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SUMMIT
SOFIA UNIVERSITY MARKING MOMENTUM FOR INNOVATION AND TECHNOLOGICAL TRANSFER

SOFIA UNIVERSITY -
MARKING MOMENTUM
FOR INNOVATION AND TECHNOLOGICAL TRANSFER

National Recovery and Resilience Plan
OF THE REPUBLIC OF BULGARIA

Research Group
Computer modelling

Research Area
Natural Sciences (Physics)

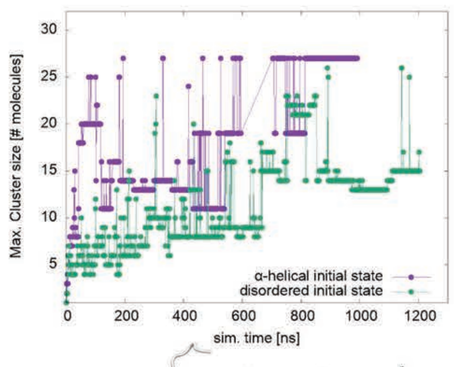
COMPLEX SYSTEMS MODELLING

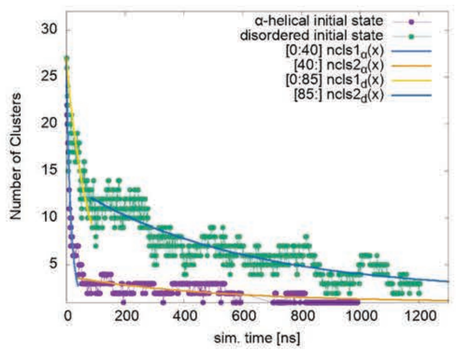
Simulations of complex systems in science are used to model and study various phenomena. Such simulations usually involve solving complex systems of differential equations using numerical methods, such as the finite difference method, finite element methods, Monte Carlo methods, etc. The goal is to understand 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.

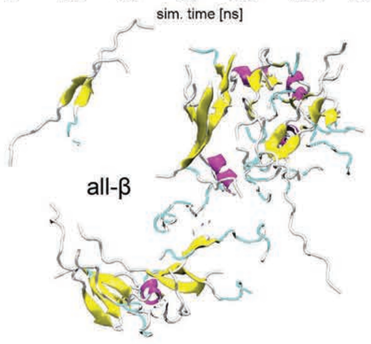
Modelling the Interactions of Antimicrobial Peptides (AMPs)

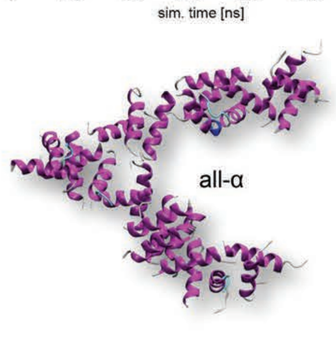
Antimicrobial peptides (AMPs) are short natural amino acid sequences with broad-spectrum activity against bacteria, fungi, viruses, and even cancer cells. They typically disrupt microbial membranes, which makes them promising candidates for novel antimicrobial therapies. Understanding their behavior in aqueous environments is crucial, including the impact of aggregation on their stability, bioavailability, and therapeutic potential. Peptide aggregation is the self-association of peptides into larger structures, ranging from soluble oligomers to insoluble amyloid formations, and depends on peptide concentration, temperature, pH, ionic strength, and the presence of other solutes.
Uperin 3.5 is isolated from the skin secretions of the Australian toadlet (Uperoleia mjobergii) and has broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative bacteria, and fungi. This AMP is known for its structural plasticity – its conformation can adapt depending on the surrounding environment. In aqueous solution Uperin 3.5 predominantly adopts a β-sheet conformation, leading to the formation of amyloid-like assemblies. When interacting with membranes, the AMP transitions to a predominantly α-helical conformation, shown to form a cross-α/cross-β chameleon functional amyloid. Due to its ability to transition between conformations, Uperin 3.5 serves as a valuable model for studying peptide-membrane interactions and AMP aggregation dynamics.
We studied the behaviour of Uperin 3.5 in water solution using Molecular Dynamics (MD) simulations and replica exchange techniques for enhanced conformational space sampling.

