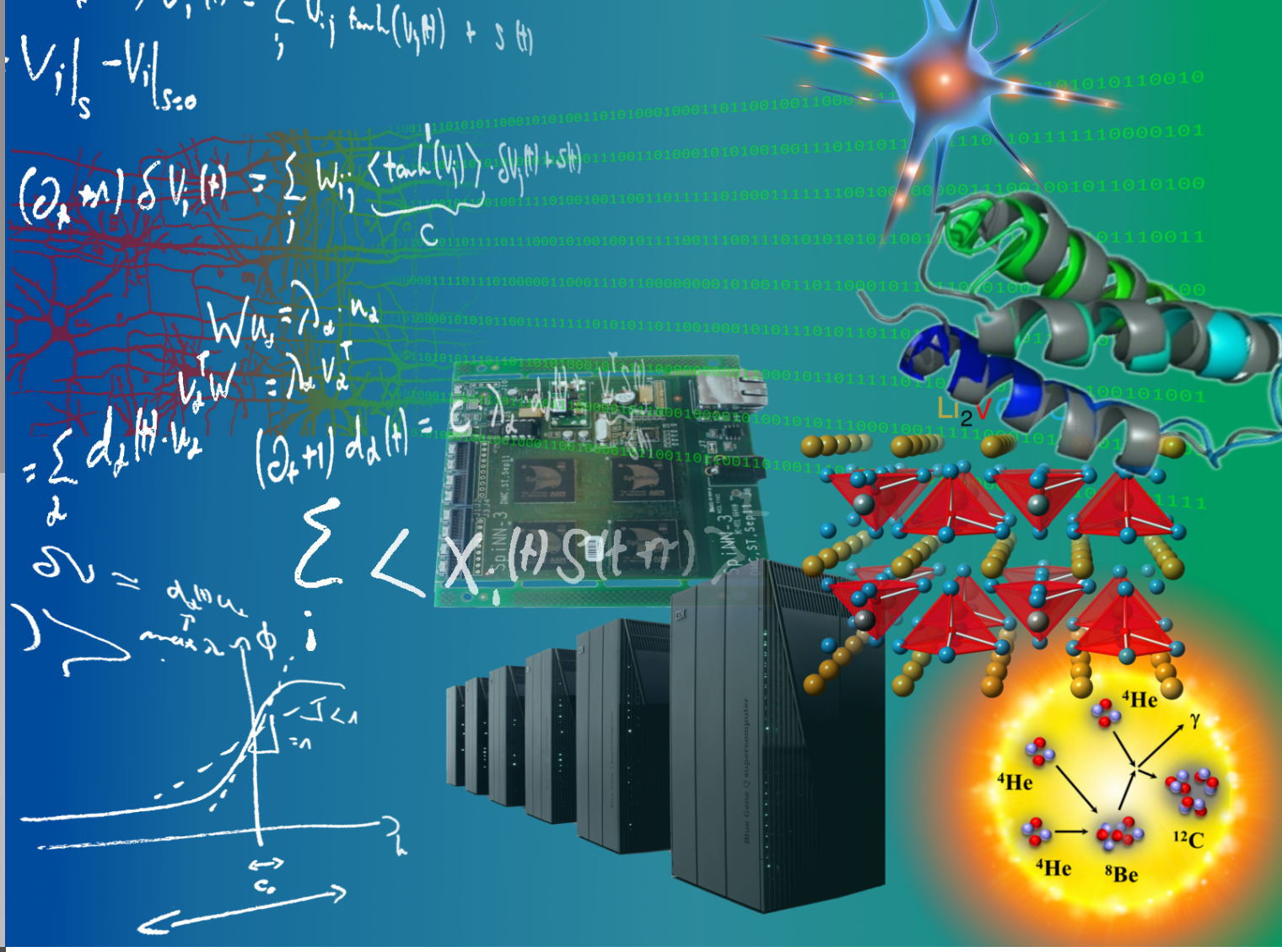

IAS Symposium 2016
Program and Abstracts

First Symposium of the
Institute of Advanced Simulation

December 5-6, 2016

Member of the Helmholtz Association

JÜLICH
FORSCHUNGSZENTRUM

Coordinator:

Thomas Luu

Organizing team:

Andreas Nogga
Dennis Terhorst
Daniel Wortmann
Eva Pavarini
Giulia Rossetti
Gerrit Vliegenthart
Julia Kämpfer
Michael Denker
Robert Speck
Sonja Grün

Cover illustration:

Dennis Terhorst

IAS Symposium 2016

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Contents

Introduction

Welcome to the first Institute for Advanced Simulation (IAS) Symposium!

The seven institutes that comprise the IAS perform research that span a diverse landscape, which, in broad brush, are the quantum behavior of materials (IAS-1), biophysics (IAS-2), nanoelectronics (IAS-3), the interactions governing quarks and gluons (IAS-4), biomedicine (IAS-5), neuroscience (IAS-6), and high-performance computing (JSC). Central to all these research areas is the use of high-performance computing (HPC) for simulation and modeling. In this regard, it is not surprising to see that the Jülich Supercomputing Centre (JSC) plays a central role within this IAS, and this is reflected in the strong representation of JSC at this symposium.

Though the systems of interests are quite different from one institute research area to another, the algorithms and methods used within any research area are not exclusive to others. The experiences gained in one research area can provide valuable insight into another area of research, and can help foster development of new methodologies and give thrust to research not just within research areas, but across research areas.

Clearly a prerequisite for developing opportunites for cross-cutting research is that scientists from each area interact and communicate with each other. The main goal of the IAS Symposium is to therefore provide a venue for this to happen. Scientists within IAS have the opportunity to present their research, either in talk or poster format, within the subject areas *Supercomputing approaches*, *Numerical methods*, *Analytical Approaches*, and *Natural Science insights*. To enhance the exchange of ideas and methodologies, we have mixed talks of different subject areas within each of the sessions.

We thank you all for your contributions to this first IAS Symposium.

Your Organizing Committee

Schedule

Monday, December 5, 2016			
10:00 -10:30		*Registration, Coffee (Foyer of the Central Library)*	
10:30 -11:45		**Opening Session: The IAS** *Chairperson: Thomas Luu*	
10:30		Thomas Luu (IAS-4)	**Welcome to the IAS-Symposium**
	IAS Colloquium – Part I		
10:45	JSC	Thomas Lippert (JSC)	Jülich Supercomputing Center
11:05	IAS-6	Markus Diesmann (INM-6)	Institute of Neuroscience and Medicine, Computational and Systems Neuroscience
11:25	IAS-5	Paolo Carloni (INM-9)	Institute for Advanced Simulations (IAS), Computational Biomedicine
11:45 -13:10		*Lunch and Poster Session (Foyer of the Central Library)*	
13:10 -15:00		**Opening Session: The IAS and Poster Spotlight Presentations** *Chairperson: Gerrit Vliegenthart*	
	IAS Colloquium – Part II		
13:10	IAS-4	Ulf-G. Meißner (IKP-3)	Institut für Kernphysik, Theorie der starken Wechselwirkung
13:30	IAS-3	David DiVincenzo (PGI-2)	Peter Grünberg Institut, Theoretische Nanoelektronik
13:50	IAS-2	Gerhard Gompper (ICS-2)	Institute of Complex Systems, Theorie der Weichen Materie und Biophysik
14:10	IAS-1	Stefan Blügel (PGI-1)	Peter Grünberg Institut, Quanten-Theorie der Materialien
14:30	**Spotlight Talks**		
14:33	P-20	Hoai Le (IAS-4)	Jacobi No-core Shell Model for Hypernuclei
14:36	P-22	Inga Blundell (IAS-6)	NESTML: A modeling language for spiking neurons
14:39	P-6	Christian Bodenstein (JSC)	Automated Soccer Scene Tracking Using Deep Neural Networks
14:42	P-13	Daniela Meister (JSC)	With Computer-Aided Drug Design Towards Selective Inhibitors for ARTD10
14:45	P-14	Viacheslav Bolnykh (IAS-5)	A Massively Parallel Hybrid Car-Parrinello QM/MM Interface
14:48	P-3	Arvind Ravichandran (IAS-2)	Computer Simulations of Cytoskeletal Filaments and Motors
14:51	P-40	Masoud Hoore (IAS-2)	von Willebrand factors and Platelets in Blood Stream: Margination and Adhesion
14:54	P-24	Jens Bröder (IAS-1)	The AiiDA plug-in for the FLEUR code and its first application on fusion relevant materials
14:57	P-15	Esmaeel Sarvestani (IAS-3)	Optical conductivity of ruthenate oxides: spin-orbit and anistropic Coulomb interaction effects
15:00 -15:30		*Coffee Break (Foyer of the Central Library)*	
15:30 -17:00		**Oral Session 1** *Chairperson: Robert Speck*	
15:30	T1	Lukas Arnold (JSC)	Fire Simulations – Fires in Underground Stations
15:45	T2	Amin Kiani (IAS-3)	Response Functions for Strongly Correlated Materials
16:00	T3	Manuel dos Santos Dias (IAS-1)	Chirality-driven orbital magnetic moments as a new probe for topological magnetic structures
16:15	T4	Christopher Körber (IAS-4)	Nuclear Lattice Investigations of Fundamental Symmetries
16:30	T5	Saltanat Sadykova (JSC)	A New Scheme for High-Intensity Laser-Driven Electron Acceleration in a Plasma
16:45	T6	Sandra Diaz-Pier (JSC)	Multiscale approach to explore the relationships between connectivity and function in whole brain simulations
17:00 -17:15		*Short Break*	

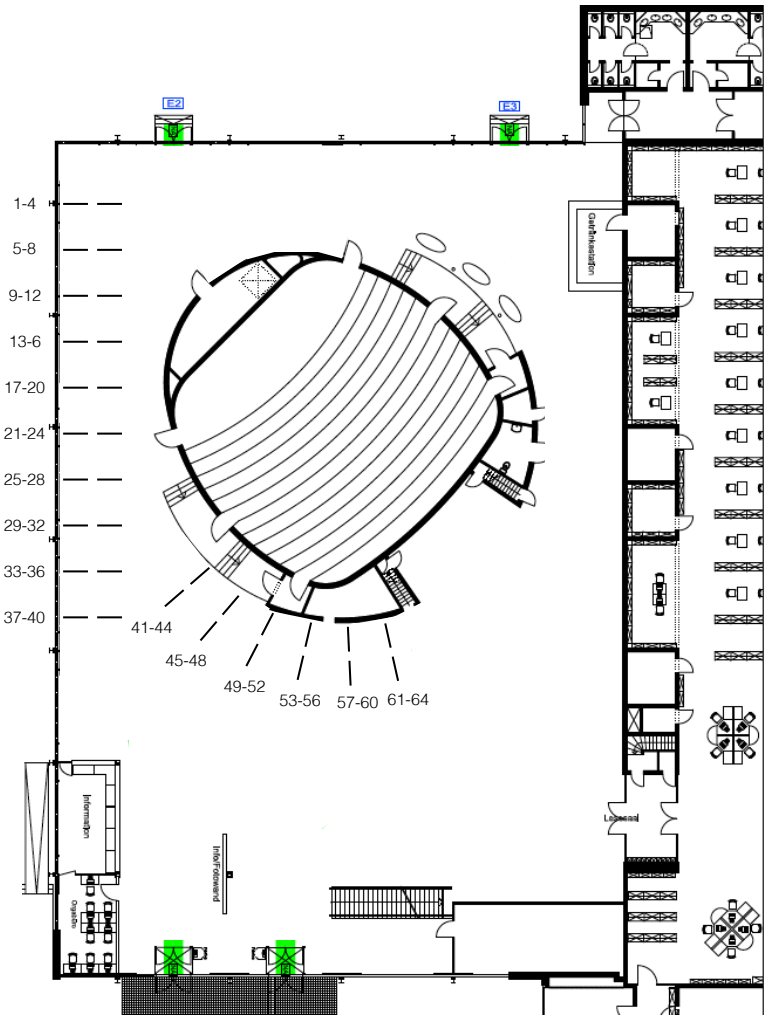
17:15		**Panel Discussion**	
-18:45		*Chairpersons: Giulia Rossetti & Dennis Terhorst*	
		IAS Directors	In this interactive session the directors of the IAS will discuss the past, now and future of the IAS. The panelists welcome questions from the audience.
18:45		**Young Scientists Poster Session**	
-21:00		**and "Häppchen und Drinks"**	
		(Foyer of the Central Library)	
18:45		Everyone!	The posters will be shown in the Foyer of the Central Library.
∼19:00			Food will be available and discussions can continue. . .
20:20		Shuttle Bus	Transportation from the library to the FZJ train station.

Tuesday, December 6, 2016			
9:00		**Oral Session 2**	
-10:30		*Chairperson: Abigale Morrison*	
9:00	T7	Myriam Czekala (JSC)	UniProv: A flexible Provenance Management System for UNICORE
9:15	T8	Andreas Kleefeld (JSC)	Adaptive Filters for Color Images: Median Filtering and its Extensions
9:30	T-25	Marisol Ripoll (IAS-2)	Self-assembly of thermophoretic swimmers
9:45	T10	Arne Graf (JSC)	Eikonal Equation in Pedestrian Dynamics
10:00	T11	Timo A. Lähde (IAS-4)	The Hoyle State in Nuclear Lattice EFT
10:15	T12	Nicolae Atodiresei (IAS-1)	Magnetic Properties of Hybrid Organic-Metal Interfaces
10:30		*Coffee Break*	
-11:00		*(Foyer of the Central Library)*	
11:00		**Oral Session 3**	
-12:30		*Chairperson: Daniel Wortmann*	
11:00	T13	Constantinos Constantinou (IAS-4)	The Complete APR Equation of State
11:15	T14	Daniel Rohe (JSC)	Hierarchical parallelisation of functional renormalisation group calculations
11:30	T15	Theo Costi (IAS-3)	Transient dynamics of the Ohmic two-state system via the time dependent numerical renormalization group method
11:45	T16	Ruth Schöbel (JSC)	Parallel-in-Time Integration with PFASST
12:00	T17	Renato Duarte (IAS-6)	Leveraging heterogeneity for neural computation with fading memory
12:15	T18	Maximilian Schmidt (IAS-6)	From single-cell spiking to large-scale interactions: A multi-scale spiking network model of macaque cortex
12:30		*Lunch and Poster Session*	
-13:30		*(Foyer of the Central Library)*	
13:30		**Oral Session 4**	
-15:00		*Chairperson: Eva Pavarini*	
13:30	T19	Rodrigo Casasnovas Perera (IAS-5)	Molecular Dynamics Simulations to design new Neuroreceptor Ligands with Optimized (un)binding Kinetics
13:45	T20	Ruyin Cao (IAS-5)	Role of the extracellular loop ECL2 and membrane lipids for ligand recognition in GPCRs.
14:00	T21	Rudolf Zeller (IAS-3)	KKRnano: Towards scientific applications on exascale computers
14:15	T22	Kristel Michielsen (JSC)	Solving Hard 2-SAT Problems on a D-Wave Two System
14:30	T23	Julian Mußhoff (IAS-3)	Continuous time quantum Monte Carlo as a quantum impurity solver
14:45	T24	Luca Pesce (IAS-5)	Predicting the apo-structures of two human NEET proteins involved in health and disease conditions
15:00			Concluding Remarks
15:15	**End of Main Meeting**		

General Information

Venue of main meeting. Lecture hall and foyer of the central library.

Posters. The suggested poster size is A0 portrait, which will comfortably fit the supplied poster boards. The locations of assigned poster boards (according to the abstract number) are shown in the accompanying figure. The poster sessions will occur during the lunch breaks on both days of the Symposium, and on the evening of Monday, December 5th, immediately after the Panel Session (described below). However, please try to mount your poster by 12:00 h on the first day of the Symposium.



Instructions for speakers. Talks are 10 minutes + 5 minutes discussion (with few exceptions). A number of poster contributions are selected to be additionally presented as a spotlight presentation to advertise the poster. A spotlight presentation is limited to 3 minutes and 1 slide. Talks and spotlight presentations are uploaded to a central computer for presentation to ensure a smooth transition of talks. Please send your talk to

ias-symposium@fz-juelich.de

before the meeting!

Projector and Laptop with some default software is provided. If you intend to use other materials, please make sure to bring them in and inform the organizers.

Finally, please remember that the audience will be composed of people from diverse scientific backgrounds. Plan your presentation accordingly!

Panel Session. We are happy to announce the participation of all IAS directors for the Panel Session titled "Past, Present, and Futrure of the IAS". The session will occur on the evening of December 5th, starting at 17:15 h. The panel participants will answer questions from the moderators related to the title of the session, and questions will also be open to the public at large.

Evening reception. After the panel session there will be a evening reception where refreshments will be offered. Here participants can continue their discussions related to the talks heard earlier in the day and to the panel session. The poster session occurs jointly during the evening reception.

Transportation. Because the evening reception and poster session ends quite late on the first day of the symposium, for your convenience we have arranged for bus transportation from the library to the FZJ train station. The bus will leave from the library at exactly 20:20 h.

The IAS Institutes

The Institute for Advanced Simulation unites simulation sciences and supercomputing under one roof. Thus, disciplinary, methodic and technological competences can be combined to manage the future challenges in the simulation sciences.

The close cooperation of the scientific users with the staff of the Jülich Supercomputing Centre leads to a prolific usage of the highly attractive European supercomputing centre in Jülich - especially in method development and scientific visualisation.

The institute consists of the Jülich Supercomputing Centre and six sections. It is planned to integrate further groups.

Managing Director: Thomas Lippert (JSC)

Institutes of Advanced Simulation

JSC	**Jülich Supercomputing Centre**
	Supercomputers for scientific simulations – The Jülich Supercomputing Centre operates supercomputers of the highest performance class. We enable scientists and engineers to solve their highly complex problems by simulations.
IAS-1 / PGI-1	**Quantum Theory of Materials**
	We calculate and analyze the complex structural, electronic and magnetic quantities of solids and molecules – for fundamental research and practical applications.
IAS-2 / ICS-2	**Theoretical Soft Matter and Biophysics**
	We explore the structure and dynamics of complex fluids, soft matter, and biological systems, from colloids and (bio)polymers to the motion of cells.
IAS-3 / PGI-2	**Theoretical Nanoelectronics**
	The quantum mechanical nature of matter is the basis of all functioning of electronic devices, and can be the basis of a new form of information processing.
IAS-4 / IKP-3	**Theory of the strong interactions**
	We investigate strongly interacting phenomena related to hadronic and nuclear processes, starting from the fundamental interactions between quarks and gluons given by Quantum Chromodynamics, to the reactions and binding energies of nuclei using nuclear effective field theory. We employ lattice Monte Carlo methods on high performance computing resources to perform our research.
IAS-5 / INM-9	**Computational Biomedicine**
	Molecular Simulation and Structural Bioinformatics towards Molecular Neuromedicine
IAS-6 / INM-6	**Theoretical Neuroscience (IAS-6) & Computational and Systems Neuroscience (INM-6)**
	Progress in the understanding of complex systems like the brain can only be achieved by integrating models on many different scales. The research performed at the institute for Computational and Systems Neuroscience develops such multi-scale models of the brain, combining data-driven development of brain theory with the bottom-up approach of directly simulated structured networks, and the top down approach, mapping functional models of higher brain function to spiking dynamics.

