicated distributed-memory infrastructure based on Global Arrays (GA). This redesign enables a true partitioned-memory representation of the simulation data.

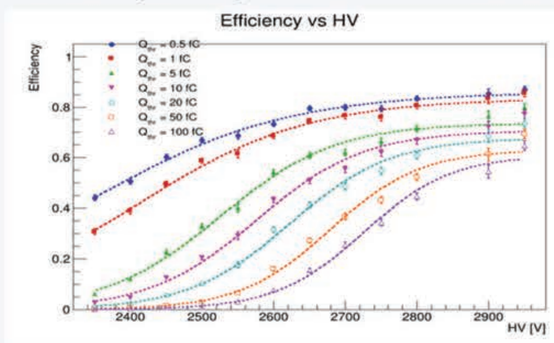
In the new implementation, the finite-element mesh geometry, electrostatic potentials, weighting fields, and auxiliary spatial search structures are stored and managed in a distributed fashion across MPI processes. This eliminates the need for full memory duplication on each process and significantly reduces the per-node memory footprint.

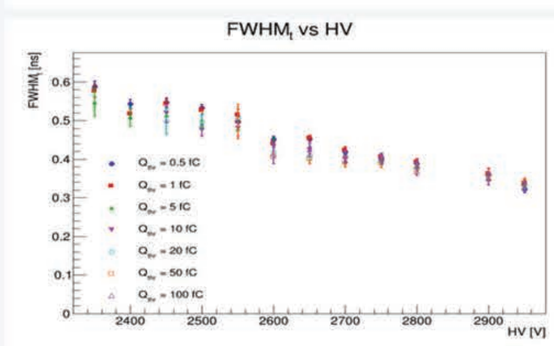
As a result, the framework exhibits improved scalability for large detector geometries and high-resolution field maps, while maintaining consistency of field access during particle tracking and avalanche simulation. The approach enables more efficient utilization of HPC resources and extends the feasible range of detector configurations that can be simulated within GARFIELD++-based workflows.

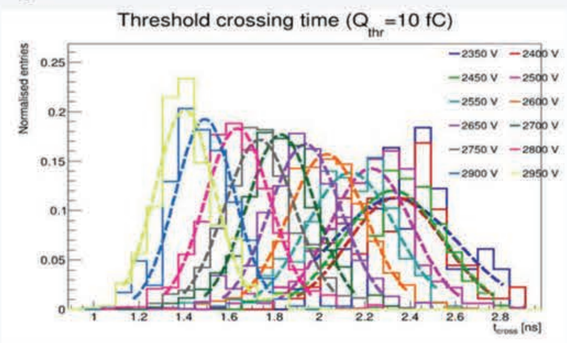
Simulation Results

An analytical model for the electrostatic and weighting fields in an RCC geometry was developed and implemented in GARFIELD++. Using this model, simulations of induced charge on the readout electrode were performed for an Ar/CO_2 gas mixture with a 0.5 mm gas gap, for 4 GeV muons, at applied voltages between 2350 V and 2950 V in 50 V steps. For each configuration, ~1000 muon events were simulated, resulting in more than 12,000 parallel simulations.

Analysis tools based on ROOT were developed to evaluate detection efficiency and time resolution for threshold charges ranging from 0.5 fC to 100 fC. The results indicate promising performance: the time resolution shows weak dependence on the discrimination threshold, reaching values of approximately 360 ps, while the minimum efficiency at the knee of the efficiency curve is about 50%. Further studies will include variations of gas mixture composition and the inclusion of space-charge effects on the electrostatic field configuration.







Publications: *P. Petkov, E. Shumka, B. Pavlov, A. Petrov, M. Pehlivanova, L. Litov, "Utilizing open-source toolkits for the simulation of avalanche formation and space-charge effects in Resistive Cylindrical Chambers",Nucl. Instrum. Methods Phys. Res. A, Vol. 1077,(2025), https://doi.org/10.1016/j.nima.2025.170550*

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