Two simulations of Uperin 3.5, starting from an all-α-helical and an all-β-sheet structure were performed. In both scenarios, the peptides sample the two local α/β minima and aggregate very rapidly.
Starting from an α-helical initial state, the monomers form fibrillar structures of trimeric, tetrameric and pentameric clusters, attached to each other in a semi-ordered strand, reminiscing of the cross-α/cross-β functional amyloids. When in the unfolded initial state, the peptide aggregates into smaller β-sheet formations, with the monomers forming multiple hydrogen bonds with the other chains, leading to an increase in β-structures in the system.







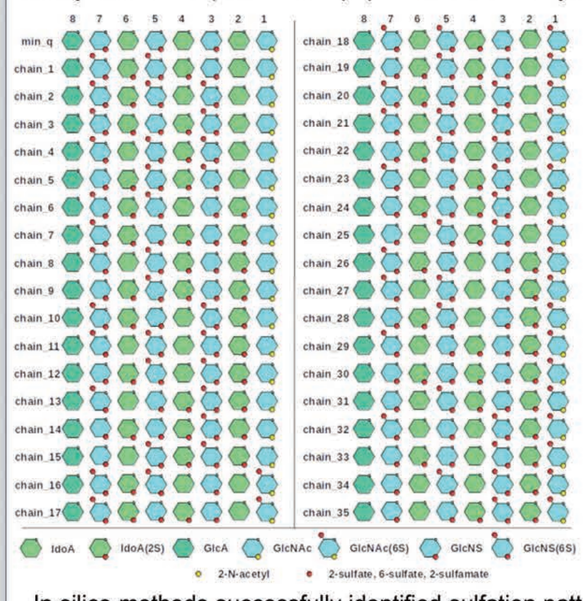


These results were reported at the IVth National Physics Congress, Sofia, Bulgaria.

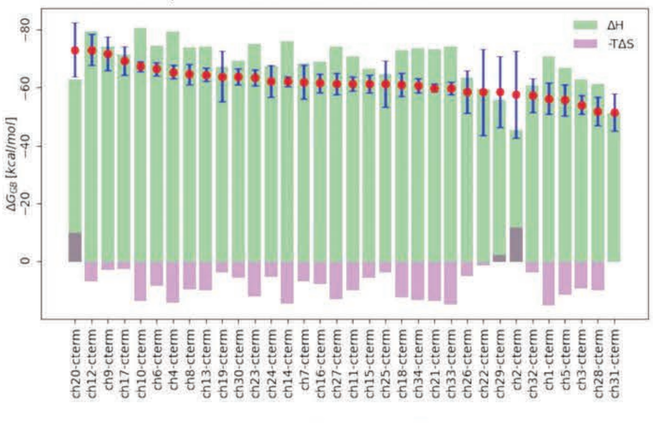
Modelling the Interactions of Interferon γ C-terminus and Heparin-like Octasaccharides

Human interferon-γ (hIFNγ) is a key immunomodulatory cytokine that binds to cell surface receptors and glycosaminoglycans such as heparan sulfate (HS) and heparin. HS is a potential target for therapeutic inhibition of the cytokine. The optimal hIFNγ ligand was experimentally found to consist of two N-sulfated octasaccharides. Currently, the sulfate group arrangements in heparin-like and HS-like chains, which influence charge distribution and potentially affect their binding affinity to the hIFNγ C-terminal peptide (hIFNγ-CT), cannot be determined precisely experimentally. Understanding the binding of heparin-like octasaccharides to the hIFNγ C-terminal domain can aid in the development of hIFNγ inhibitors.

We used MD simulations, molecular mechanics with generalized Born and surface area (MM-GBSA) and quasi-harmonic approximation (QHA) to estimate the free energy of binding to investigate how different sulfate group arrangements in of heparin– and HS-like octasaccharides with one acetyl and seven sulfate groups affect their binding affinity to the hIFNγ C-terminal peptide and to identify the most favorable sulfation patterns for strong binding.



35 different octasaccharide sequences were studies. Chains 10, 12, 9, 17, and 20 exhibited the highest affinity. Chains 31, 28, 3, 5, and 1 were the worst binders. A preference for single sulfation over double sulfation at position 2 and sulfation over non-sulfation at position 5 was observed.



In silico methods successfully identified sulfation patterns that enhance the binding affinity of HS-like octasaccharides to hIFNγ. These findings can inform experimental synthesis efforts aimed at designing hIFNγ inhibitors for inflammatory and autoimmune conditions. Further studies will integrate additional computational techniques to refine binding affinity predictions.