Talks

Fire Simulations – Fires in Underground Stations

Lukas Arnold[1]

[1] **Jülich Supercomputing Centre (JSC)**

Contact: `l.arnold@fz-juelich.de`

Keywords: *fire safety science; computational fluid dynamic; smoke and fire dynamics; underground stations.*

Complex buildings pose a challenge for fire safety engineers as these are hardly covered by prescriptive regulations. Numerical models, like zone and field models, provide tools for performance based approaches, which can be applied to any building structures. These models describe the mass and heat transport from fires. Field models are based on computational fluid dynamics (CFD) and allow for the most detailed description of phenomena like turbulent flows, combustion, radiative and conducting heat transfer and pyrolysis – at the cost of complexity and high computational demands.

The mainly applied CFD software in fire safety engineering is FDS (Fire Dynamics Simulator). It is a LES (Large Eddy Simulation) code with a multitude of sub-models with a hybrid OpenMP and MPI parallelization. It uses second order finite differences for the spatial discretization and an explicit time stepping method. Depending on the problem size, it scales up to a few hundred cores of JURECA. The application of FDS in this project ranges from the modelling of bench scale (few centimeter) pyrolysis experiments up to real scale (hundred meter) field experiments.

This talk presents one of the multiple topics the team “Fire Simulations” of the division “Civil Safety and Traffic” is working on: the simulation of smoke spread in complex underground stations. This work is part of the ORPHEUS project, in which both numerical simulations as well as real scale experimental fires in Berlin’s underground stations are considered. The safety of the passengers in a fire accident is one of the main safety targets. The simulation of the smoke spread results in an estimation of the available safe egress time for the passengers. This time strongly depends on the scenario choice, i.e. positon of the fire, underground climate conditions or the heat release rate. Therefore, a design of experiment is created to cover the reasonable scenarios. The computed data, e.g. smoke density, may then be coupled to an evacuation model to compute the requested safe egress time. Both times, the available and requested, safe egress times are used to assess the safety level.

The talk concludes with an overview of the other topics covered by the group. These are activities on model- and software development of adaptive mesh refinement techniques and GPU based predictive real-time simulations of smoke dynamics. They are amended by small scale validation experiments, that focus on high precision flow measurement techniques, like particle image velocimetry (PIV) and laser Doppler velocimetry (LDV).

Acknowledgements. *This work is part of the BMBF funded project ORPHEUS, Teilvorhaben "Brand- und Personenstromsimulationen in unterirdischen Verkehrsanlagen" (13N13266). The author gratefully acknowledges the computing time granted (project jjsc11) on the supercomputer JURECA at Jülich Supercomputing Centre (JSC).*

Response Functions for Strongly Correlated Materials

Amin Kiani[1], **Eva Pavarini**[1,2]

[1] **Institute for Advanced Simulation (IAS-3)**

[2] **JARA High-Performance Computing, RWTH Aachen University, 52062 Aachen, Germany**

Contact: `a.kiani@fz-juelich.de`

Keywords: *Strongly correlated systems; Dynamical mean field theory; Response functions; Magnetic susceptibility; High temperature superconducting cuprates.*

Strongly correlated materials are a vast class of systems ranging from unconventional metals and superconductor to Mott insulators and frustrated systems. Their characteristic behavior is due to the strong electron-electron coulomb repulsion within partially filled d- or f-, and sometimes p-shells. Due to the complexity of the associated many-body problem, the theoretical description of these materials remains to date a major challenge. The state-of-the-art method, density functional theory (DFT) + dynamical mean field theory (DMFT), combines ab-initio approaches based on density-functional theory and many-body techniques. In order to exploit the power of the DFT+DMFT method, one needs to connect theory and experiment. This is possible via the calculation of linear response functions which relate the *small* external field $\mathcal{F}$, applied on the sample in an experiment, and the measured observable X. Within the DFT+DMFT method, we calculate the general form of the response functions which enables us to describe almost all experiments.

As representative results, we focus on high temperature superconducting cuprates, one of the family of systems among strongly correlated materials. We study the magnetic properties of a representative material, $La_{2-x}Sr_xCuO_4$, above the superconducting in the normal phase. We calculate the magnetic response function for a wide range of temperatures and hole doping. We show that our theoretical results are in very good agreement with neutron scattering and nuclear magnetic resonance experiments.

Acknowledgements. *We acknowledge financial support from the Deutsche Forschungsgemeinschaft through research unit FOR 1346.*

Chirality-driven orbital magnetic moments as a new probe for topological magnetic structures

Manuel dos Santos Dias[1,2], **Juba Bouaziz**[1,2], **Mohammed Bouhassoune**[1,2], **Stefan Blügel**[1,2], **Samir Lounis**[1,2]

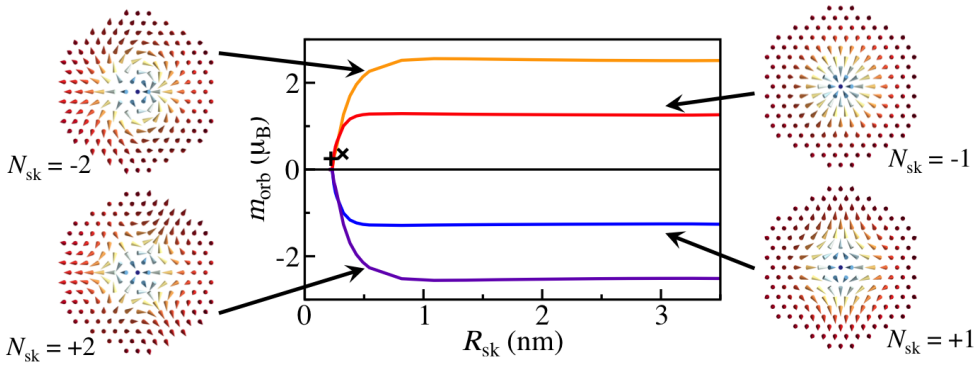
[1] **Institute for Advanced Simulation (IAS-1)**

[2] **Peter Grünberg Institut, Forschungszentrum Jülich, Germany**

Contact: `m.dos.santos.dias@fz-juelich.de`

Keywords: *skyrmions; orbital magnetism; topological properties; density functional theory; x-ray magnetic circular dichroism.*

When electrons are driven through unconventional magnetic structures, such as skyrmions, they experience emergent electromagnetic fields that originate several Hall effects. Independently, ground state emergent magnetic fields can also lead to orbital magnetism, even without the spin-orbit interaction. The close parallel between the geometric theories of the Hall effects and of the orbital magnetization raises the question: does a skyrmion display topological orbital magnetism? Here we first address the smallest systems with non-vanishing emergent magnetic field, trimers, characterizing the orbital magnetic properties from first-principles. Armed with this understanding, we study the orbital magnetism of skyrmions, and demonstrate that the contribution driven by the emergent magnetic field is topological. This means that the topological contribution to the orbital moment does not change under continuous deformations of the magnetic structure. Furthermore, we use it to propose a new experimental protocol for the identification of topological magnetic structures, by soft x-ray spectroscopy.



Topological orbital magnetic moments in skyrmionic structures of 961 atoms

Acknowledgements. *MdSD would like to thank B. Dupé, S. Heinze and Y. Mokrousov for insightful discussions. This work is supported by the HGF-YIG Programme VH-NG-717 (Functional Nanoscale Structure and Probe Simulation Laboratory - Funsilab) and the ERC Consolidator grant DYNASORE. SB acknowledges funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 665095 (FET-Open project MAGicSky).*

References

[1] accepted in Nature Communications; see arXiv:1609.07529

Nuclear Lattice Investigations of Fundamental Symmetries

Christopher Körber[1,2], **Jordy de Vries**[3]

[1] **Institute for Advanced Simulation (IAS-4)**

[2] **IKP 3**

[3] **Nikhef, Theory Group, Amsterdam, The Netherlands**

Contact: `c.koerber@fz-juelich.de`

Keywords: *Dark Matter; Nuclear Lattice Effective Field Theory; Nuclear Physics; Hybrid Monte-Carlo Algorithms.*

Introduction. As there are several indications for the existence of so-called 'Dark Matter' (DM) from an astrophysical point of view, direct detection of a candidate particle in a lab has not been successful this far. A set of direct detection experiments, which use different targets, could potentially test the various types of DM interactions with different properties of nuclei. To connect possible future measurements of DM signals to a candidate DM particle, these DM experimental signals must be propagated through nuclear cores — composed of many protons and neutrons — to the fundamental level of the DM theory. Due to the complexity in describing the many-body nucleus, this propagation has historically been done in a model-dependent fashion. As a candidate for propagating possible experimental data to the level of protons and neutrons, Nuclear Lattice Effective Field Theory (NLEFT) provides an approach which systematically enables the reduction of uncertainties.

Methods. Statistical algorithms, more specifically Hybrid Monte-Carlo integration algorithms are employed to compute a path integral composed of an action with nuclear degrees of freedom. The sampled observables can be associated with possible interactions of dark matter with nuclear matter.

References

[1] The Effective Field Theory of Dark Matter Direct Detection - A. Fitzpatrick, W. Haxton, E. Katz, N. Lubbers, Y. Xu - JCAP 1302 (2013) 004

[2] Lattice simulations for few- and many-body systems - D. Lee - Prog.Part.Nucl.Phys. 63 (2009) 117-154

A New Scheme for High-Intensity Laser-Driven Electron Acceleration in a Plasma

Saltanat Sadykova[1], **Anri Rukhadze**[2], **Paul Gibbon**[1]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Prokhorov General Physics Institute, RAS, Vavilov Street 38, Moscow, 119991, Russia**

Contact: **s.sadykova@fz-juelich.de**

Keywords: *plasma acceleration; Raman forward scattering; electron acceleration; laser-driven accel..*

During the past few decades plasma accelerators have attracted increasing interest of scientists from all over the world due to its compactness, much cheaper construction costs compared to those for conventional one and various applications ranging from high energy physics to medical and industrial applications. 3 M€ of funding have been awarded to 16 laboratories and universities from 5 EU member states within the European Union's Horizon 2020 programme – EuPRAXIA (European Plasma Research Accelerator with eXcellence in Applications). They will be joined by 16 associated partners that make additional in-kind commitments. The goal of this ambitious project is to produce a conceptual design report for the worldwide first high energy plasma-based accelerator that can provide industrial beam quality and user areas. At the Forschungszentrum Jülich in a frame of the JuSPARC project it is planned to establish a short-pulse, petawatt laser facility (pulse duration of 10 fs). This will be utilized to produce ultra-short pulsed X-rays based on the laser-driven electon acceleration (LDEA) concept, providing probes for materials science and biology applications relying on both high spatial and temporal resolution. In the standard LDEA, a short laser pulse excites a trailing plasma wave that can trap and accelerate electrons to high energy with the very high electric field gain. Unlike light sources of comparable wavelength such as the planned XFEL (x-ray free electron laser) at DESY, the laser-driven techniques potentially offer a much more compact and convenient operating environment with obvious advantages for FZJ-based research teams. Owing to the complex, nonlinear nature of the latter, only detailed numerical modelling and theoretical analysis will be able to provide the quantitative guidance necessary to optimize the beam characteristics required for a particular application. Establishment of collaboration between the various European institutes and FZJ in a frame of the JuSPARC and EuPRAXIA projects could be mutually beneficial. The idea to accelerate the charged particles in a plasma medium using collective plasma fields belongs to Budker, Veksler, and Fainberg. Later on, another acceleration schemes were proposed including the laser plasma acceleration. In our earlier work we proposed a A New Scheme for High-Intensity LDEA in a Plasma [1]. In our present work, we discuss and study further the suggested scheme taking into account different factors which can influence for example the plasma instability, consequently, the plasma wave amplification. Due to the stimulated scattering of a laser pulse by electrons the longitudinal plasma wave is generated. When the instability increases the much higher magnitudes of electric fields compared to the conventional accelerators can be gained. It is known that the wakefield generating instability induced by the stimulated back-scattering (backwards the laser pulse) has a maximum increment. However, this acceleration scheme is not suitable for particle acceleration because the wave vector of a plasma wave is equal to the double magnitude of that of a laser pulse, i.e. the phase velocity of a plasma wave is quite low. Due to this fact the wave leaves behind both the laser and the backward-scattered waves getting localized at the back to the front of the laser pulse. As a result the plasma wave gets soon out of the acceleration phase with the laser wave, and the relativistic electron beam, injected into the plasma, gets soon out of a phase with the plasma wave what halts the acceleration process. Due to the laser forward scattering a forward wave is generated. In this case, the plasma wave and the injected electrons can stay in acceleration phase for a much longer time. We determine additional conditions, not considered earlier, for such a resonance at which the maximum electron acceleration energy can be gained, make an estimation of a plasma, injected electron bunch parameters, maximum amplitude of the generated electric field and assist them with simulations using the EPOCH-code. As the basis parameters and for comparison we use those set in the planned plasma acceleration experiment at SPARC LAB facility of INFN-LNF, Frascati, Italy, with external electron Injection [2].

References

[1] A. A. Rukhadze and S. P. Sadykova, T. G. Samkharadze, CPP 55, Issue 8, (2015) ;

[2] A. R. Rossi, et al.,Proceedings of IPAC2012, USA,WEEPPB002

Multiscale approach to explore the relationships between connectivity and function in whole brain simulations

Sandra Diaz-Pier[1], Christian Nowke[2], Alexander Peyser[1], Benjamin Weyers[2], Bernd Hentschel[2], Abigail Morrison[1,3,4], Torsten W. Kuhlen[2]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Visual Computing Institute, RWTH Aachen University, Germany**

[3] **Institute for Advanced Simulation (IAS-6)**

[4] **Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr-University Bochum, Germany**

Contact: `s.diaz@fz-juelich.de`

Keywords: *neural networks; interactive; visualization; structural plasticity; multiscale simulations; steering.*

Introduction. In this work we describe an approach to explore the relationships between structure and function combining point-neuron network simulations with dynamic neuron mass models.

Methods. We use an interactive tool designed to visualize and steer the evolution of structural plasticity in complex multi-population networks to complement connectivity data for whole brain simulations. This multiscale setup is constructed for a whole brain parcellated into 68 regions based on the work described in Deco et al. 2014 [1]. Each region is modeled as dynamic neural mass, and in parallel, we also model each region as small point-neuron populations in NEST [2]. Structural plasticity in NEST is used to calculate the missing inner inhibitory connectivity required to match experimentally observed firing rates. We allow the point-neuron network to self-generate the missing connectivity following simple homeostatic rules. To stably bring all the regions in the NEST simulation to their ideal firing range, we use the interactive tool designed for this project to steer the structural plasticity algorithm by altering control parameters. The inner connectivity information can later be reused in the dynamic mass model simulation, producing an output which can be iteratively compared to experimental fMRI data in order to find correlations between structure and function.

Results. Using this approach and our interactive tool, it is possible to fill gaps in connectivity data of highly coupled multi-population networks and explore the impact of structure in function at different scales.

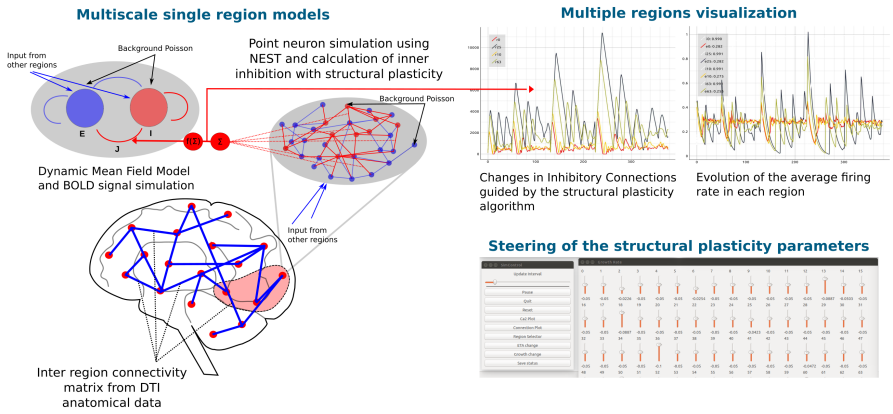


Diagram of our multiscale approach where large brain regions are simulated with a dynamic mass model and point-neuron networks are used to complement their inner inhibitory connectivity using structural plasticity (left). The interactive visualization and steering tool is used to bring all regions to their ideal firing activity (right).

Acknowledgements. *The authors would like to acknowledge the support by the Excellence Initiative of the German federal and state governments, the Jülich Aachen Research Alliance – High-Performance Computing and the Collaborative Research in Computational Neuroscience (CRCNS) grant. In addition, this project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 720270 (HBP SGA1).*

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UniProv: A flexible Provenance Management System for UNICORE

André Giesler[1], **Myriam Czekala**[1], **Björn Hagemeier**[1], **Richard Grunzke**[2]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Technische Universität Dresden**

Contact: `m.czekala@fz-juelich.de`

Keywords: *reproducibility; interoperability; provenance; scientific workflows.*

We present a flexible provenance managment system called UniProv. UniProv is an ongoing development project providing provenance tracking in scientific workflows and data management particularly in the field of neuroscience, thus allowing users to validate and reproduce tasks and results of their experiments.

The primary goal is to equip the commonly used Grid middleware UNICORE and its incorporated workflow engine with the provenance capturing mechanism of UniProv. We also explain an approach for using predefined patterns to ensure compatibility with the W3C PROV data model and to map the provenance information properly to a graph database.

In the past few years, scientific workflows have been often used to automatize and execute a range of experiments in many domains. As scientific work often comprises joint effort, there is a growing demand for a repository that allows everyone involved to store and query scientific workflow provenance information. Here, it is particularly important that such a repository must provide interoperability, since provenance data may be collected from various systems. Moreover, the storage of provenance must also be considered in terms of maintance and an efficient query processing. This work presents UniProv which adresses three main requirements: (i) enabling the traceability of scientifc workflows exemplarily in the domain of neuroimaging by designing a flexible provenance management system that can be conveniently integrated in the existing UNICORE workflow system; (ii) building an interoperable framework so that further potential provenance information providers can make use of the system; (iii) and designing a suitable storage management system, so that the provenance graph can be mapped efficiently and arbitrary analytics on its data can be performed.

We met the first requirement by implementing a modular architecture of UniProv that allows to connect different provenance providers mapping proprietary source information to the framework by making use of a predefined set of provenance patterns applying the emerging W3C PROV standard and addresses the interoperability requirement. Finally, we chose the scalable Neo4j graph database that supports Cypher, an expressive query language. Furthermore, Neo4j provides a convenient web interface to query and visualize the tracked provenance data.

Adaptive Filters for Color Images: Median Filtering and its Extensions

Andreas Kleefeld[1]

[1] **Jülich Supercomputing Centre (JSC)**

Contact: **a.kleefeld@fz-juelich.de**

Keywords: *matrix field; color image; median filter; M-smoother; amoeba filter.*

Abstract. In this talk, the construction of structure-preserving denoising filters for color images is explained. This is based on a recently proposed transformation from the RGB color space to the space of symmetric 2×2 matrices that has already been used to transfer morphological operations such as dilation and erosion from matrix-valued data to color images (see [1]). The applicability of this framework is shown for the construction of color-valued median filters. Additionally, spatial adaptivity is introduced into this approach by morphological amoebas that offer excellent capabilities for structure-preserving filtering. Furthermore, color-valued amoeba M-smoothers as a generalization of the median-based concepts are defined. The experiments confirm that all these methods work well with color images. They demonstrate the potential of the new approach to define color processing tools based on matrix field techniques (refer to [2]).

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von Willebrand factors and Platelets in Blood Stream: Margination and Adhesion

Masoud Hoore[1], **Kathrin Rack**[1,2], **Dmitry A. Fedosov**[1], **Gerhard Gompper**[1]

[1] **Institute for Advanced Simulation (IAS-2)**

[2] **Simulation and Software Technology, German Aerospace Center, 51147, Cologne, Germany**

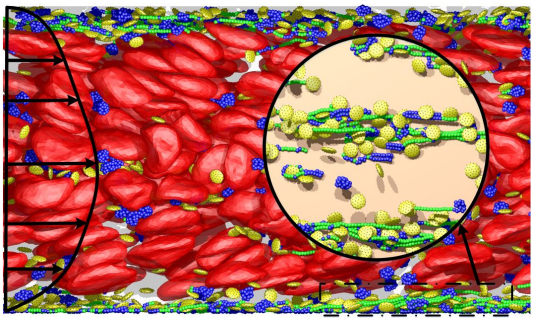
Contact: `m.hoore@fz-juelich.de`

Keywords: *Hemostasis; Mesoscopic modeling; Microfluidics; Margination; Adhesion.*

To stop bleeding, platelets must adhere to the injured endothelium and plug the opening. Although platelet adhesion to the injured substrate is effective in low shear rates, they are unable to firmly adhere to the surface by their own in shear rates higher than $900\ \mathrm{s}^{-1}$ [1]. In such conditions, von Willebrand factors (VWFs), the largest soluble proteins in blood stream play the crucial role [2]. They unwrap in high shear rates and adhere to the injured site; at the same time, they adhere to platelets and tether them from flowing in the blood flow. VWFs are long concatemers of VWF dimers bound to each other end to end [3]. The conformation of VWF polymer is such that in the absence of shear stress, the polymer remains globular, thus hiding its adhesive sites (A1 domains) for binding platelet receptors (Glycoprotein Ibα) or collagen. At sufficiently high shear rates, the VWF stretches making the interaction of its adhesive domain with platelet receptors or collagen possible.

For adhesion to occur, the platelets and VWFs must migrate to the proximity of tha injured walls. Indeed, the presence of red blood cells (RBCs) in blood stream facilates it by a process called margination. Accordingly, RBCs move to the center of the vessel and leave a RBC free layer near the walls. Then, the other micro-scale components such as ultra-large VWFs and platelets are pushed to this layer and populate there making hemostasis more probable. In addition, VWFs must be stretched to be hemostatically active since their adhesive domains are shielded from platelet receptors if the VWF polymer is coiled. Since VWFs are known to be coiled in low shear rates and stretched critically in sufficiently high shear rates [5], their adhesion occurs only in high shear rates.

By using meso-scale simulations, we study the behavior of VWFs and platelets in blood flow. It is shown that although platelets margination is enhanced by either increasing volume fraction of RBCs or by increasing shear flow, the margination of VWFs is non-trivially dependent on these two properties. It is also shown that VWF-platelet adhesion and aggregation are critically dependent on shear flow. The presence of ultra-large micro-scale VWFs is necessary in this process since they marginate and make big aggregates.



A snapshot of the simulation of blood clotting in blood stream. Platelet-VWF aggregates forming on the adhesive substrate are shown.

Acknowledgements. *M.H. and K.R. are thankful for the support by the DFG Research Unit FOR 1543 SHENC - Shear Flow Regulation in Hemostasis. D.A.F. acknowledges funding by the Alexander von Humboldt Foundation. We also gratefully acknowledge a CPU time grant by the Jülich Supercomputing Center.*

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Eikonal Equation in Pedestrian Dynamics

Arne Graf[1], **Mohcine Chraibi**[1]

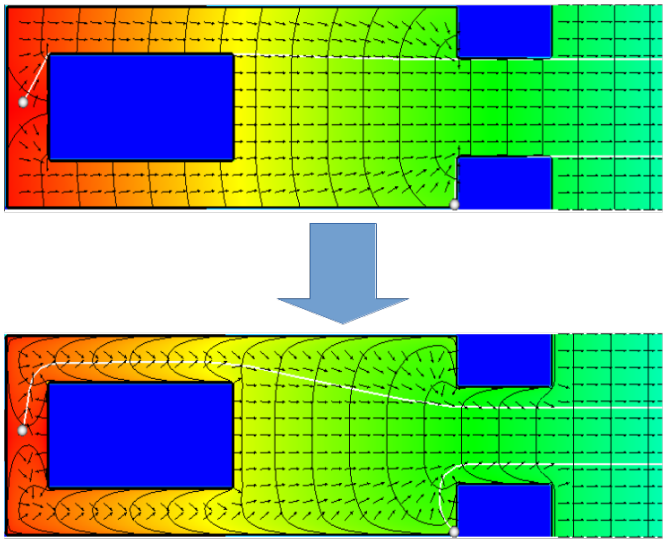
[1] **Jülich Supercomputing Centre (JSC)**
Contact: `ar.graf@fz-juelich.de`

Keywords: *simulation; floor field; pedestrian dynamics; navigation.*

Floor fields, as the solution of a well-posed Eikonal equation, are being used in a broad variety of applications, ranging from image processing, computer vision [1, 2, 3], optimal control [4], robotic path planning [5] to pedestrian dynamics.

In simulations of pedestrian dynamics, the routing and navigation of agents is an integral part. Routing can be seen as the composition of two aspects: the global path finding throughout a given geometry and the local avoidance of static or dynamic obstacles (like walls or other agents). To takle this task, cellular automaton (CA) models make use of static and dynamic floor fields [6], which were further developed to fit in various scenarios [7]. Floor fields gained popularity not only in CA but were also transferred to continuous models [8, 9]. They show exceptionally potential in directing agents through even very complex geometries without generating more effort compared to simple geometries.

In this work besides using floor fields as a tool to navigate through buildings, we modify the Eikonal equation by introducing a wall-distance-dependent speed factor, which helps avoiding walls and keeping an adjustable distance to static obstacles. An analogue modification to avoid other dynamical phenomena e.g. congestion seems likely, further extending its potential. Computationally, this method is optimal, since we calculate the necessary floor fields before hand (offline) and use them to navigate the agents through the building. Thus we avoid the necessity to calculate the agent-wall interactions at each time step and make only use of the information already at hand.



Comparison of conventional (above) and altered (below) Eikonal floor field: Isometrics of arbitrary unit "time-cost" to reach right border. Sample trajectories for two starting points (white). Negative gradients are visible (arrows).

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The Hoyle State in Nuclear Lattice EFT

Timo A. Lähde[1,2,3]

[1] **Institute for Advanced Simulation (IAS-4)**

[2] **IKP-3, Forschungszentrum Jülich, D-52425 Jülich, Germany**

[3] **Jülich Center for Hadron Physics, Forschungszentrum Jülich, D-52425 Jülich, Germany**

Contact: `t.laehde@fz-juelich.de`

Keywords: *Lattice Monte Carlo; Nuclear Structure; Effective Field Theory.*

The Hoyle state is a resonance in the spectrum of Carbon-12, which appears fortuitiously placed to enable the synthesis of elements heavier than Helium in evolved red-giant stars. Recently, Monte Carlo calculations of Nuclear Lattice EFT have begun to shed light on the spectrum, structure and transitions of the low-lying resonances of Carbon-12 from first principles. I will review this progress along with the possibly anthropic role of the Hoyle state, and discuss recent algorithmic developments in Nuclear Lattice EFT studies of the properties of Carbon-12 and the Hoyle state.

Magnetic Properties of Hybrid Organic-Metal Interfaces

Nicolae Atodiresei[1]

[1] **Institute for Advanced Simulation (IAS-1)**

Contact: `n.atodiresei@fz-juelich.de`

Keywords: *magnetism; interfaces; organic; graphene; ab intio; DFT.*

The density functional theory provides a framework with predictive power that can be used to describe organic-metal hybrid systems in a realistic manner. In this respect, ab initio studies elucidate how the subtle interplay between the electrostatic, the weak van der Waals and the strong chemical interactions determine the geometric, electronic and magnetic structure of hybrid organic-metal interfaces. More precisely, the interaction between the π-like electronic cloud of organic materials with the magnetic states of a metal influences the (i) spin-polarization, (ii) magnetic exchange coupling, (iii) magnetic moments and (iv) their orientation at the hybrid interfaces.

In this talk I will briefly summarize how first-principles calculations (i) provide the basic insights needed to interpret surface-science experiments and (ii) are a key tool to design novel materials with tailored properties that can be integrated in carbon-based spintronic devices.

Acknowledgements. *Supported by German Research Foundation (DFG), Japan Society for the Promotion of Science, VolkswagenStiftung and Jülich Supercomputing Centre.*

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The Complete APR Equation of State

Constantinos Constantinou[1], **Brian Muccioli**[2], **Madappa Prakash**[2], **James M. Lattimer**[3]

[1] **Institute for Advanced Simulation (IAS-4)**

[2] **Department of Physics and Astronomy, Ohio University, Athens, OH 45701**

[3] **Department of Physics and Astronomy, Stony Brook University, Stony Brook, NY 11794**

Contact: `c.constantinou@fz-juelich.de`

Keywords: *equation of state; thermal effects; hot and dense matter.*

The equation of state (EOS) of dense nucleonic matter at zero and finite temperature is essential in the modeling of neutron stars, core-collapse supernovae, and binary mergers. The cold component of the EOS determines the structure of old neutron stars and is a factor in the pre-merger progression of a binary system. Thermal effects are important in the hydrodynamic evolution of supernovae, during a merger where mass transfer can lead to shock heating, and in the post-event fate of the remnant.

We employ the Skyrme-like Hamiltonian density of Akmal, Pandharipande, and Ravenhall [1] in order to construct the equation of state (EOS) for conditions relevant to the aforementioned astrophysical phenomena. This Hamiltonian density, which is fit to the properties of more microscopic calculations of Akmal and Pandharipande [2], incorporates the long scattering lengths of nucleons that determine the low density characteristics.

We begin with the bulk homogeneous phase and calculate its thermodynamic properties (free energy, pressure, chemical potentials, isospin susceptibilities, etc.,) as functions of baryon density, proton-to-baryon ratio and temperature. The validity of the exact numerical computations is established by comparing to approximate results corresponding to analytical expressions valid in the non-degenerate and degenerate limits.

The subnuclear regime is treated in the Lattimer-Swesty [3] (LS) approach whereby the total free energy of the system receives contributions from bulk nucleons, light nuclei, heavy nuclei (described by the liquid-drop model), electrons and photons. Chemical and mechanical equilibrium as well as the optimum size of nuclei are obtained by minimizing the free energy under the constraints of strong and electromagnetic equilibrium.

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Hierarchical parallelisation of functional renormalisation group calculations

Daniel Rohe[1]

[1] **Jülich Supercomputing Centre (JSC)**

Contact: `d.rohe@fz-juelich.de`

Keywords: *Hybrid Parallelisation; functional Renormalisation Group; HPC Tools.*

We report on recent work of a multi-level parallelisation of functional Renormalisation Group calculations in condensed matter systems. By means of MPI, OpenMP and in part vectorisation a speed up of the code by several orders of magnitude is possible.

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Transient dynamics of the Ohmic two-state system via the time dependent numerical renormalization group method

Theo Costi[1,2], **Hoa Nghiem**[1,2], **Dante Kennes**[3], **Christian Klöckner**[3], **Volker Meden**[3]

[1] **Institute for Advanced Simulation (IAS-3)**

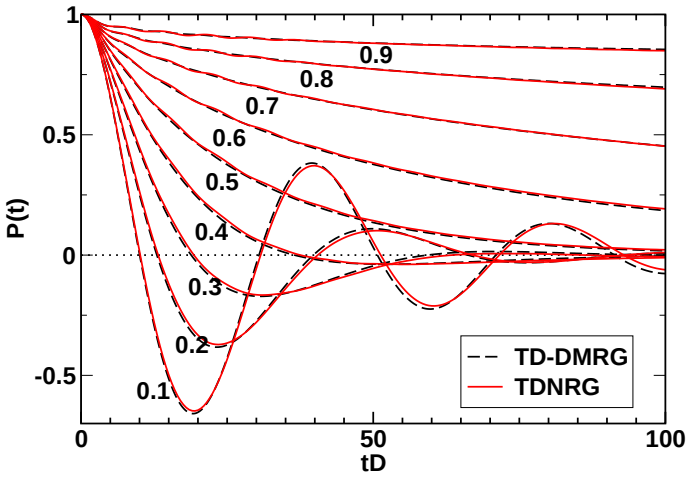
[2] **Institute for Theoretical Nanoelectronics (PGI-2), FZJ**

[3] **Institut für Theorie der Statistischen Physik, RWTH Aachen University**

Contact: `t.costi@fz-juelich.de`

Keywords: *time evolution of quantum systems; numerical renormalization group; two-level systems; quantum dissipation; Kondo effect; Interacting resonant level model.*

We investigate the transient dynamics of the Ohmic two-state system for a range of dissipation strengths, α, ranging from weak ($\alpha \ll 1$) to strong ($1/2 \leq \alpha \leq 1$) dissipation, by exploiting equivalences to fermionic models and applying the time-dependent numerical renormalization group (TDNRG) [1,2,3], the time-dependent density matrix renormalization group (TD-DMRG) and the functional renormalization group (FRG) approaches [4]. For the transient dynamics of the two-level system coordinate $P(t) \equiv \langle \sigma_z(t) \rangle$, we compare our TDNRG results with results from the noninteracting-blip approximation (NIBA) and the TD-DMRG, finding excellent agreement with results from the latter, on short to intermediate time scales, but significant differences with the results from the NIBA [4]. This quantifies the accuracy of the TDNRG on the above time scales and also quantifies the size of the errors within the NIBA on the same time scales. Our TDNRG results for $P(t)$ could serves as useful benchmarks for future techniques simulating spin-boson problems [5].



Comparison between TDNRG (solid lines) and TD-DMRG (dashed lines) for the time evolution of the two-level system coordinate $P(t) = \langle \sigma_z(t) \rangle$ of the Ohmic two-state system on short to intermediate time scales for a bare tunneling amplitude $\Delta_0/\omega_c = 0.1$ and a range of dissipation strengths $0.1 \leq \alpha \leq 0.9$ as indicated by the labelled curves [4]. The excellent agreement demonstrates the quantitative accuracy of the TDNRG method at finite (short to intermediate) times. All calculations have been performed on the equivalent interacting resonant level model within both TDNRG and TD-DMRG using a semi-elliptic density of states with bandwidth $W = 2D = 2$.

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Parallel-in-Time Integration with PFASST

Ruth Schöbel[1], **Robert Speck**[1], **Dieter Moser**[1]

[1] **Jülich Supercomputing Centre (JSC)**

Contact: `r.speck@fz-juelich.de`

Keywords: *time parallel; Finite Elements; Gray Scott equations.*

The challenges arising from the extreme levels of parallelism required by today's and future HPC systems mandates the development of new numerical methods that feature a maximum degree of concurrency. In particular, iterative time integration methods that can provide parallelism along the temporal axis have become increasingly popular over the last years. The recently developed "parallel full approximation scheme in space and time" (PFASST) can integrate multiple time-steps simultaneously in a multigrid-fashioned way. Based on multilevel spectral deferred corrections, PFASST is able to make use of different coarsening strategies in space and time to improve parallel performance. In this talk, we will describe the basic concept of parallel-in-time integration and discuss the different components of PFASST. We will show recent results on successful combinations of space-parallel solvers, highlighting extreme-scale benchmarks with a multigrid solver on up to 448K cores of the IBM Blue Gene/Q installation JUQUEEN.

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Leveraging heterogeneity for neural computation with fading memory

Renato Duarte[1,4,5], **Alex Seeholzer**[6], **Abigail Morrison**[1,2,3]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Faculty of Psychology, Institute of Cognitive Neuroscience, Ruhr-University Bochum**

[3] **Jülich Supercomputing Centre (JSC)**

[4] **Bernstein Center Freiburg, Albert-Ludwig University of Freiburg**

[5] **Institute for Adaptive and Neural Computation, School of Informatics, University of Edinburgh**

[6] **Laboratory of Computational Neuroscience, Ecole Polytechnique Federale de Lausanne**

Contact: `r.duarte@fz-juelich.de`

Keywords: *Heterogeneity; Online Processing; Cortical microcircuits.*

Computational studies addressing the dynamics and computational properties of biologically inspired spiking neurons and networks tend to assume (often for the sake of analytical tractability) a great degree of homogeneity in both neuronal and connectivity parameters (e.g. [1]). The biophysical reality, however, is radically different from a homogeneous system and multiple levels of complex heterogeneous properties coexist and shape a local circuit's emergent collective dynamics and information processing properties. Within each cortical module, the characteristic patterning of the microcircuit's building blocks and their mechanistic interactions give rise to rich dynamics, which subserves local computation by shaping the spatiotemporal features of population responses. Despite their varying molecular, morphological and physiological features, cortical modules can be seen as variations on a common theme [2]. In essence, notwithstanding the complex laminar patterning and differential input-output relations which might give rise to additional structural and functional sub-parcellations, cortical modules are large recurrently coupled neuronal networks, whose interactions are achieved primarily via spike-triggered excitatory and inhibitory transmission [3]. The combined complexity of these heterogeneous building blocks can be leveraged by cortical microcircuits to provide a rich dynamical space where complex relational constructs, spanning multiple timescales, can be learned, represented and used for online information processing. In this study, we set out to systematically evaluate the role played by different sources of heterogeneity (structural, neuronal and synaptic) in the characteristics of population dynamics and the circuit's capacity for online stimulus processing with fading memory, using cortical layer 2/3 microcircuits as a core inspiration for the circuit specification. We cross-reference various sources of experimental data regarding the composition and patterning of these microcircuits, accounting for different phenomena of interest (e.g. neuron types and corresponding subthreshold characteristics, conductance properties of different receptor types, circuit-level connectivity and activity statistics, etc.), across different cortical regions, assuming a certain degree of generalization is possible. The methods applied in this study to quantify the dynamics and generic processing properties, being system-independent, can provide a valuable set of tools for microcircuit benchmarking. As carefully curated and organized datasets become increasingly available, it will become possible in the near future to apply increasingly realistic constrains and comparatively study the properties of realistic microcircuits, built to model specific cortical regions and input-output relations.

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From single-cell spiking to large-scale interactions: A multi-scale spiking network model of macaque cortex

Maximilian Schmidt[1], **Rembrandt Bakker**[1,2], **Kelly Shen**[3], **Gleb Bezgin**[4], **Claus-Christian Hilgetag**[5,6], **Markus Diesmann**[1,7,8], **Sacha Jennifer van Albada**[1]

[1] **Institute of Neuroscience and Medicine (INM-6) and Institute for Advanced Simulation (IAS-6) and JARA BRAIN Institute I, Jülich Research Centre, Jülich, Germany**

[2] **Donders Institute for Brain, Cognition and Behavior, Radboud University, Nijmegen, Netherlands**

[3] **Rotman Research Institute, Baycrest, Toronto, Ontario M6A 2E1, Canada**

[4] **McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montreal, Canada**

[5] **Department of Computational Neuroscience, University Medical Center Eppendorf, Hamburg, Germany**

[6] **Department of Health Sciences, Boston University, USA**

[7] **Department of Psychiatry, Psychotherapy and Psychosomatics, Medical Faculty, RWTH Aachen University, Aachen, Germany**

[8] **Department of Physics, Faculty 1, RWTH Aachen University, Aachen, Germany**

Contact: `max.schmidt@fz-juelich.de`

Keywords: *simulation; supercomputer; cortex; neural networks; brain anatomy; brain dynamics.*

Even in the absence of a particular sensory stimulus or behavioral task, mammalian cortex features complex dynamical behavior on multiple scales. On the single-cell level, neurons spike irregularly with increasing intrinsic time scales along the visual hierarchy [1]. Cortical layers and cell types show heterogeneous average firing rates. On a global scale, cortical areas form clusters with covarying activity, so-called resting-state networks [2]. These dynamics emerge on a substrate of complex connectivity on the level of cell types, layers and areas. With increasing knowledge on cortical structure, it is a growing challenge to integrate this information into a consistent picture of cortical connectivity. To jointly characterize the connectivity and spontaneous dynamics of cortex, we present a spiking multi-scale model of macaque visual cortex connected according to a new connectivity map based on multiple sources. It thus makes the non-trivial step from a population description [3] to a spiking description of this system. Visual cortex serves as an example system on which we develop the necessary tools to simulate spiking networks of this scale with realistic population-level connectivity, enabling analogous models of further cortical regions in future. The network connectivity combines data from numerous tracing studies, collected in a new release of the CoCoMac database [4], with a recent quantitative dataset [5] and is refined using dynamical constraints [6]. The model for each area is an adaptation of a microcircuit model of early sensory cortex [7] to the specific laminar structure of the given area. Simulations on the JUQUEEN supercomputer show that plausible dynamics emerge from the network, mimicking experimental findings on cortical dynamics on multiple scales, from single-cell spiking properties [1] to the large-scale interaction patterns of cortical areas [2]. Furthermore, cortico-cortical interactions propagate predominantly in the feedback direction, akin to experimental observations during sleep or visual imagery [8]. Our study demonstrates that such multi-scale dynamics can emerge from the connectivity on the level of areas and populations, thereby separating network effects from the influence of cell-type specific intrinsic dynamics. Our working model can easily be extended to other cortical areas, and it provides a substrate on which functional features at the spiking level can be added.