The results were reported in two papers, which have been accepted for publication:
- **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*, 2025 (in press).
- **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, 2025, Springer , DOI: 10.1007/978-3-031-76782-1_11.

Modelling Gaseous Particle Detectors

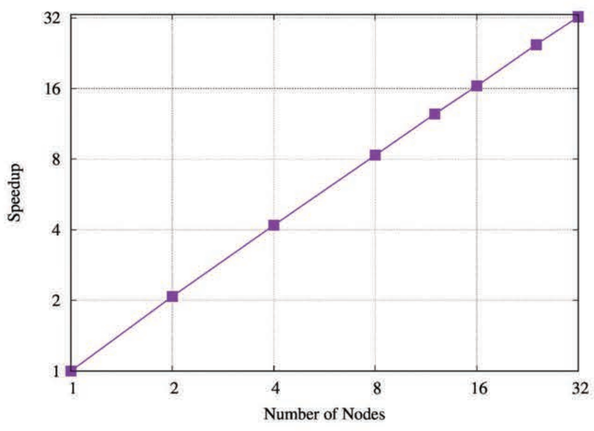
In modern high-energy physics, various software tools are used for detector simulation, such as Garfield++ for electron transport and avalanche simulations, ANSYS/ELMER for electrostatic field modeling, and Geant4 for particle interactions.
Our study aims to develop a high-performance simulation framework for gaseous detectors with resistive electrodes by integrating advanced computational tools and leveraging high-performance computing (HPC) resources. The framework combines Garfield++ for modeling gaseous detector behavior, PETSc for solving large-scale partial differential equations (PDEs) in electrostatics, and FEniCSx/DOLFINx for a flexible and efficient finite element method (FEM) interface.
This approach enables precise avalanche simulations and detailed modeling of space charge effects, which play a crucial role in Resistive Plate Chambers (RPCs) and the recently proposed Resistive Cylindrical Chambers (RCCs). The framework supports various detector types; as a case study, we implemented an RCC simulation, chosen due to the limited number of studies and its complex electric field geometry.

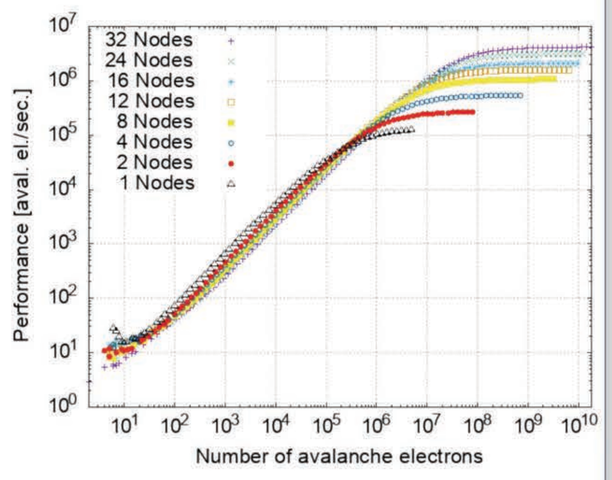
DIstributed memory parallelisation of electron avalanche simulation with Garfield++

The computational challenges come from the significant memory requirements for simulation of large electron avalanches. To overcome this problem, we utilize the MPI to develop parallel algorithms for electron avalanche simulations. The simulation process is divided into discrete steps, each defined by a specific time window. At the beginning of each time window, the electron population is uniformly distributed across the available MPI ranks to ensure balanced workload distribution.

Results

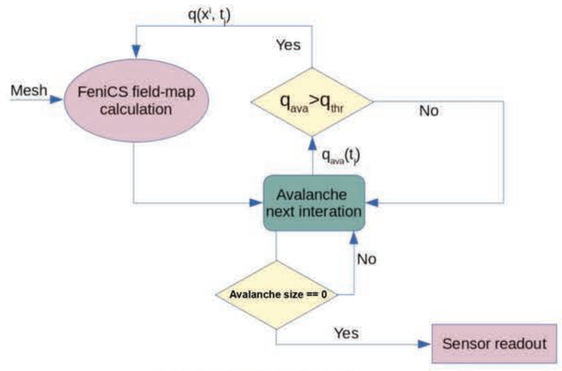
To evaluate the performance of the implemented parallel version, we used a single gap RPC model consisting of two resistive parallel plates with a thickness of 2 mm and a 2 mm wide gap filled with a gas mixture of C2H2F4 - 90%, iso − C4H10 - 5%, and SF6 - 5% at temperature 23°C and pressure 1 atm. The electric field was set at an intensity of 55 kV/mm in the gas gap. The simulations were run on up to 32 nodes of the cluster module of the DEEP-EST supercomputer at the Juelich Supercomputing Center, Juelich, Germany. Numerical experiments with 1, 2, 4, 8, 12, 16, 24, and 32 nodes were conducted with 24 MPI tasks per node. The results of the performance evolution in wall clock time can be seen in figures below.