Acknowledgements. *VSR computation time grant JINB33, Helmholtz Portfolio SMHB, EU Grant 269921 (BrainScaleS), EU Grant 604102 (Human Brain Project, HBP), SFB936 /A1, Z1 and TRR 169 /A2.*

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Molecular Dynamics Simulations to design new Neuroreceptor Ligands with Optimized (un)binding Kinetics

Rodrigo Casasnovas Perera[1,2], **Vittorio Limongelli**[3,4], **Pratyush Tiwary**[5], **Paolo Carloni**[1,2], **Michele Parrinello**[6]

[1] **Institute for Advanced Simulation (IAS-5)**

[2] **Institute of Neuroscience and Medicine (INM-9) Forschungszentrum Jülich, Jülich, Germany**

[3] **Università della Svizzera Italiana (USI), Faculty of Informatics, Institute of Computational Science - Center for Computational Medicine in Cardiology, via G. Buffi 13, CH-6900 Lugano, Switzerland**

[4] **Department of Pharmacy, University of Naples "Federico II", via D. Montesano 49, I-80131 Naples, Italy.**

[5] **Department of Chemistry, Columbia University, 10027 New York, United States of America**

[6] **Department of Chemistry and Applied Biosciences, ETH Zurich , and Faculty of Informatics, Institute of Computational Science, Università della Svizzera Italiana, via G. Buffi 13, CH-6900 Lugano, Switzerland**

Contact: `r.casasnovas.perera@fz-juelich.de`

Keywords: *Protein-ligand unbinding kinetics; Molecular Dynamics simulations; Enhanced Sampling methods; Metadynamics simulations.*

Small molecule ligands targeting neuroreceptors are used in imaging techniques to study brain anatomy and physiology as well as for medical diagnosis and therapy. While traditional ligand design strategies focused on finding molecules with high affinity for their targets, novel strategies are aiming also at optimizing the kinetics of binding and/or unbinding. This strategy provides control of the ligand-target complex residence times and allows improving selectivity and, therefore, reducing drug dose and side effects.

Rational optimization of the binding and unbinding events ultimately requires structural knowledge of the relevant transition states, which is extremely difficult to obtain by experimental means. On the contrary, atomistic Molecular Dynamics (MD) simulations provide detailed structural knowledge while their main limitation is that the binding and unbinding timescales are too large to be observed in standard simulations. We overcome this limitation by accelerating artificially the protein-ligand binding and unbinding with a method called Metadynamics [1] and later we use statistical mechanics to recover the real times of the non-accelerated process [2].

As a test case we study the p38 MAP Kinase, an enzyme activated by stress signals that participates in the molecular development of Alzheimer's disease and Amyotrophic Lateral Sclerosis [3-6] and derivatives of BIRB 796, which entered Phase II human clinical trials for the treatment of autoimmune disorders. We show that this methodology provides kinetic constants in very good agreement with experiment and provides a detailed description of the unbinding mechanism, rate-limiting steps and the structure of the associated transition states. In our next investigations we aim at applying this technique to brain research and propose new ligands targeting the M2 muscarinic receptor that can potentially be used in brain imaging.

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Role of the extracellular loop ECL2 and membrane lipids for ligand recognition in GPCRs.

Ruyin Cao[1,2], **Giulia Rossetti**[1,2,3], **Dirk Bier**[4], **Paolo Carloni**[1,2]

[1] **Institute for Advanced Simulation (IAS-5)**

[2] **Institute of Neuroscience and Medicine INM-9, Forschungszentrum Jülich, Wilhelm-Johnen-Straße, D-52428, Jülich, Germany**

[3] **Jülich Supercomputing Centre (JSC)**

[4] **Institute of Neuroscience and Medicine INM-5, Forschungszentrum Jülich, Wilhelm-Johnen-Straße, D-52428, Jülich, Germany**

Contact: `r.cao@grs-sim.de`

Keywords: *metadynamics; GPCR; ligand binding.*

Extracellular loops (ECLs) of GPCRs are very diverse in lengths and sequence compositions, and increasing evidence suggests their key role in early stages of ligand recognition. By using metadynamics simulations [1] we uncover the role of the extracellular loops in the multi-step dissociation pathways of the high affinity antagonist ZM241385 [2] from the orthosteric binding site of human adenosine receptor type 2A ($hA_{2A}R$) [3]. We discover two precedently undecribed vestibular binding sites, where ECL1 and ECL2 use lipid-specific interaction patterns to stabilize the ligand. Moreover, we also showed that these two vestibular binding sites are evolutionally correlated to the deep orthosteric binding site, strongly suggesting the presence of an allosteric pathway connecting these topologically distinct regions of the receptor. We further found a solvent-exposed binding site on the ECL2, whose existence is confirmed by mutagenesis experiments, pointing toward a role of ECL2 in early ligand recognition step. By extending our analysis to other human GPCRs for which structural information are available, we found that the evolutionary coupling between ECLs and orthosteric binding site also exists for 22 human GPCRs, in 18 of which, the ECL2 is involved. Our finding uncover a potentential allosteric modulation of the extracellular loops, ECL2 being the key player, on to the deep orthosteric binding site.

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KKRnano: Towards scientific applications on exascale computers

Rudolf Zeller[1]

[1] **Institute for Advanced Simulation (IAS-3)**

Contact: `ru.zeller@fz-juelich.de`

Keywords: *electronic structure; exascale computing; density-functional calculatiosn.*

A basic-quantum mechanical treatment of material properties is an indispensable tool for the development of advanced 21st century applications. While systems with several hundred atoms can be treated routinely by density-functional calculations, larger systems with many thousand atoms represent a serious problem since the computational effort in standard codes increases with third power of the number of atoms. In the last years we have developed KKRnano, a new computer code which overcomes this problem. The basic concepts of the code will be described and it will be shown that KKRnano enables to treat systems with many thousand atoms with up to more than a million of parallel tasks. It will be discussed that the calculations can be made very precise by exploiting a new concept which approximates the electronic potential by non-local angular projection potentials.

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Solving Hard 2-SAT Problems on a D-Wave Two System

Kristel Michielsen[1,2], **Lukas Hobl**[1], **Fengping Jin**[1], **Hans De Raedt**[3]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **RWTH Aachen University, Aachen, Germany**

[3] **Zernike Institute for Advanced Materials, University of Groningen, Groningen, The Netherlands**

Contact: `k.michielsen@fz-juelich.de`

Keywords: *quantum annealing; adiabatic quantum computation; 2-satisfiability; Landau-Zener transitions; D-Wave quantum computer.*

Solving a 2-satisfiability (2-SAT) problem amounts to finding whether a collection of two-valued variables with constraints on pairs of variables can be assigned values satisfying all the constraints. 2-SAT problems can be solved in polynomial time, in contrast to the general k-SAT problems which are NP-complete. We consider computationally hard 2-SAT problems with a unique satisfying assignment, that is with a unique ground state [1]. Other characteristics of these hard 2-SAT problems are that the energy gap between the ground state and the first-excited state is small and that they have a highly degenerate first-excited state. The first makes it hard to solve the problem by quantum annealing as can be seen from the Landau-Zener transition formula and the latter makes a classical search in terms of simulated annealing hard as the chance of getting trapped in a local minimum is high.

We study 2-SAT problems with 8, 12 and 18 variables (or Ising spins in the physics language). For these problems we numerically calculate the exact value of the gap between the ground state and the first-excited states which gives information about the computational complexity for solving the problems with quantum annealing.

We report about a comparison of the frequencies for finding the ground state, as obtained with the D-Wave Two and a digital computer emulating the dynamics of an ideal adiabatic quantum computer by solving the time-dependent Schrödinger equation for a system of interacting, localized spin-1/2 particles at zero temperature. Our analysis indicates that the D-Wave Two processor does not perform “ideal” quantum annealing and that more research is necessary to investigate the effects of e.g. temperature, imperfections etc.

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Continuous time quantum Monte Carlo as a quantum impurity solver

Julian Mußhoff[1,2], **Amin Kiani**[1], **Eva Pavarini**[1]

[1] **Institute for Advanced Simulation (IAS-3)**

[2] **RWTH Aachen University, Germany**

Contact: `j.musshoff@fz-juelich.de`

Keywords: *continuous time; quantum Monte Carlo; dynamical mean-field theory; quantum impurity model; hybridization expansion.*

In modern solid-state physics many interesting effects like high-temperature superconductivity, the Kondo effect or anti-ferromagnetism occur because of strong correlations between electrons. These correlations, due to Coulomb repulsion, lead to an exponential growth of degrees of freedom, which makes it impossible to solve the problem exactly. In a quantum impurity model correlations are only considered for the electrons on the impurity, which is embedded in a bath of uncorrelated electrons. Solving a quantum impurity model with only one bath site is already sufficient to understand the nature of the Kondo problem [1]. Beneath direct physical application impurity models play the central role in the dynamical mean-field theory (DMFT) [2]. This method describes the mapping of a correlated lattice model (Hubbard model) onto an effective impurity model [3]. Our group uses this theory to map multi-orbital crystal structures with multiple sites per unit cell to impurity models. To solve this multi-orbital models, which is the most time consuming part in DMFT, we use the continuous time quantum Monte Carlo (CT-QMC) solver [4]. In this talk we will introduce the basics of the QMC method and details of the CT hybridization expansion [5][6]. We show the possibility of massive parallelization and measurement of one and two-particle Green functions. This functions are essential in the response theory [7], which is the connection to experiments.

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Predicting the apo-structures of two human NEET proteins involved in health and disease conditions

Luca Pesce[1], **Vania Calandrini**[1], **Giulia Rossetti**[1,2,3], **Rachel Nechushtai**[4], **Paolo Carloni**[1]

[1] **IAS-5/INM-9, Computational Biomedicine**

[2] **Hematology and Stem Cell Transplantation University Hospital Aachen, RWTH Aachen University, Germany**

[3] **Jülich Supercomputing Centre (JSC)**

[4] **The Alexander Siberman Life Science Institute and the Wolfson Center for Applied Structural Biology, The Hebrew University of Jerusalem, Edmond J. Safra Campus at Givat Ram, Jerusalem 91904, Israel**

Contact: `l.pesce@fz-juelich.de`

Keywords: *NEET proteins; molecular dynamics simulaitons; REST2.*

mitoNEET and NAF-1 are homologous proteins, belonging to the NEET family. These feature two intertwining monomers, each of which contains a labile 2Fe-2S cluster[1-3]. Despite the functions of these proteins still need to be elucidated, experimental observations support the hypothesis that their function involves the gather/release of the FeS from/to holo-donor/apo-acceptor proteins[4,5].

The lack of structural information for these proteins in absence of the iron-sulfur cluster(s) has so far hampered a molecular understanding of the key processes involving the cluster release. Here, we propose to predict the structural determinants of these proteins without one (holo-apo state) and two (apo-apo state) clusters in aqueous solution. We plan to use Replica Exchange Solute Tempering (REST)2 enhanced simulations[6,7]. This method allows performing a faster and extensive exploration of the conformational space compared to classical MD[6]. The initial models was built based on the crystal structure of mitoNEET and NAF-1 in the holo form[2,3,8] after removal of one or two clusters.

Our theoretical predictions will be compared with our spectroscopic data. This information is key for our planned future works aimed at finding molecular partners potentially able to interfere with the cluster release.

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Posters

Design of ligands interfering with aberrant subcellular processes in Huntington's.

Anna Bochicchio[1,2], Giulia Rossetti[1,3,4], Serena Massari[5], Jenny Desantis[5], Kamyar Hadian[6], Kenji Schorpp[6], Oriana Tabarrini[5], Sybille Krauss[7], Paolo Carloni[1,3]

[1] **Institute for Advanced Simulation (IAS-5)**

[2] **Computational Biophysics, German Research School for Simulation Sciences (GRS)**

[3] **Institute of Neuroscience and Medicine INM-9, Forschungszentrum Jülich, Wilhelm-Johnen-Straße, D-52428, Jülich, Germany**

[4] **Jülich Supercomputing Centre (JSC)**

[5] **Dipartimento di Scienze Farmaceutiche, Università di Perugia, Via del Liceo 1, 06123 Perugia, Italy**

[6] **Institute for Molecular Toxicology and Pharmacology, Helmholtz Zentrum München German Research Center for Environmental Health (GmbH), Ingolstädter Landstr. 1, D-85764, Neuherberg, Germany**

[7] **German Center for Neurodegenerative Diseases (DZNE), Sigmund-Freud-Str. 25, D-53127, Bonn, Germany.**

Contact: `a.bochicchio@fz-juelich.de`

Keywords: *Huntington disease; md; ligands.*

Huntington's disease (HD) is a fatal and devastating neurodegenerative genetic disorder for which there is currently no cure. The gene responsible for the disease encodes the Huntingtin protein (HTT), essential for brain development [1]. The disease is caused by an expanded CAG repeat in the 5'-end of HTT. HD penetrance is related to the number n of CAG repeats. Mounting evidences suggested that HTT mRNA transcripts with expanded CAG repeats contribute to the pathogenesis, regulate aberrantly several cellular mechanisms and they bind to proteins in a repeat size-dependent manner to form pathological complexes. One of those involves the Midline-1 protein (MID1) in complex with protein phosphatase 2A (PP2A) [2], as recently shown by one of us (S.K.). Inhibiting the formation of this pathological mRNA-proteins complex, targeting the expanded CAG mRNA transcript, can significantly reduce the HTT overproduction effect [2]. Yet, the rational design of molecules specifically targeting the expanded CAG repeats is critically limited by the lack of structural information. Here, we used well-tempered-metadynamics based free energy calculations to investigate pose and affinity of the two ligands targeting CAG repeats for which affinities have been so far measured [3]. Our calculations, consistent with the experimental affinities, uncover the recognition pattern between ligands' and their RNA target. They also provide the molecular bases of their different specificity of the two ligands for CAG repeats [4]. By capitalizing on this investigation, we have identified new compounds with chemical and shape similarity to the highest affinity ligand. The calculated free energy of unbinding to CAG repeats is in accord with that derived by the K_d, as measured here. Most importantly, RNA pull-down assays performed show a clear inhibition of the MID1-mRNA CAG complex by this compound. This work, along with that of other groups [3], suggests that advanced computational physics investigations can help the design of new molecules targeting RNA with possible beneficial effects for neurodegenerative diseases.

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Path Integral Formalism in Momentum Space for Carbon Nano-systems

Ahish Vishwanatha[1,2], **Thomas Luu**[1]

[1] **Institute for Advanced Simulation (IAS-4)**

[2] **German Research School for Simulation Sciences, RWTH Aachen University, Germany**

Contact: `ahishv@gmail.com`

Keywords: *Path Integral Formalism; Momentum Space Lattice Monte Carlo; Nanosystems; Graphene.*

Path Integral Formalism is a very well established technique commonly applied to solve problems in Quantum Field Theory. It was then noticed that it is equally applicable to lattice structures at the nanoscale, and was subsequently implemented to study carbon nanosystems (such as graphene and carbon nanotubes).

Previous developments in this field have mostly been limited to solving problems in real space which turn out to be rather computationally expensive, mostly due to problem size and complexity.

We develop on such earlier work and implement the formalism as applicable to graphene nanosystems. This makes use of the geometric symmetries intrinsic to the system under consideration, and simplifies some of its computationally expensive features. It also eliminates the momentum projection step necessary at the end of real-space computations (since the formalism operates entirely in the momentum space). This decreases solve times, thereby allowing one to solve larger and more complex problems.

This is the first time the Monte Carlo formalism for graphene has been developed entirely in momentum space, and it can also be straightforwardly extended to account for carbon nanotubes and similar systems.

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Computer Simulations of Cytoskeletal Filaments and Motors

Arvind Ravichandran[1], **Thorsten Auth**[1], **Gerrit Vliegenthart**[1], **Gerhard Gompper**[1]

[1] **Institute for Advanced Simulation (IAS-2)**

Contact: `a.ravichandran@fz-juelich.de`

Keywords: *cytoskeleton; microtubule; molecular motor; cytoplasmic streaming; brownian dynamics.*

Motor proteins, such as kinesins, are molecular machines that hydrolyse ATP to perform mechanical work on microtubules (MTs) to drive motility in cells. This is important for processes such as cytokinesis, localization of organelles, and cytoplasmic streaming [1]. The recent work of Lu et al. has shown in vivo that microtubule sliding, induced by kinesin-1 is important for normal oocyte cytoplasmic rotation, a process required for efficient localization of mRNAs and proteins during oogenesis in Drosophilia [2]. Namely, free microtubules are observed to move against cortically anchored microtubules generating forces that contribute to cytoplasmic streaming.

To elucidate the relation of microscopic mechanisms to the macroscopic properties, we use a two dimensional Brownian dynamics model [3]. Circularly confined polar filaments are modelled as a linear rigid chain of penetrable beads that mutually attract each other by depletion forces. Motors are harmonic force dipoles that move on the filaments in the direction of MT polarisation, and pull cross-linked filaments with them [4]. In this work we study the effect of both, tetrameric and dimeric motors. Tetrameric motors have two motile arms that cross-link two neighbouring MTs, while dimeric motors have one motile arm, and another anchored arm, similar to kinesin-1.

We show that tetrameric motors bundle MTs, and do not lead to motility. Unlike tetrameric motors that induce relative tangential stress only in the case of aligned MTs, kinesin-1-like, dimeric motors induce stresses in the case of both anti-aligned and aligned MTs. This leads to perpetual motility in a layer of MTs close to the confinement edge, where filaments are distinctly more anti-aligned than the center of the confinement. Higher densities of motors do not change the organization of filaments, but induce more stress and propel filaments faster. The structures consist of large nematically aligned droplets with point defects at the boundary.

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Collective behavior of swimmers with density-dependent motility

Clara Abaurrea Velasco[1,2], **Masoud Abkenar**[1,2,3], **Kristian Marx**[1,2], **Thorsten Auth**[1,2], **Gerhard Gompper**[1,2]

[1] **Institute for Advanced Simulation (IAS-2)**

[2] **Institute of Complex Systems (ICS-2)**

[3] **Soft Matter Theory, Fakultät für Physik, Technische Universität München, 85748 Garching, Germany**

Contact: `c.abaurrea@fz-juelich.de`

Keywords: *microswimmers; cytoskeleton; collective behaviour; Brownian dynamics simulations; self-propelled particles; swarming.*

Microswimmers span from bacteria to human-made nanorobots [1]. To simulate collective behavior, generic models allow to study a large number of particles and to still maintain certain characteristics, such as the aspect ratio. Because many biological swimmers are anisotropic, we use self-propelled rods in two dimensions that interact with a soft repulsive potential. Our capped interaction potential allows rods to cross each other [2]. This makes our simulations suitable for studying quasi-2D experiments, such as microtubule motility assays or a thin layer of swimming bacteria.

The phase behavior of monodisperse rods with constant self-propulsion has been characterized systematically [2, 3]. While for low densities cluster formation is observed, at high densities laning is found. However, many biological swimmers show density-dependent motility, such as quorum sensing phenomena in bacteria [4]. Density-dependent self-propulsion can be characterized by the ratio of the propulsion velocity of a single rod and a rod in a dense environment, and by and exponential dependence with the number of neighboring particles. We study for the first time self-propelled rods with physical interactions and a density dependent propulsion force. We show that by decreasing the self-propulsion of the rods with the local density of swimmers the polar alignment and phase segregation are favored. Enhanced phase segregation helps bacterial colonies in biofilms become more compact, which increases their resistances against external chemical agents.

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Graph properties of the functional connected brain under the influence of Alzheimer's disease

Claudia Bachmann[1], **Heidi Jacobs**[2,3,4], **Kim Dillen**[5], **Simone Buttler**[1], **Gereon R. Fink**[5,6], **Juraj Kukolja**[5,6], **Abigail Morrison**[1,7,8]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Faculty of Health, Medicine and Life Science, School for Mental Health and Neuroscience (MHeNS), Alzheimer Centre Limburg, Maastricht University Medical Centre, PO Box 616, 6200 MD Maastricht, The Netherlands**

[3] **Department of Radiology & Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA**

[4] **Faculty of Psychology and Neuroscience, Department of Cognitive Neuroscience, Maastricht University, PO BOX 616, 6200 MD Maastricht, The Netherlands**

[5] **Cognitive Neuroscience, Inst. of Neuroscience and Medicine (INM-3), Jülich Research Centre, Jülich, Germany**

[6] **Department of Neurology, University Hospital of Cologne, Cologne, Germany**

[7] **Computational Neuroscience, Bernstein Center Freiburg, Freiburg, 79104, Germany.**

[8] **Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr-University Bochum, 44801 Bochum, Germany**

Contact: `c.bachmann@fz-juelich.de`

Keywords: *fMRI data; data analysis.*

Diagnosing Alzheimer's Disease (AD), especially in the early stage, is costly and burdensome for the patients, since it comprises a battery of psychological tests and an extraction of disease specific biomarkers from the cerebrospinal fluid. A cheaper and more convenient procedure would be a diagnosis based on images obtained through fMRI. Based on previous polymodal studies demonstrating disrupted inter- and intra-cortical connectivity in AD [1], we argue that the functional connectivity of the whole cortex might be a good predictor for the cause of the disease. In resting state fMRI, previous attempts to analyze graph properties of whole brain networks contradict each other [2]. In our opinion there are two general critical points in the methodology of these studies that are likely to contribute to the variability of the results. First, we criticize that the activities of the brain areas (graph nodes) that are used to calculate the functional connectivities (weights of the graph edges) are composed of functionally inhomogeneous signals,as individual brains are often mapped onto a standard atlas brain of known functional coherent areas [2,3]. The second problem consists in converting the resulting weighted graphs into simple graphs, by setting weights above an arbitrary threshold $w_{\min}$ to 1, and those below it to 0 [2]. The drawback here is that there is no validation for an optimal threshold, and information that might be relevant in AD may be lost. In this work we address the first problem by applying an activity-driven, region-growing clustering algorithm derived from image processing [4]. In order to guarantee functionally homogeneous clusters, the threshold for inclusion of a voxel in a region is regulated by a heterogeneity criterion [3]. Applying this algorithm, we end up with undirected weighted graphs with varying numbers of nodes for three sets of data: healthy elderly controls, mild cognitive impairment and Alzheimer's disease. Targeting the second problem, we analyze the dependence of graph theoretic measures (shortest path length, in- and out-degree distribution, clustering coefficient, modularity and minimal spanning tree [5]) on $w_{\min}$. Finally, we investigate the distribution of these measures for each data set to determine candidates for a predictive measure.

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Automated Soccer Scene Tracking Using Deep Neural Networks

Christian Bodenstein[1,2], **Markus Götz**[1,2], **Morris Riedel**[1,2]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **University of Iceland, Iceland**

Contact: `c.bodenstein@fz-juelich.de`

Keywords: *Computer Vison; Tracking; Machine Learning; Deep Learning; Sport; Soccer.*

Sport events fascinate audiences around the whole globe. While some events are privileged to gather a large audience through television or internet broadcasts, most can only be seen on-site or on shaky amateur videos. A proper sports broadcast requires two things: first, a infrastructure including cameras, servers and a joinable event channel for the viewers. Second, a camera director or cinematographer that catches the important scene in the playground, allowing the viewer at home to follow the event. While there are companies providing low-cost broadcasting infrastructures, the director comes at high cost as it requires manual labor. We would like to change the game by providing a computerized video analysis pipeline, which is able to select the scene of interest in soccer games fully automatically. The approach is based on modern deep learning techniques—or more precise Convolutional Neural Networks (CNN). CNNs are the state-of-the-art for image and voice recognition, but have not been widely applied to object or scene tracking problems yet. In this scenario, the supervised learning algorithm is learning proper camera angles and zooms by "viewing" already recorded games captured of cameramen. We are showing the viability of these algorithms by automatically directing captures of regional soccer league matches from a number of cameras. The resulting video can then be streamed to viewers at home or stores for later review by fans or coaches.

Significance Test for Detection of Sequences of Synchronous Events in Massively Parallel Spike Trains

Carlos Canova[1], Emiliano Torre[1], Michael Denker[1], Moritz Helias[1], George Gerstein[2], Sonja Grün[1,3]

[1] **Inst. of Neuroscience & Medicine (INM-6) and Inst. for Advanced Simulation (IAS-6), Jülich Research Center & JARA Brain I, Jülich, Germany**

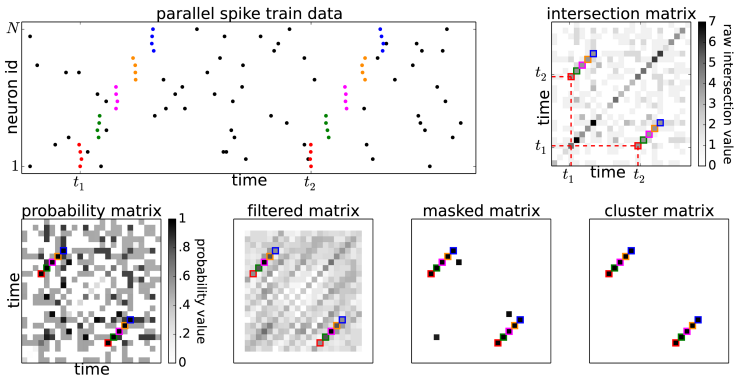
[2] **Department of Neuroscience, University of Pennsylvania, Philadelphia, USA**

[3] **Theoretical Systems Neurobiology, RWTH Aachen University, Aachen, Germany**

Contact: `c.canova@fz-juelich.de`

Keywords: *data analysis; stochastic simulation; pattern detection.*

Schrader et al [1] proposed a method for the detection of a repeatedly active synfire chain (SFC) [2]. After binning of the time axis (bin width of a few ms) of the parallel spike trains, the overlap of neuron ids active in any two bins (i,j) are evaluated and entered at the corresponding time bins in the intersection matrix. A repeated activation of a SFC would appear as diagonal entries with high neuron id overlaps. Active SFCs were identified in that approach by visual inspection. Building on this idea, we worked out an automatized detection of such diagonal structures (DS) and the neuron ids therein based on a mathematical framework that enables the assessment of the significance of the matrix entries. The analysis is composed of a sequence of steps. First we calculate for each pair of bins (i,j) the probability of finding the observed overlap in the matrix element (i,j) given the local firing rates and under the hypothesis of Poisson statistics. In the next step the matrix is filtered by a diagonal filter emphasizing diagonal structures of high entries. The significance of the diagonal structures is evaluated by comparison to randomized matrices, i.e. where the values of the entries are kept but their temporal order is destroyed (see also [3]). Matrix elements that pass both tests are marked as significant. Significant elements which are 'close by' are consecutively belonging clustered into DS. Finally, we extract the neuron ids composing significant DS such that we can identify the (groups of) neurons being part of the SFC and their occurrence times. We calibrate the method via stochastic simulations of parallel activities of many neurons with different non-stationary and non-homogeneous background scenarios and inserted sequences of synchronous events (SSEs). We show that the SSEs are identified with low false negative and low false positive levels. The application to electrophysiological, massively parallel spike data will be demonstrated.



Detecting sequences of synchronous events

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Effective (field) theories as a tool to deal with multi-scale problems

Christoph Hanhart[1,2]

[1] **Institute for Advanced Simulation (IAS-4)**

[2] **IKP-3**

Contact: **c.hanhart@fz-juelich.de**

Keywords: *effective fiel theory; multi-scale problems; analytic methods.*

Effective (field) theories as a tool to deal with multi-scale problems. Effective field theories allow one to systematically analyze multi-scale problems as long as the systems are characterized by a clear separation of scales. On the poster it is demonstrated on various examples that the technology is of great use not only to understand complicated physics systems but also to optimize numerical efforts. This includes extrapolations in parameter space to connect regimes where simulations are cheaper to the real world, calculations of complex systems to isolate quantities that allow for straightforward simulations and how effective theories allow one to interpret certain results found in numerical simulations.

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Bandstructure Theory of Topological Materials

Chengwang Niu[1], **Bihlmayer Gustav**[1], **Daniel Wortmann**[1], **Stefan Blügel**[1], **Yuriy Mokrousov**[1]

[1] **Institute for Advanced Simulation (IAS-1)**

Contact: `c.niu@fz-juelich.de`

Keywords: *topological insulators; topological crystalline insulators; quantum anomalous Hall insulators; Bandstructure Theory; first-principles calculations.*

The topological insulators (TIs), topological crystalline insulators (TCIs), and quantum anomalous Hall insulators (QAHIs) are new classes of quantum states which exhibit metallic boundary states. [1,2] Here, based on first-principles calculations and band structure analyses, we theoretically investigate and predict topological materials with TI, TCI, and QAHI phases. We reveal that the band gap of two-dimensional TIs and QAH states can be as large as 1.01 and 0.35 eV in an H-decorated Bi(111) film. [3] The origin of this giant band gap lies in both the large spin-orbit interaction of Bi and the H-mediated exceptional electronic and structural properties. Moreover, we find that the QAH state also possesses the properties of a quantum valley Hall state, thus intrinsically realizing the so-called valley-polarized QAH effect.

In addition, we predict that monolayers of SnTe, PbTe, TlS, and TlSe can be characterized as two-dimensional TCIs, confirmed by the calculated mirror Chern number n_M = -2 and the emergence of two pairs of gapless edge states in an one-dimensional nanoribbon [4,5]. Embedded in NaCl or NaBr films, both the electronic and topological characteristics can be tuned via the cladding-layer thickness, and the topological characteristics survive even when the middle layers of the quantum wells are also trivial insulators [6]. Remarkably, the electrostatic potential, i.e., Madelung potential of the cladding-layer NaCl (NaBr) acts on the middle layers, leads to the band inversion, resulting in a phase transition from trivial insulator to 2D TCIs. In addition, under uniaxial strain, a topological phase transition between 2D TCIs and 2D TIs is revealed with the calculated spin Chern number C_S = -1 for the 2D TI. [5]

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Investigations of $\Lambda_b^0 \to J/\psi K^-(\pi^-)p$ decays

C. W. Xiao[1]

[1] **Institute for Advanced Simulation (IAS-4)**

Contact: **c.xiao@fz-juelich.de**

Keywords: P_c *states; s-channel contribution; interaction.*

Recently LHCb experiments found two P_c states in the $\Lambda_b^0 \to J/\psi p\pi^-$ decays. In this work, we investigate both the $\Lambda_b^0 \to J/\psi K^- p$ and the $\Lambda_b^0 \to J/\psi p\pi^-$ decays, continuing the investigations of our former works on the interactions of $J/\psi N$ with its coupled channels by considering the s-/u- channel contributions. We obtain consistent results of the line-shape of the $J/\psi N$ invariant mass distribution with the LHCb experiments, and favour the $P_c(4450)$ state as a $\bar{D}^*\Sigma_c$ bound state with $J = 1/2^-$.

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Characterization of small anisotropic colloids by means of time-resolved flow dichroism

Run Li[1], Marisol Ripoll[1], Jan K. G. Dhont[2], Ruben Dierick[3], Zeger Hens[3], Christian Clasen[4], Naveen K. Reddy[4]

[1] **Institute for Advanced Simulation (IAS-2)**

[2] **Soft-Matter, Institute of Complex Systems, Forschungszentrum Jülich, 52425 Jülich, Germany**

[3] **Department of Inorganic and Physical Chemistry, Ghent University, 9000 Ghent, Belgium**

[4] **Department of Chemical Engineering, KU Leuven, Celestijnenlaan 200F, 3001 Leuven,Belgium**

Contact: `ru.li@fz-juelich.de`

Keywords: *Smoluchowki equation; Numerical solution; Flow dichroism; Average size; Polydispersity; Rod-like colloids.*

The average size and size-polydispersity of suspensions of anisotropic colloids that are much smaller than the wavelength of visible light can be determined by means of time-resolved dichroism measurements by applying step-up shear flow [1] to an isotropic and dilute suspension. The time-period of the alternating orientation angle with respect to flow direction, as well as the decay of its amplitude are sensitive to size and polydispersity. Flow dichroism measurements offer a sensitive method for their characterization. We extend previous work[1,2] to rod-like particles of arbitrary aspect ratio by a numerical solution of the rotational Smoluchowki equation with shear flow. The developed algorithm allows us to fit the time-dependent flow dichroism data with respect to the average size and polydispersity of the anisometric colloids in the sample. Experimental data on tumbling of small anisotropic colloids will be presented together with the results of the fits with this new algorithm. These small rods are CdSe-CdS rods, CuInS2 tiles, and CdSe, quantum dots with average dimensions on the order of O(10 nm).

Acknowledgements. *We thank the EU for funding through the project DiStruc (Grant Agreement No 641839)*

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Distribution of pair-wise covariances in neuronal networks

David Dahmen[1], **Markus Diesmann**[1,2,3], **Moritz Helias**[1,2]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Dept. of Psychiatry, Psychotherapy and Psychosomatics, Medical Faculty, RWTH Aachen University, Aachen, Germany**

[3] **Dept. of Physics, Faculty 1, RWTH Aachen University, Aachen, Germany**

Contact: `d.dahmen@fz-juelich.de`

Keywords: *networks; correlations; meta-statistics; beyond self-averaging.*

Massively parallel recordings of spiking activity in cortical networks show that spike count covariances vary widely across pairs of neurons [Ecker et al., Science (2010)]. Their low average is well understood [Renart et al., Science (2010), Tetzlaff et al., PLoS CB (2012)], but an explanation for the wide distribution in relation to the static (quenched) disorder of the connectivity in recurrent random networks was so far elusive. Starting from spin-glass techniques [Sompolinsky and Zippelius, Phys. Rev. B (1982)] and a generating function representation for the joint probability distribution of the network activity [Chow and Buice, J. Math. Neurosci. (2015)], we derive a finite-size mean-field theory that reduces a disordered to a highly symmetric network with fluctuating auxiliary fields. The exposed analytical relation between the statistics of connections and the statistics of pairwise covariances shows that both, average and dispersion of the latter, diverge at a critical coupling. At this point, a network of nonlinear units transits from regular to chaotic dynamics. Applying these results to recordings from the mammalian brain suggests its operation close to this edge of criticality.

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With Computer-Aided Drug Design Towards Selective Inhibitors for ARTD10

Daniela Meister[1,2], Julien Engel[2], Arno Claßen[2], Valeria Losasso[3], Patricia Verheugd[4], Bernhard Lüscher[4], Carsten Bolm[2], Giulia Rossetti[1,5,6]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Institute of Organic Chemistry, RWTH Aachen University, Germany**

[3] **Scientific Computing Department, STFC Daresbury Laboratory, Daresbury, Warrington WA4 4AD, United Kingdom**

[4] **Insitute of Biochemistry and Molecular Biology, University Hospital Aachen, RWTH Aachen University, Germany**

[5] **Department of Oncology, Hematology and Stem Cell Transplantation, University Hospital Aachen, RWTH Aachen University, Germany**

[6] **IAS-5/INM-9: Computational Biomedicine - Institute for Advanced Simulation (IAS) / Institute of Neuroscience and Medicine (INM) Forschungszentrum Jülich, Germany**

Contact: `g.rossetti@fz-juelich.de`

Keywords: *Drug Design; Macrodomains; Docking; Molecular Dynamics Simulations.*

ADP-ribosylation is a post-translational modification in which the ADP-ribose moiety of NAD^+ is transferred onto a substrate protein.[1] This transformation is performed by, amongst other, ADP-ribosyl transferases (ARTDs). Depending on the sequence of a three amino acid signature in the active center, ARTDs have been classified as mono- and poly-ADP-ribosyl transferases.[2] ARTD10 is a mono-ADP-ribosylating enzyme, that participates in DNA repair, signaling pathways of NFκB- and GSK3β and interacts with cMyc.[3,4,5,6] Therefore, the search of selective ARTD10 inhibitors is an emerging field of research in medicinal chemistry.[7,8,9] Recently, Lehtiö and coworkers revealed that OUL-35 is a potential selective ARTD10 inhibitor.[10]

Here we show the results of molecular dynamics simulations on ARTD10 with OUL-35 and 3-aminobenzamide, an unselective inhibitor for the ARTD-family.[11,12,13] Moreover, we established a QSAR[14,15] model to reveal further potential inhibitors. This identification of structural determinants of ARTD10 inhibition is a key information for future research on selective inhibitors for the ARTD protein family.

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A Massively Parallel Hybrid Car-Parrinello QM/MM Interface

Jógvan Magnus Haugaard Olsen[3], Viacheslav Bolnykh[1,2,4,7], Simone Meloni[5], Emiliano Ippoliti[1,2], Paolo Carloni[1,2,4], Teodoro Laino[8], Valery Weber[8], Alessandro Curioni[8], Ursula Rothlisberger[6]

[1] **Institute for Advanced Simulation (IAS-5)**

[2] **INM-9**

[3] **University of Southern Denmark, Odense M, Denmark**

[4] **RWTH Aachen University, Germany**

[5] **Sapienza University of Rome, Italy**

[6] **EPFL, Lausanne, Switzerland**

[7] **CaSToRC, The Cyprus Institute, Nicosia, Cyprus**

[8] **IBM, Zurich Research Laboratory, Zurich, Switzerland**

Contact: **v.bolnykh@fz-juelich.de**

Keywords: *QM/MM interface; CPMD code; multiscale approach.*

Many quantum biological applications (e.g. simulations of enzymatic reactions) usually require dealing with large systems (typically of the order of 10^4˘10^5 atoms), making first principles quantum mechanical strategies far too costly. This motivates using a multiscale approach, in which the part of the system that is of particular interest (e.g. the active site of an enzymatic reaction) is treated at quantum level (QM part), while the rest of the system is handled by a classical force field (MM part). Such a hybrid QM/MM approach allows a significant decrease of the size of the computationally expensive part, while keeping the ability to represent the processes that can only be treated by quantum chemistry (e.g. chemical reactions). Unfortunately, most of the current implementations of QM/MM codes do not scale very well, limiting tremendously the domain of applications of this otherwise very powerful approach. In an effort at coding a truly HPC code, we are building a coupling scheme based on the CPMD code [1]. This is a highly efficient massively parallel first-principles (quantum) molecular dynamics software package. It can scale up to a few million threads with extremely high efficiency [2]. The current implementation of such a multiscale modeling QM/MM method in CPMD has a set of issues that prevent its usage on large-scale neurobiological applications. First, the scalability of the MM description is limited, thus, simulating large systems becomes time consuming. Second, the number of classical force fields that can be used is restricted to AMBER [3] and GROMOS96 [4] formats. Finally, because of the tight coupling of CPMD to routines from the GROMOS96 [5] code, which is used to handle the classical part of the simulation, the user needs to buy a commercial GROMOS96 license in order to be able to run QM/MM simulations. We are currently developing a new QM/MM interface using a loose coupling scheme to connect CPMD with a generic client MM code. The loose coupling requires the use of a communication layer in order to establish data interaction between the independent codes. This approach allows us to benefit from the highly efficient parallelization schemes of both CPMD and the MM code. It also provides us with a flexible and easily extendable framework that potentially will allow the support of any kind of MM code and any type of force field. Finally, the loose coupling allows overriding licensing issues that can arise when coupled codes have not permissive licenses.