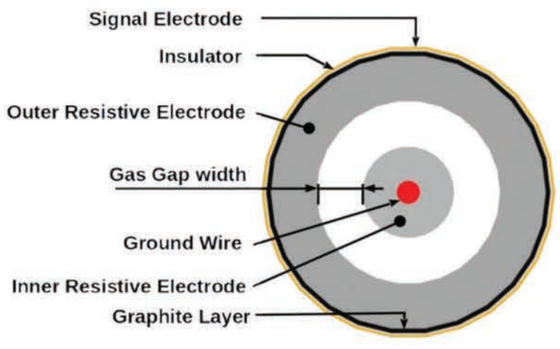




Parallel framework for accounting for space charge effects in simulations of gaseous detectors

We propose using Python wrappers of Garfield++ and FEniCSx for modeling avalanche multiplication is gaseous detectors and solving electrostatic field therein, respectively. The parallel versions of the Garfield++ classes (developed in the project) and the FEniCSx FEM calculations run in one and the same MPI environment. Under user defined conditions, the charge density is constructed within the active volume of the detector, the electrostatic field is calculated by means of the FEM method and then taken into account in the gas multiplication simulation.



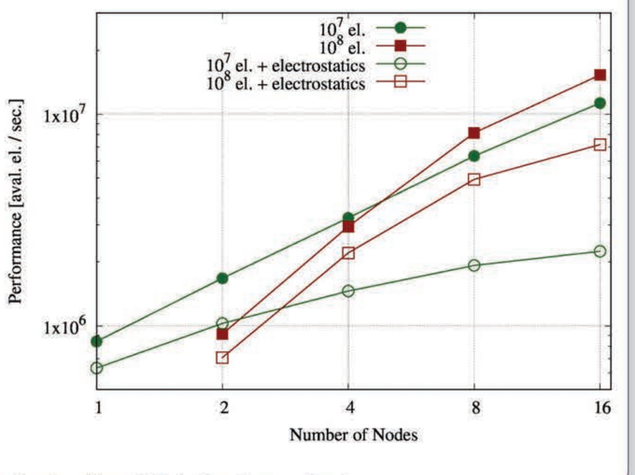


Digital model of a simple Resistive Cylindrical Chamber

Based on the research on RCC design presented in [Cardarelli et al., 2021] [Cardarelli et al., 2024], and in alignment with the simulation framework development discussed here, we consider a simplified RCC model consisting of coaxial cylindrical layers, as illustrated in figure on the left. A copper grounding wire runs along the central axis of the cylindrical layers, surrounded by the inner resistive electrode. The gas gap is enclosed by the outer resistive electrode, which features a graphite coating on its external surface. The outermost layer consists of a metallic signal electrode, typically made of copper, which is electrically insulated from the graphite layer using a high-voltage insulating material.

Results

For testing the RCC model simulations were run on the Discoverer supercomputer located at TechPark Sofia in Bulgaria. The simulated geometry consists of a central wire electrode (1 mm radius), a gas gap (2–4 mm radius), and an outer electrode (7 mm radius) with resistive electrodes (εr = 8). The gas mixture was Ar (80%) and CO_2 (20%), at 23°C, 1 atm, with a 4100 V potential difference.
Avalanche development was simulated in 0.1 ns steps, with the electrostatic field recalculated using FEM once the avalanche exceeded 10^7 electrons. Performance was tested on 1, 2, 4, 8, and 16 nodes with 128 MPI ranks per node, assigning one FEM process per node. The figure compares performance with and without electrostatic field calculations.



The results were reported at "RPC'2024 conference", September 2024, Santiago, Spain

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