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Optical conductivity of ruthenate oxides: spin-orbit and anistropic Coulomb interaction effects

Esmaeel Sarvestani[1], **Guoren Zhang**[1], **Evgeny Gorelov**[1], **Eva Pavarini**[1,2]

[1] **Institute for Advanced Simulation (IAS-3)**

[2] **JARA High-Performance Computing, RWTH Aachen University, 52062 Aachen, Germany**

Contact: `e.sarvestani@fz-juelich.de`

Keywords: *Optical conductivity; Ruthenate oxides; LDA+DMFT.*

When an electromagnetic field is applied to an electron system, a charge-current is induced in the system. The induced current is proportional to the applied electric field. The *optical conductivity* is the quantity which links the external electric field to the current induced in the system. The Kubo formula, in the linear response theory, expresses the conductivity in terms of the current-current correlation function.
In this work we calculate the in-plane and out-of-plane optical conductivity for two materials: single-layered and double-layered ruthenate oxides, Sr_2RuO_4 and $Sr_3Ru_2O_7$. To this end, we use the combination of density functional theory and dynamical mean-field theory. We investigate the effects of the electron-electron interaction, the spin-orbit coupling and the low- symmetry Coulomb interaction in the optical spectra. We show that including the spin-orbit coupling improves the agreement with experimental data while the anisotropic Coulomb interaction does not change the in-plane optical spectrum. We find that, contrary to the out-of-plane conductivity, the in-plane conductivity changes considerably by changing temperature and Coulomb interaction and by including the spin-orbit coupling. We explain the difference in the behaviour of in-plane and out-of-plane conductivities in terms of the corresponding non-interacting transport functions.

DPDE Simulation of Thermophoretic Particles

Fatemeh Alidadi Soeymani[1], **Fedosov Dmitry**[1], **Marisol Ripoll**[1], **Gerhard Gompper**[1]

[1] **Institute for Advanced Simulation (IAS-2)**

Contact: `f.alidadi.soleymani@fz-juelich.de`

Keywords: *Janus particles; thermophoretic phenomena; DPDE(Dissipative Particle Dynamics with Energy conservation).*

DPDE Simulation of Thermophoretic Particles. Collisions of suspended micro-particles with molecules leads to Brownian motion or particle diffusion. Additionally self-propelled particles take up energy from their environment and convert it into directed motion[1]. Examples range from chemotactic cells and bacteria to artificial micro-swimmers. Artificial systems are be powered, e.g., by artificial flagella[2] or magnetic field[3]. Another approach is physico-chemical, where non-equilibrium concentration fields or temperature distribution[4] in the fluid environment are generated around the swimmer and are employed for propulsion, without any movable parts of the swimmer itself. Janus particles with a gold capped illuminated by light in a fluid perform active motion[5]. We try to investigate the behavior of a thermophoretic janus colloid in its own temperature gradient using dissipative particle dynamics method with energy conservation (DPDE). The simulation results show how local fluid-colloid interactions and temperature gradients near the colloid's surface control its swimming velocity[6].

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Ligand binding to human bitter taste receptors studied by multiscale molecular dynamics simulations

Fabrizio Fierro[1,2], Thomas Tarenzi[1,2], Eda Suku[3], Vania Calandrini[1,2], Alejandro Giorgetti[3], Paolo Carloni[1,2]

[1] **Institute for Advanced Simulation (IAS-5)**

[2] **Institute of Neuroscience and Medicine (INM-9)**

[3] **Department of Biotechnology, University of Verona, Ca' Vignal 1, Strada le Grazie 15, 37134 Verona, Italy**

Contact: `f.fierro@fz-juelich.de`

Keywords: *bitter taste receptors; molecular dynamics simulations; protein/ligand interaction.*

The perception of bitter taste in mammals occurs through specific receptors belonging to the G-protein coupled receptors (GPCRs) family, the largest family of plasma membrane receptors (including 800 members in human genome) (1). Bitter taste receptors (TAS2Rs, 25 members in humans) accomplish this function by binding small molecules to their 7-transmembrane (7-TM) helix bundle. The structural determinants of TAS2Rs and their complexes with agonists are mostly lacking. Homology modeling and docking approaches are then the method of choice to get structural insight on TAS2Rs and on their binding cavity. However, because of the low sequence identity (13-20%) between templates and targets, the resulting receptors' models can be quite inaccurate (2). In order to improve the reliability of the structural prediction of protein/ligand complexes, we use a hybrid molecular mechanics/coarse-grained (MM/CG) scheme developed by us (3). This MM/CG approach provides the atomic description of the intermolecular ligand/protein interactions and it is appropriate for homology models (4, 5). In particular, by restricting the atomistic representation to a limited region of interest (the binding site), MM/CG simulations allow side chains to relax much more quickly than in an all-atom simulation. Our work will focus on characterization of human bitter taste receptors across all the receptor/agonist complexes for which experimental data (site-directed mutagenesis) are available. Specifically, we plan to predict the binding poses for the agonists and mapping the critical residues/positions involved in agonist binding. This study will help find common traits across TAS2Rs members, as well as to rationalize their different specificities. Understanding the nature of the intermolecular interactions between human bitter taste receptors and their agonists may provide important hints on the effect of genetic variability on bitter taste sensing, as well as a new opportunity for designing more subtype-specific ligands.

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Simulations for testing the validity of the Jarzynski relation for non-Gibbsian initial states in isolated quantum spin systems

F. Jin[1], R. Steinigeweg[2], H. De Raedt[3], K. Michielsen[1,5], M. Campisi[4], J. Gemmer[2]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Department of Physics, University of Osnabrück, D-49069 Osnabrück, Germany**

[3] **Zernike Institute for Advanced Materials, University of Groningen, NL-9747AG Groningen, The Netherlands**

[4] **NEST, Scuola Normale Superiore & Istituto Nanoscienze-CNR, I-56126 Pisa, Italy**

[5] **RWTH Aachen University, D-52056 Aachen, Germany**

Contact: `f.jin@fz-juelich.de`

Keywords: *Jarzynski relation; Quantum spin system; Simulation.*

Quantum spin systems provide rich opportunities to study properties of collective quantum behavior. There exist various numerical algorithms to simulate the real- and imaginary-time evolution of quantum spin systems, such as the second-order product formula [1] and Chebyshev polynomial algorithms [2]. These algorithms can easily simulate systems with up to 36 spins on current supercomputers. The system size is much larger than the size one can simulate with the exact diagonalization approach. We present large-scale simulation results for a spin ladder system to test the validity of the Jarzynski relation for non-Gibbsian initial states [3].

Since the introduction of the Jarzynski equality many derivations of this equality have been presented in both, the classical and the quantum context. While the approaches and settings greatly differ from one to another, they all appear to rely on the initial state being a thermal Gibbs state. Here, we present an investigation of work distributions in driven isolated quantum systems, starting off from pure states that are close to energy eigenstates of the initial Hamiltonian. We find that, for the nonintegrable system in quest, the Jarzynski equality is fulfilled to good accuracy.

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How network structure shapes responses to oscillatory stimuli

Hannah Bos[1,2], **Jannis Schuecker**[1,2], **Moritz Helias**[1,2,3]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Institute of Neuroscience and Medicine (INM-6), Jülich Research Centre, 52425 Jülich, Germany**

[3] **Department of Physics, Faculty 1, RWTH Aachen University, 52074 Aachen, Germany**

Contact: `h.bos@fz-juelich.de`

Keywords: *oscillations; neural network; mean-field theory.*

Applications of oscillatory stimuli in optogenetical studies have been used to gather evidence that γ oscillations are generated by the interaction of inter-neurons (also termed the inter-neuron γ or ING mechanism) [1,2]. We elaborate the pitfalls of inferring the origin of the oscillation from absolute (response spectra) as well as relative (power ratios) changes in spectra of neural activity induced by oscillatory input. We consider minimalistic models that isolate the difficulties and limitations arising in the interpretation of response spectra. The described effects generalize to more realistic models. This is demonstrated in simulations of a multi-laminar model of V1 composed of leaky-integrate- and-fire (LIF) model neurons [3], where the ground truth regarding the sub-circuits generating the oscillations is known [4]. In this structured model these effects combine and yield misleading results. By extending mean-field theoretical descriptions of population dynamics [5] by oscillatory input, we can close the loop to the condensed models. We identify three main complications: First, the input can modify the excitability of the population in a linear or non-linear fashion, yielding significantly different changes in the spectra. Second, depending on the properties of the system, the input to the populations is potentially low pass filtered before it enters the system. Since this low pass filter is reflected in the response spectra, without revealing information regarding the internal dynamics of the network, we propose a stimulation protocol counteracting this effect by emphasizing high frequencies. Third, in general, the stimulation of a single population excites a mixture of dynamical modes. One frequency is generated by one dynamical mode that can be mapped to its anatomical origin [4]. Since the observable response is composed of an inseparable mixture of modes, the mode generating the oscillation cannot easily be isolated. Hence reconstructing the underlying connectivity as well as identifying the role of the stimulated population in the generation of the rhythm is not straightforward. Instead, the stimulus vector needs to reflect the structure of the circuit generating the oscillation in order to allow insights into the dynamically relevant components of the system. These problems can be regarded as a sub-set of challenges that need to be faced when interpreting the results of circuits composed of more complex units. The proposed solutions may be used to construct new experimental stimulation protocols.

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Jacobi No-core Shell Model for Hypernuclei

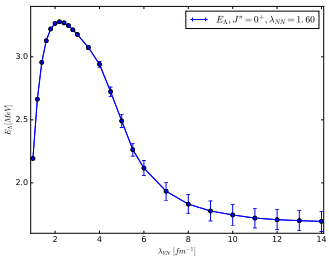
Hoai Le[1]

[1] **Institute for Advanced Simulation (IAS-4)**

Contact: `h.le@fz-juelich.de`

Keywords: *No-core shell model; hypernuclei; Similarity renormalization group.*

In this poster, I present our first results for hypernuclei up to $A = 5$ using the translationally invariant Jacobi no-core shell model (NCSM). I start with a brief introduction to the method focusing on the computational needs. In our calculations, we employ the realistic chiral based nucleon-nucleon and hyperon-nucleon interactions. To accelerate the convergence of the method, the Hamiltonian is evolved via a similarity renormalization group (SRG). The SRG dependences for ${}^{4}_{\Lambda}$He (see Fig.1) and ${}^{5}_{\Lambda}$He are shown, and the implications for further calculations are discussed.



Dependence of Λ-seperation energy on the SRG cutoff λ_{YN} for ${}^{4}_{\Lambda}$He, $J^\pi = 0^+$

Time Evolution of Kondo Impurity Systems in Response to General Pulses

Hoa Nghiem[1], **Theo Costi**[1]

[1] **Institute for Advanced Simulation (IAS-3)**

Contact: `h.nghiem@fz-juelich.de`

Keywords: *numerical renormalization group; time evolution of Kondo impurity system.*

We generalize the time-dependent numerical renormalization group method (td-NRG) to study the time evolution of an observable of interacting quantum impurity system after a sudden quench at an arbitrary temperature without truncating the length of Wilson chain [1]. This generalization requires the use of the full density matrix, and determining all the terms of the projected density matrix appearing in the time evolution. To evaluate these terms, we introduce the recursion relations which are efficient for calculating. The numerical results show to be exact at the short time limit, while, at the long time limit, strongly depend on the discretization parameter of NRG. We also consider the time evolution due to general pulses, which vary continuously in a finite time interval [2]. The calculation is done by discretizing a pulse into a sequence of small quenches, and generalizing the td-NRG to an arbitrary number of quenches.

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NESTML: A modeling language for spiking neurons

Inga Blundell[1], **Dimitri Plotnikov**[2,3], **Jochen Martin Eppler**[2], **Abigail Morrison**[1,2,4], **Bernhard Rumpe**[3,5]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Jülich Supercomputing Centre (JSC)**

[3] **RWTH Aachen University, Chair of Software Engineering, Jülich Aachen Research Alliance (JARA), Aachen, Germany**

[4] **Ruhr-University Bochum, Faculty of Psychology, Institute of Cognitive Neuroscience, Bochum, Germany**

[5] **Fraunhofer FIT, Aachen, Germany**

Contact: `i.blundell@fz-juelich.de`

Keywords: *Simulation; NESTML; NEST; Neuroscience; Biological neural networks; code generation.*

Biological nervous systems exhibit astonishing complexity. Neuroscientists aim to capture this complexity by modeling and simulation of biological processes. Often very complex models are necessary to depict the processes, which makes it difficult to create these models. Powerful tools are thus necessary, which enable neuroscientists to express models in a comprehensive and concise way and generate efficient code for digital simulations. Several modeling languages for computational neuroscience have been proposed [1, 2]. However, as these languages seek simulator independence they typically only support a subset of the features desired by the modeler. In this article, we present the modular and extensible domain specific language NESTML, which provides neuroscience domain concepts as first-class language constructs and supports domain experts in creating neuron models for the neural simulation tool NEST. NESTML and a set of example models are publically available on GitHub.

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Functional classification of homologous basal-ganglia networks

Jyotika Bahuguna[1], **Tom Tetzlaff**[1], **Arvind Kumar**[2,3], **Jeanette H. Kotaleski**[3], **Abigail Morrison**[1,2]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Computational Neuroscience, Bernstein Center Freiburg, Freiburg, 79104, Germany**

[3] **Computational Brain Science, Dept. of Computational Science and Technology, School of Computer Science and Communication, KTH, Royal Institute of Technology, Stockholm.**

Contact: `j.bahuguna@fz-juelich.de`

Keywords: *Basal ganglia; Firing rate models.*

The basal ganglia (BG) are a set of nuclei that play an important role in motor and cognitive functions. Indeed many brain diseases such as Parkinson's disease (PD) can be attributed to dysfunction of one or more BG nuclei. The classical model of basal ganglia has been regularly updated with discoveries of new sub-populations within a nucleus or new projections from existing nuclei in recent years. It is unclear how these new insights on the structure of the BG network foster our understanding of its function. The effective connectivities among these recently identified BG sub-populations are only partially known. In the framework of a simple firing-rate model subjected to a genetic algorithm, we identified effective BG connectivities which are consistent with experimentally established firing-rate and phase relationships in Subthalamic Nucleus (STN) and two GPe subpopulations (arkypallidal [GPe-TA] and prototypical [GPe -TI]) in both healthy and PD states [1].This is in extension to an earlier model that identified effective connectivities for the STN-TA-TI- sub circuit [2].

As expected, we found that multiple parameter combinations can fit the data [1]. We re-classified these homologous networks that reproduced the healthy and PD state, on the basis of two dynamical features: suppression of GPi activity and susceptibility of the BG network to oscillate in the presence of cortical input. These features were chosen because task execution requires GPi suppression while oscillations in the STN-GPe subnetwork are characteristic of PD. We found that most putative pathological networks showed insufficient suppression of GPi activity and high susceptibility to oscillations whereas most putative healthy networks showed sufficient suppression of GPi activity and low susceptibility to oscillations. This is consistent with experimental data that shows that lack of GPi suppression [3] or oscillations [4,5] is correlated with Parkinsonian symptoms such as stymied movement and tremor. A small fraction of networks, however, in both cases show deficiency in only one of the features. This could indicate the configurations of healthy networks that might be more pathology prone and in contrast configurations of pathological networks that might be easier to push into a healthy state. Further analysis of estimated BG connectivity revealed that transitions between the putative PD and healthy networks were possible by modifying the strength of the relevant projections. Most of the transitions involved changes in corticostriatal, striatopallidal and pallidopallidal projections.Finally, the variance observed in the functional classification of putative pathological and healthy networks might hint at the variance observed in manifestation of Parkinson's disease (PD).

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The AiiDA plug-in for the FLEUR code and its first application on fusion relevant materials

Jens Bröder[1,2], Gregor Michalicek[1], Daniel Wortmann[1], Martin Köppen[2], Christian Linsmeier[2], Stefan Blügel[1]

[1] **Institute for Advanced Simulation (IAS-1)**

[2] **Institut für Energie- und Klimaforschung – Plasmaphysik, Forschungszentrum Jülich GmbH, 52425 Jülich, Germany**

Contact: `j.broeder@fz-juelich.de`

Keywords: *FLEUR; DFT; FLAPW; AiiDA; material design; PostgreSQL.*

In this poster we present the AiiDA [1] (Automated Interactive Infrastructure and Database for Computational Science) plug-in for the all-electron linearized augmented plane-wave density-functional theory code FLEUR [2]. The interface layout and some common usage examples of the important classes are shown.

Adapted to the usage of the FLEUR code, the plug-in consists of three parts: one for the FLEUR input generator, one part for FLEUR, and a data structure called FleurinpData. Everything is fully implemented in python and stands under the MIT license. Further we point out the benefit for creating a reference database of materials relevant to plasma wall interaction in a fusion reactor. Which will be one of the first use cases for the plug-in.

One of the key challenges for the lifetime prediction of future fusion devices, like e.g. ITER lies in understanding the evolution of wall materials mostly consisting of W and Be. Here, experiments performing a chemical analysis by photoelectron spectroscopy are very important. Density functional theory simulations with an all-electron code can assist by relating the measured core-level shift to the chemical environment and therefore support the evaluation of such core-level spectra. For many relevant materials literature data is scarce and therefore broad-scale and reliable predictions from simulations are important.

Acknowledgements. *We acknowledge financial support in part from MAX (Materials design at the eXascale) Horizon 2020 EINFRA-5.*

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Effect of Heterogeneity on Decorrelation Mechanisms in Spiking Neural Networks: A Neuromorphic-Hardware Study

Jakob Jordan[1], **Thomas Pfeil**[2], **Tom Tetzlaff**[1], **Andreas Grübl**[2], **Johannes Schemmel**[2], **Markus Diesmann**[1,3,4], **Karlheinz Meier**[2]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Kirchhoff-Institute for Physics, Heidelberg University, 69120 Heidelberg, Germany**

[3] **Department of Psychiatry, Psychotherapy and Psychosomatics, Medical Faculty, RWTH Aachen University, 52074 Aachen, Germany**

[4] **Department of Physics, Faculty 1, RWTH Aachen University, 52074 Aachen, Germany**

Contact: `j.jordan@fz-juelich.de`

Keywords: *neuromorphic hardware; simulations; correlations; noise.*

High-level brain function such as memory, classification or reasoning can be realized by means of recurrent networks of simplified model neurons. Analog neuromorphic hardware constitutes a fast and energy efficient substrate for the implementation of such neural computing architectures in technical applications and neuroscientific research. The functional performance of neural networks is often critically dependent on the level of correlations in the neural activity. In finite networks, correlations are typically inevitable due to shared presynaptic input. Recent theoretical studies have shown that inhibitory feedback, abundant in biological neural networks, can actively suppress these shared-input correlations and thereby enable neurons to fire nearly independently. For networks of spiking neurons, the decorrelating effect of inhibitory feedback has so far been explicitly demonstrated only for homogeneous networks of neurons with linear sub-threshold dynamics. Theory, however, suggests that the effect is a general phenomenon, present in any system with sufficient inhibitory feedback, irrespective of the details of the network structure or the neuronal and synaptic properties.

Here, we investigate the effect of network heterogeneity on correlations in sparse, random networks of inhibitory neurons with non-linear, conductance-based synapses [Pfeil et al. (2016), Phys. Rev. X 6, 021023]. Emulations of these networks on the analog neuromorphic hardware system Spikey allow us to test the efficiency of decorrelation by inhibitory feedback in the presence of hardware-specific heterogeneities. The configurability of the hardware substrate enables us to modulate the extent of heterogeneity in a systematic manner. We selectively study the effects of shared input and recurrent connections on correlations in membrane potentials and spike trains. Our results confirm that shared-input correlations are actively suppressed by inhibitory feedback also in highly heterogeneous networks exhibiting broad, heavy-tailed firing-rate distributions. In line with former studies, cell heterogeneities reduce shared-input correlations. Overall, however, correlations in the recurrent system can increase with the level of heterogeneity as a consequence of diminished effective negative feedback.

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Perfect detection of spikes via time-reversal

Jeyashree Krishnan[1,2,3], **Pier Gian Luca Porta Mana**[1,2], **Moritz Helias**[1,2], **Markus Diesmann**[1,2], **Edoardo Di Napoli**[3,4]

[1] **Institute of Neuroscience and Medicine(INM)-6**

[2] **Institute for Advanced Simulation (IAS-6)**

[3] **Aachen Institute for advanced study in Computational Engineering Science (AICES)**

[4] **Jülich Supercomputing Centre (JSC)**

Contact: `j.krishnan@fz-juelich.de`

Keywords: *NEST; precise models; LIF neuron; time-driven simulations; state-space analysis.*

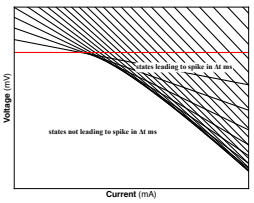
In the discrete-time of the NEST simulator [1,2], the dynamics of each neuron is propagated by a pre-defined simulation step. Various pitfalls of this approach such as artificial synchronization have been addressed previously by embedding event-driven methods in a globally time-driven simulation[4,5] applicable to a certain class of neuron models [3] whose sub-threshold dynamics can be exactly integrated by applying methods that process spikes in continuous-time.

However, the accuracy of these continuous-time "precise" models of the NEST simulator has not been systematically investigated yet. One source of imprecision is the possibility to miss spikes caused by brief and unnoticed excursions of the membrane potential beyond threshold. We here develop a new spike detection algorithm based on state-space analysis of variables governing the linear system of a LIF neuron with exponential currents.

Conventional spike detection methods in time-driven simulations propagate the state of neuron forward i.e. from t to $t + \Delta t$ (or) $t_{\text{incoming\_event}}$ and check whether there has been a threshold crossing only at the end of time interval. If the neuron dynamics is such that its voltage is below threshold at t and $t + \Delta t$ (or) $t_{\text{incoming\_event}}$ and supra-threshold between, this leads to a spike miss. The idea of this work is to understand whether such voltage excursions occur and if so, how frequent they are and what is their effect on accuracy the of the LIF model.

Instead of propagating the neuron state forward, we propagate the threshold plane backward in time to find the set of initial conditions (spiking states) that would cross threshold in the future. By doing so, we get two distinct regions in state-space: the initial states leading to a spike, and those not leading to a spike, within a simulation step as illustrated in Fig(1).

This algorithm confirms that the precise LIF model in NEST rarely misses spikes. The reason is that frequently arriving synaptic impulses effectively induce a fine-grained grid of check points making brief excursions above threshold extremely unlikely.



In state space, back-propagation of the threshold plane (red line) swipes the spiking region (states that lead to spikes in $\Delta t ms) and non-spiking region (states not leading to spikes in $t ms)

Acknowledgements. *This work was supported by DFG Grant: GSC11; Helmholtz association: VH-NG-1028 and SMHB; EU Grant 604102 (HBP); Juelich Aachen Research Alliance (JARA).*

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Towards Flexible Open Data Management Solutions

Jedrzej Rybicki[1], **Benedikt von St Vieth**[1]

[1] **Jülich Supercomputing Centre (JSC)**

Contact: `j.rybicki@fz-juelich.de`

Keywords: *data management; object stores; graph databases; search algorithms.*

The requirement to share research data is becoming commonplace for many reasons. In the first line, such sharing enables the verification of obtained results by facilitating repeatability, and reproducibility. Also economical aspects are important: Data reuse can reduce the research costs. The implementation of data sharing is, however, quite challenging. It demands both storage resources and services that can deal with the increasing amounts of data in an efficient and cost-effective way while remaining user-friendly. We would like to present our experiences and solutions from the field of research data management.

A very promising technology for storing different kinds of data are object stores. They offer scalability, cost-effectiveness, maintainability, and extensibility. In short, data objects are stored in a distributed system of interdependent storage elements. Since the objects are distributed across available resources with help of hash functions, workload is spread evenly across the storage elements and “hot spots” are avoided. The far-reaching autonomy of the storage elements increases fault-tolerance and throughput as transfers from/to different storages are independent from each other. Although object stores are widely used, there is an aspect of their operation which is not yet properly addressed. It is the object replication across different administrative domains. Such a replication is surprisingly popular for scientific data. Many times community data centers require additional replicas of their data in generic data centers (like JSC) for data safety reasons. At the same time, they want to keep the local copies to maintain control over the data. We would like to present a solution to this problem which we implemented in the EUDAT Project.

Object stores have many advantages. The advantages come, however, at the cost of some limitations. Probably the most important one, from a users perspective, is the lack of hierarchical directory structure as known from file systems. Object identifiers are used to address data form a “flat” space. We address this challenge and enabled flexible namespaces for research data which are independent from the way the data are stored. We are convinced that it is vital to account for all kinds of storages, especially those which provide only limited namespaces, like object stores. On the other hand, for the same set of data different namespaces could be created (e.g. different researchers can have different views on the same data). This requirement is not easily supported even by modern file systems.

One way of creating flexible namespaces is to use graph databases. Graphs are very powerful abstractions often used in computer science. They can capture different domain models i.e., views on the data. Graphs can also be used for efficient search. Currently, the most popular approaches to search research data are based on indexing of metadata. This reassembles the very beginning of the Internet search engines, where also keyword-based indexes were used. The revolution of the Internet search started by Google was propelled by graph algorithms. Google uses a graph-based heuristics to identify the most popular web pages containing a phrase searched for. The popularity metrics works very well with web pages but might not be the best option for research data. Researchers could, for instance, be more interested in the least popular data which were not analyzed very often and they have potential to generate new findings. To this end, we work on the possibility to give the users power to run their own search algorithms on the stored data.

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Transition to chaos in random neural networks in the presence of noise

Jannis Schuecker[1], **Sven Goedeke**[1], **Moritz Helias**[1,2]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Department of Physics, Faculty 1, RWTH Aachen, Aachen, Germany**

Contact: `j.schuecker@fz-juelich.de`

Keywords: *Random neural network; Chaos; Noise.*

Networks of randomly coupled rate neurons display a transition to chaos at a critical coupling strength [1]. These networks exhibit optimal information processing capabilities close to the transition – at the edge of chaos – and have been a focus both in neuroscience and machine learning. In the absence of noise or time-dependent inputs the transition is well understood by a dynamical mean-field theory describing the fluctuations of a single unit [1]. In particular, the transition to chaos occurs exactly when the trivial fixed point becomes unstable and hence can be predicted by linear stability analysis. Moreover, chaos is uniquely indicated by a decaying autocorrelation function. However, in nature and technology, these networks operate in the presence of noise or time-dependent inputs, rendering their dynamics stochastic or nonautonomous.

Previously it was found that noise shifts the transition to chaos to larger coupling strengths in simpler discrete-time systems [2], where the critical coupling corresponds to the point at which the system becomes locally unstable. The absence of temporal correlations on the one hand greatly simplifies the analysis, but on the other hand makes it impossible to transfer the results to continuous-time systems considered here. Kadmon et al. [3] studied the effect of small noise on the autocorrelation function and showed that noise smooths the transition. However, the fundamental mechanism by which noise affects the maximum Lyapunov exponent and the location of the transition are not understood.

Here, we investigate the effect of additive white noise on the transition to chaos. We develop the corresponding dynamical mean-field theory yielding the self-consistent autocorrelation function. As expected, the autocorrelation function always decays due to the noise and cannot be used as an indicator for chaotic dynamics. A transition to chaos must therefore be qualitatively different from the noiseless case. To find the transition we determine the maximum Lyapunov exponent, which describes the asymptotic growth of infinitesimal perturbations also for stochastic dynamics. We derive an exact condition for the transition from stable to chaotic dynamics. The transition is shifted to significantly larger coupling strengths than predicted by linear stability analysis of the local Jacobian matrix. This hints toward a dynamic mechanism by which noise suppresses chaos in continuous-time systems [4].

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A Simulation-Analysis Workflow for Computational Neuroscience integrated into a Collaboration Platform

Johanna Senk[1,11], Alper Yegenoglu[1,11], Olivier Amblet[2], Yury Brukau[2], Andrew Davison[3], David Lester[4], Anna Lührs[5], Pietro Quaglio[1], Vahid Rostami[1], Andrew Rowley[4], Bernd Schuller[5], Alan Stokes[4], Sacha J. van Albada[1], Daniel Zielasko[6,7], Markus Diesmann[1,8,9], Benjamin Weyers[6,7], Michael Denker[1], Sonja Grün[1,10]

[1] **Institute of Neuroscience and Medicine (INM-6) and Institute for Advanced Simulation (IAS-6) and JARA BRAIN Institute I, Forschungszentrum Jülich, Jülich, Germany**

[2] **Human Brain Project, École Polytechnique Fédérale de Lausanne, Geneva, Switzerland**

[3] **3 Unité de Neurosciences, Information et Complexité (UNIC), Centre National de la Recherche Scientifique, Gif-sur-Yvette, France**

[4] **Dept. of Computer Science, University of Manchester, Manchester, United Kingdom**

[5] **Jülich Supercomputing Centre (JSC), Forschungszentrum Jülich, Jülich, Germany**

[6] **Visual Computing Institute, RWTH Aachen University, Aachen, Germany**

[7] **JARA - High-Performance Computing, Aachen and Jülich, Germany**

[8] **Dept. of Psychiatry, Psychotherapy and Psychosomatics, Medical Faculty, RWTH Aachen University, Aachen, Germany**

[9] **Dept. of Physics, Faculty 1, RWTH Aachen University, Aachen, Germany**

[10] **Theoretical Systems Neurobiology, RWTH Aachen University, Aachen, Germany**

[11] **equal contribution**

Contact: `j.senk|a.yegenoglu@fz-juelich.de`

Keywords: *high-performance computing; workflows; collaboration; simulation; neuromorphic hardware; comparative data analysis.*

Workflows for the acquisition and analysis of data in the natural sciences exhibit a growing degree of complexity and heterogeneity, are increasingly performed in large collaborative efforts, and often require the use of high-performance computing (HPC). Here, we explore the reasons for these new challenges and demands and discuss their impact with a focus on the scientific domain of computational neuroscience [1]. We argue for the need for software platforms integrating HPC systems that allow scientists to construct, comprehend and execute workflows composed of diverse processing steps using different tools. As a use case we present a concrete implementation of such a complex workflow, covering diverse topics such as HPC-based simulation using the NEST software [2], access to the SpiNNaker neuromorphic hardware platform [3], complex data analysis using the Elephant library [4], and interactive visualizations. Tools are embedded into a web-based software platform under development by the Human Brain Project, called Collaboratory [5]. On the basis of this implementation, we discuss the state-of-the-art and future challenges in constructing large, collaborative workflows with access to HPC resources.

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odML-tables: A graphical approach to metadata management based on odML

Julia Sprenger[1], **Carlos Canova**[1], **Jana Pick**[1], **Lyuba Zehl**[1], **Sonja Grün**[1,2], **Michael Denker**[1]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Theoretical Systems Neurobiology, RWTH Aachen University, Germany**

Contact: `j.sprenger@fz-juelich.de`

Keywords: *Metadata Management; odML; Data Analysis.*

Central to quantitative sciences is the measurement of data with the aim to capture empirical, experimental observations or the outcome of model simulations. These primary data, and derived data resulting from post-processing steps, are always accompanied by information about the origin of the data and the circumstances of recording. Such information is typically called metadata. It is relevant to facilitate the communication between members of a project and is essential for the interpretation of the data. Metadata also enables queries to answer scientific questions that researchers did not previously consider (e.g. transversal studies) and is one of the main components to realize reproducibile science [1]. In neuroscience, and in particular experimental neurophysiology, the development of approaches to metadata management are still an ongoing effort [2]. A promising metadata framework in this field is odML (open metadata Markup Language) [3]. This XML-based language is designed to represent complex metadata collections hierarchically organized as key-value pairs.

In practice however, embedding odML-based metadata within multiple collaborations of INM-6 [4] revealed that setting up an odML document involves extensive programming and the manual entry of metadata into it during or after the experiment is cumbersome. The lack of software support effectively prevented our experimental partners from using odML to capture metadata into one coherent collection. To address this shortcoming, we developed odML-tables, a software solution that bridges the gap between hierarchical odML and a tabular representation of metadata and which is suitable for easy editing.

odML-tables is accessible by a graphical user interface as well as from a Python interface and offers multiple features which simplify the generation and modification of odML metadata files:

- Generation of a template (tabular) structure facilitating the initial design of an odML structure
- Conversion of existing odML files to more easily accessible tabular formats (.xls, .csv) in order to enable manual entry and modifications using common graphical software tools (e.g., Microsoft Excel, LibreOffice).
- Reverse transformation of the modified data in a standardized tabular format to the odML format
- Filtering odML metadata by defined search criteria to generate overview files or simplify access parts of a complex odML structure
- Merging of multiple odML files
- Generation of a comparison table of similar entries within an odML file

We show how odML-tables serves to complement a sustainable workflow for metadata management in an example use case, where we illustrate the practical usage of odML-tables ranging from structuring available metadata to daily enrichment of the metadata collection (cf. also [1,2]).

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Stochastic Sampling Method: Analytic Continuation of Quantum Monte Carlo Data

Khaldoon Ghanem[1], **Erik Koch**[1]

[1] **Jülich Supercomputing Centre (JSC)**

Contact: `k.ghanem@fz-juelich.de`

Keywords: *analytic continuation; QMC data; stochastic sampling; bayesian inference.*

We apply Bayesian inference to the analytic continuation of quantum Monte Carlo (QMC) data from the imaginary axis to the real axis. Demanding a proper functional Bayesian formulation of any analytic continuation method leads naturally to the stochastic sampling method (StochS) as the Bayesian method with the simplest prior, while it excludes the maximum entropy method and Tikhonov regularization.

We present a new efficient algorithm for performing StochS that reduces computational times by orders of magnitude in comparison to earlier StochS methods. We apply the new algorithm to a wide variety of typical test cases: spectral functions and susceptibilities from DMFT and lattice QMC calculations. Results show that StochS performs well and is able to resolve sharp features in the spectrum.

Added value in convection-permitting WRF climate simulations for central Europe

Sebastian Knist[1,2,4], **Klaus Goergen**[3,4], **Clemens Simmer**[2,4]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Meteorological Institute, University of Bonn, Germany**

[3] **Agrosphere (IBG-3), Forschungszentrum Jülich, Jülich, Germany**

[4] **Centre for High Performance Scientific Computing in Terrestrial Systems, Geoverbund ABC/J, Germany**

Contact: **s.knist@fz-juelich.de**

Keywords: *RCM; climate simulation; model evaluation; convection permitting; EURO-CORDEX.*

High-resolution regional climate models with a more detailed representation of heterogeneous land surface properties, as well as an explicit treatment of deep convection can lead to an improved simulation of the climate system on the local scale. Added value is found especially on the sub-daily scale in the reproduction of intensities, diurnal cycle and spatial extent of precipitation. In this study, results from 10 years of convection-permitting WRF hindcast simulations at 3 km spatial resolution for a central European model domain are analyzed. The 3km-resolved domain is nested into the pan-European Coordinated Regional Downscaling Experiment (CORDEX) EUR-11 (12km) model grid, driven by ERA-Interim reanalysis data. The simulated time spans (1992-1995, 2002-2003, 2010-2013) cover much of the variability of central European weather conditions. Results from both resolutions are compared with each other and evaluated against high-resolution reanalysis data and gridded observations. Hourly precipitation data over three regions with a very moderate, low mountain and high mountain topography and for different seasons exhibit significant differences between the simulations and added value in the statistics of extremes as simulated with the 3 km runs. The largest differences occur during the summer months, when convective precipitation is dominant.

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Fully coupled terrestrial water cycle simulations with TerrSysMP: Features and applications

Ketan Kulkarni[1,4], Klaus Goergen[3,4], Fabian Gasper[3,4], Jessica Keune[2,4], Wolfgang Kurtz[3], Lukas Poorthuis[1,4], Bernd Schalge[2], Wendy Sharples[1,4], Prabhakar Shrestha[2], Mauro Sulis[2], Markus Uebel[2], Harrie-Jan Hendricks-Franssen[3], Stefan Kollet[3,4], Clemens Simmer[2,4]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Meteorological Institute, Bonn University**

[3] **Agrosphere (IBG-3), Juelich Research Centre**

[4] **Centre for High Performance Scientific Computing in Terrestrial Systems (Geoverbund ABC/J), Germany**

Contact: **k.kulkarni@fz-juelich.de**

Keywords: *Terrestrial systems; water cycle; coupled models; hydrological modeling; regional modeling; HPC.*

Fully coupled terrestrial water cycle simulations with TerrSysMP: Features and applications. The Terrestrial Systems Modelling Platform (TerrSysMP) is a fully coupled scale-consistent physics-based numerical model system, currently consisting of the COSMO NWP (v4.11) model, the Community Land Model (CLM, v.3,5) and the ParFlow (v3.1) variably saturated surface and subsurface hydrological model, coupled with the external coupler OASIS3(-MCT). TerrSysMP allows for a physically-based representation of transport processes across scales down to sub-km resolution with explicit feedbacks between the individual compartments, including groundwater dynamics and a full representation of the terrestrial hydrological cycle. Ongoing developments and extensions are e.g., improvements in the coupling, updates of the component models CLM to v4.5 and COSMO to v5.1, first steps towards the consideration of bio-geochemical cycles by including CO2 coupling, the implementation of a parallel data assimilation framework in ParFlow+CLM, and steps towards an improved big data readiness in the complete modelling system. TerrSysMP is operated on mutiple HPC systems, ranging from Linux clusters to highly scalable systems such as IBM BG/Q. TerrSysMP and its component models are used in a range of ongoing projects that nicely demonstrate the system's capabilities: It is the core modelling tool in a Collaborative Research Centre on interactions and processes related to patterns in the critical zone; here, the spatial focus of the model runs is on high-resolution (1km and sub-km) model domains and river catchments. In a Research Unit on data assimilation for improved characterization of fluxes across compartmental interfaces, TerrSysMP is used with so-called virtual catchments at very high resolution. Continental evaluation simulations are run over the pan-European 12km EURO-CORDEX model domain in fully coupled mode to e.g., investigate the impact of coupled groundwater and groundwater schemes at this scale on extreme events such as droughts and floods, sub-surface surface atmosphere coupling processes and to generate river runoff. Further model developments, optimisations and setups are supported for example by extensive validation studies, a model intercomparison with the coupled ParFlow.WRF and investigations on the impact of coupling functionalities and settings. Both, the technical features and developments in combination with the ongoing applications are evolving towards an earth system modelling approach at a regional scale.

Nanoparticle wrapping via receptor-mediated adhesion

Karandeep Singh[1], **Sabyasachi Dasgupta**[2], **Thorsten Auth**[1], **Gerhard Gompper**[1]

[1] **Institute for Advanced Simulation (IAS-2)**

[2] **Mechanobiology Institute, National University of Singapore**

Contact: `k.singh@fz-juelich.de`

Keywords: *Membranes; Nanoparticles.*

Nanoparticle wrapping via receptor-mediated adhesion. Biological cells internalize cargo via different pathways. In all cases, the cargo is encapsulated within a carrier that interacts with the plasma membrane of a cell via wrapping. Understanding the mechanisms involved in this internalization process is important both from a fundamental science and from an application point of view. For example, in drug delivery and nanomedicine, nanoparticles can be used as carriers. Furthermore, nanoparticles are used for food processing and in technological applications, therefore a better understanding of their toxicity is required. Towards understanding the complex wrapping process, we study wrapping of a spherical nanoparticle decorated with ligands that interacts with a lipid-bilayer membrane via receptor-ligand bonds.

Theoretical calculations have shown that the wrapping state of nanoparticles depends both on particle properties, such as size and shape, the membrane properties, such as bending rigidity and tension, and the strength of the adhesive interaction [1-3]. We calculate the deformation energy of the fluid membrane using the Helfrich curvature Hamiltonian. We take into account receptor-ligand binding energy and receptor entropy [4]. For a given fraction of a particle being wrapped by the membrane, we obtain an optimum number of bound receptors at equilibrium. For low-receptor densities and high receptor-ligand bond energies, we find stable partial-wrapped states. We show that in this regime the kinetics of receptor-mediated wrapping can determine the number of nanoparticles that attach to a cell, which is important to understand dosage effects for nanoparticle-cell interaction.

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Towards the design of allosteric ligands binding to the muscarinic receptor M2

Luca Maggi[1,2,6], **Giulia Rossetti**[1,2,5], **Rodrigo Casasnovas**[1,2], **Katrin Amunts**[3,4], **Paolo Carloni**[1,2,6]

[1] **Institute for Advanced Simulation (IAS-5)**

[2] **Institute of Neuroscience and Medicine (INM-9)**

[3] **Institute of Neuroscience and Medicine (INM-1) , Forschungszentrum Jülich, 52425 Jülich, Germany**

[4] **C. & O. Vogt Institute for Brain Research, Heinrich-Heine-University Duesseldorf, Germany**

[5] **Jülich Supercomputing Centre (JSC)**

[6] **RWTH Aachen University, 52074 Aachen, Germany**

Contact: `l.maggi@fz-juelich.de`

Keywords: *Allosteric Modulation; GPCRS; Molecular Dynamics Simulations.*

Allosteric ligands (ALs) activate neuro-receptors by binding in protein region other than the orthosteric sites [1]. They are usually more specific than the traditional agonist/antagonist [2], making them highly amenable for brain imaging applications [3].

Here we plan to identify ALs targeting the five members of the muscarinic receptors subclass (M1-M5) [4-6] of G-Protein Coupled Receptors (GPCRs). Located mostly in the cerebral cortex and subcortical nuclei [7], these receptors are implicated in many physiological and pathological brain functions [8]. We plan to apply structure-based virtual screening to detect novel potential candidates for allosteric modulation. The calculations will be based on the X-ray structure of M2, in complex with the LY2119620 allosteric ligand [9]. The structural determinants of the intracellular domain (165 aa in M2), lacking in the X-ray structure [9], will be predicted by enhanced sampling techniques. The screening will be performed by building a 3D pharmacophore model [10]. This model will filter apt ligands across ZINC Clean Leads database [11]. This database contains about 500.000 compounds. The promising ALs candidates will be tested experimentally using receptor autoradiography [12]. The molecular basis of the allosteric effect associated with the most promising ligands will be unraveled by advanced molecular simulation approaches, such as metadynamics.

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Predicting the apo-structures of two human NEET proteins involved in health and disease conditions

Luca Pesce[1], **Vania Calandrini**[1], **Giulia Rossetti**[1,2,3], **Rachel Nechushtai**[4], **Paolo Carloni**[1]

[1] **IAS-5/INM-9, Computational Biomedicine**

[2] **Hematology and Stem Cell Transplantation University Hospital Aachen, RWTH Aachen University, Germany**

[3] **Jülich Supercomputing Centre (JSC)**

[4] **The Alexander Siberman Life Science Institute and the Wolfson Center for Applied Structural Biology, The Hebrew University of Jerusalem, Edmond J. Safra Campus at Givat Ram, Jerusalem 91904, Israel**

Contact: `l.pesce@fz-juelich.de`

Keywords: *NEET proteins; molecular dynamics simulaitons; REST2.*

mitoNEET and NAF-1 are homologous proteins, belonging to the NEET family. These feature two intertwining monomers, each of which contains a labile 2Fe-2S cluster[1-3]. Despite the functions of these proteins still need to be elucidated, experimental observations support the hypothesis that their function involves the gather/release of the FeS from/to holo-donor/apo-acceptor proteins[4,5].

The lack of structural information for these proteins in absence of the iron-sulfur cluster(s) has so far hampered a molecular understanding of the key processes involving the cluster release. Here, we propose to predict the structural determinants of these proteins without one (holo-apo state) and two (apo-apo state) clusters in aqueous solution. We plan to use Replica Exchange Solute Tempering (REST)2 enhanced simulations[6,7]. This method allows performing a faster and extensive exploration of the conformational space compared to classical MD[6]. The initial models was built based on the crystal structure of mitoNEET and NAF-1 in the holo form[2,3,8] after removal of one or two clusters.

Our theoretical predictions will be compared with our spectroscopic data. This information is key for our planned future works aimed at finding molecular partners potentially able to interfere with the cluster release.

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Exploring the DNA-protein interface of cisplatin-modified DNA and HMGB1 box-A under in vivo post-translational modifications

Wenping Lyu[1,2,3], Giulia Rossetti[2,4,5], George Christophides[3,6], Giovanni Natile[7], Fabio Arnesano[7], Paolo Carloni[2]

[1] **Faculty of Mathematics, Computer Science and Natural Sciences, RWTH-Aachen University, 52056 Aachen, Germany**

[2] **Computational Biophysics, German Research School for Simulation Sciences, and Computational Biomedicine, Institute for Advanced Simulation IAS-5 and Institute of Neuroscience and Medicine INM-9, Forschungszentrum Jülich, 52425 Jülich, Germany**

[3] **Cyprus Inst, Computat Based Sci & Technol Res Ctr, 2121 Aglantzia, Nicosia, Cyprus**

[4] **Jülich Supercomputing Centre (JSC)**

[5] **Department of Oncology, Hematology and Stem Cell Transplantation, RWTH Aachen University, Aachen, Germany**

[6] **Univ London Imperial Coll Sci Technol & Med, Fac Nat Sci, Dept Life Sci, South Kensington Campus, London SW7 2AZ, England**

[7] **Department of Chemistry, University of Bari "A. Moro", via Edoardo Orabona 4, I-70125 Bari, Italy**

Contact: `g.rossetti@fz-juelich.de`

Keywords: *DNA-Protein interaction; HMGB1A; Cisplatin-DNA; Post-translational modifications; Replica exchange sampling; Molecular dynamics simulation.*

Cisplatin is a potent anticancer drug targeting the DNA of cancerous cells. Unfortunately, cisplatin-based treatments are plagued by resistance mechanism, which greatly limits the efficacy of the drug. One of these mechanism is the enzyme-based repair of the platinum lesions [1]. The high mobility group box 1 (HMGB1) protein binds to the distorted DNA [2], inhibiting the repair of the cisplatin–DNA damage in vitro [3, 4] and in cell [5], thus favoring drug resistance mechanisms [6]. Understanding the details of the HMGB1 recognition of cisplatin-DNA adducts in vivo is key for a strategy aiming to increase the efficacy of platinum-based drugs. Recently, several HMGB1 isoforms bearing extensive acetylation and phosphorylation were identified in vivo and found to be able to bind cisplatin-DNA adducts with high affinity [7]. This prompted us to investigate how the multisite modifications can impact on the interaction network at the DNA-protein interface at the atomic-level. In this work the molecular interactions between four post-translationally modified (PTM) isoforms of HMGB1 box A and a cisplatin-modified DNA oligomer have been investigated using enhanced sampling computational methods and the results compared with those obtained with un-modified HMGB1A [8]. A regulatory PTM-depended mechanism emerged, which might rationalize the higher affinity between cisplatin-modified DNA and PTM HMGB1A proteins with respect to unmodified HMGB1A.

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Spin-wave excitations and electron-magnon scattering from many-body perturbation theory

Mathias C. T. D. Müller[1], **Christoph Friedrich**[1], **Stefan Blügel**[1]

[1] **Institute for Advanced Simulation (IAS-1)**

Contact: `m.c.t.d.mueller@fz-juelich.de`

Keywords: *Spin waves; Bethe-Salpeter equations; Perturbation theory, applied to electronic structure of solids; Excited states solids electronic structure calculations.*

Spin-wave excitations and electron-magnon scattering from many-body perturbation theory. Spin excitations form a fundamental class of excitations in magnetic materials. We study the magnetic excitations of bulk Fe, Co, and Ni within the framework of many-body perturbation theory (MBPT) as implemented in the full-potential linearized augmented plane-wave (FLAPW) method. Starting from the GW approximation we obtain a Bethe-Salpeter equation for the magnetic susceptibility treating single-particle Stoner excitations and magnons on the same footing. At high energies the spin waves are heavily damped due to the coupling to single-particle Stoner excitations. The obtained results are in good agreement with available experimental data. Due to approximations used in the numerical scheme, the acoustic magnon dispersion exhibits a small but finite gap at Γ. We analyze this violation of the Goldstone mode and present an approach that implements the magnetic susceptibility using a renormalized Green function instead of the Kohn-Sham (KS) one, leading to a substantial improvement of the Goldstone-mode condition. As a cheap alternative, we discuss a correction scheme that involves an adjustment of the KS exchange splitting. The new exchange splittings turn out to be closer to experiment. Finally, we employ the solution of the Bethe-Salpeter equation to construct a self-energy that describes the scattering of electrons and magnons. We show results of the renormalized band structure including lifetime effects for the elementary ferromagnets iron, cobalt, and nickel.

Towards reproducible workflows for electrophysiology data using the *Elephant* analysis framework

Michael Denker[1,2,3], **Alper Yegenoglu**[1,2,3], **Sonja Grün**[1,2,3,4]

[1] **Institute of Neuroscience and Medicine (INM-6)**

[2] **Institute for Advanced Simulation (IAS-6)**

[3] **JARA BRAIN Institute I, Jülich Research Centre, Germany**

[4] **Theoretical Systems Neurobiology, RWTH Aachen University, Aachen, Germany**

Contact: `m.denker@fz-juelich.de`

Keywords: *electrophysiology; software; workflows; data analysis; multielectrode recordings; neuroscience.*

The degree of complexity when working with data from electrophysiological experiments has reached a level where well-structured and defined workflows for data and metadata acquisition, pre-processing, and subsequent analysis are becoming a necessity. The implementations of such workflows are often heterogeneous across researchers and experiments, dependent on custom-written codes, and far from being automatized. As such, they place a high burden and workload on the individual researchers in charge of defining the workflows and translating them into software. While in the meantime a number of generic software solutions to support some parts of such workflows are under development, software covering other aspects of the workflow are still lacking. This situation has serious consequences regarding the degree of reproducibility of data capture and data analysis in that it leads to ineffective and unsustainable science.

Here we outline how already today existing software tools can be combined to construct partial workflows that are capable of addressing some of the resulting challenges facing researchers, as summarized in [1]. To this end, we introduce a case study that links emerging software tools to form a reproducible analysis workflow based on the Python programming language. At the heart of this workflow we identified and partly developed three open-source software tools that represent the scaffold from which the analysis is built. First, we demonstrate how data of different origins can be represented in a standard form using the *Neo* framework [2]. Second, we demonstrate how the complex metadata accumulating in an electrophysiological experiment [3] can be gathered and stored using the open metadata markup language (*odML*) for metadata management [4]. These metadata are suitable to be combined with the actual data in the Neo framework, leading to a common representation of both data and metadata for subsequent use in the analysis workflow. Finally, as the key component of such workflows, we introduce the Electrophysiology Analysis Toolkit (*Elephant*, http://neuralensemble.org/elephant/) as a recent community-centered initiative to develop an analysis framework for multi-scale activity data based on this data representation. As such, *Elephant* represents a modular software component that provides generic library functions to perform standard and advanced analysis processes. In an outlook, we outline how this workflow can be extended by additional tools and technologies to handle access to high-performance computing, provenance tracking of the results, and work in a highly collaborative environment (see also [5]). In part, the work presented in this abstract is detailed in [6].

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von Willebrand factors and Platelets in Blood Stream: Margination and Adhesion

Masoud Hoore[1], **Kathrin Rack**[1,2], **Dmitry A. Fedosov**[1], **Gerhard Gompper**[1]

[1] **Institute for Advanced Simulation (IAS-2)**

[2] **Simulation and Software Technology, German Aerospace Center, 51147, Cologne, Germany**

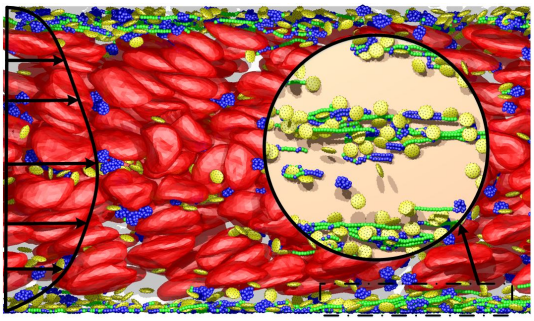
Contact: `m.hoore@fz-juelich.de`

Keywords: *Hemostasis; Mesoscopic modeling; Microfluidics; Margination; Adhesion.*

To stop bleeding, platelets must adhere to the injured endothelium and plug the opening. Although platelet adhesion to the injured substrate is effective in low shear rates, they are unable to firmly adhere to the surface by their own in shear rates higher than $900\ \mathrm{s}^{-1}$ [1]. In such conditions, von Willebrand factors (VWFs), the largest soluble proteins in blood stream play the crucial role [2]. They unwrap in high shear rates and adhere to the injured site; at the same time, they adhere to platelets and tether them from flowing in the blood flow. VWFs are long concatemers of VWF dimers bound to each other end to end [3]. The conformation of VWF polymer is such that in the absence of shear stress, the polymer remains globular, thus hiding its adhesive sites (A1 domains) for binding platelet receptors (Glycoprotein Ibα) or collagen. At sufficiently high shear rates, the VWF stretches making the interaction of its adhesive domain with platelet receptors or collagen possible.

For adhesion to occur, the platelets and VWFs must migrate to the proximity of tha injured walls. Indeed, the presence of red blood cells (RBCs) in blood stream facilates it by a process called margination. Accordingly, RBCs move to the center of the vessel and leave a RBC free layer near the walls. Then, the other micro-scale components such as ultra-large VWFs and platelets are pushed to this layer and populate there making hemostasis more probable. In addition, VWFs must be stretched to be hemostatically active since their adhesive domains are shielded from platelet receptors if the VWF polymer is coiled. Since VWFs are known to be coiled in low shear rates and stretched critically in sufficiently high shear rates [5], their adhesion occurs only in high shear rates.

By using meso-scale simulations, we study the behavior of VWFs and platelets in blood flow. It is shown that although platelets margination is enhanced by either increasing volume fraction of RBCs or by increasing shear flow, the margination of VWFs is non-trivially dependent on these two properties. It is also shown that VWF-platelet adhesion and aggregation are critically dependent on shear flow. The presence of ultra-large micro-scale VWFs is necessary in this process since they marginate and make big aggregates.



A snapshot of the simulation of blood clotting in blood stream. Platelet-VWF aggregates forming on the adhesive substrate are shown.

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Developing inhibitors of the enzyme "TRMT2A" for the treatment of PolyQ diseases

M. A. Margreiter[1], A. Voigt[2], J. B. Schulz[2,3], N. J. Shah[4], G. Rossetti[1,2]

[1] **Institute for Advanced Simulation (IAS-5) and Institute of Neuroscience and Medicine (INM-9)**

[2] **Department of Neurology, RWTH University Aachen, Aachen, Germany**

[3] **Institute of Neuroscience and Medicine (INM-11)**

[4] **Institute of Neuroscience and Medicine (INM-4)**

Contact: `m.margreiter@fz-juelich.de`

Keywords: *polyQ diseases; drug discovery; lead optimization; virtual screening.*

Polyglutamine (polyQ) diseases are a heterogenic group of neurodegenerative disorders including Huntington's disease, for which no cure is available at this time. [1] Their common feature is an expanded CAG repeat in the coding region of the gene, which results in an extended Q tract in the corresponding protein. These uninterrupted polyQ stretches lead to the formation of toxic aggregates.

Recently, experimental evidence produced by Dr. Voigt, in Prof. Schulz's group, showed that inhibiting tRNA methyltransferase 2 homolog A (TRMT2A) function might cause an error-prone translation, leading to increased number of non-Q amino acid insertions in the otherwise uninterrupted polyQ stretch. These interruptions, in turn, decrease the probability of polyQ stretches to form toxic aggregates. Upon silencing the TRMT2A gene, decreased polyQ aggregation was observed in yeast, flies and HEK293T cells.

We report our first steps towards the development of a potent and non-toxic inhibitor for TRMT2A with computer-aided drug discovery and development strategies. TRMT2A features a catalytic domain (CD) and an RNA recognition motif (RRM). Successful inhibition of one of the two is thought to hamper TRMT2A function. We first followed a ligand-based pharmacophore model approach across known tRNA methyltransferase inhibitors against the CD. This was combined with structural models of the domain to allow educated guesses about spatial requirements of the binding pocket and protein-ligand interaction hotspots. The resulting molecules of this first ligand-based *in silico* screening are currently being tested in HEK293 cells by Dr. Voigt's lab in Prof. Schulz's group.

On the other hand, we are analyzing the structural and dynamic properties of the RRM (recently crystalized by Dr. Dierk Niessing's lab) by molecular dynamic simulations. The aim is to identify a druggable binding pocket, specific for TRMT2A, to perform a structure-based virtual screening.

In cell experiments will be complemented with *ex vivo* and *in vivo* magnetic resonance imaging on healthy and transgenic mice brains in Prof. Shah's lab.

Finally, we are also modeling uninterrupted and interrupted polyQ stretches to rationalize at the molecular level how the insertion changes the probability of aggregation. [2]

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Shape-Induced Hydrodynamic Effects in Thermophoretic Microswimmers

Martin Wagner[1], **Marisol Ripoll**[1]

[1] **Institute of Complex Systems, Forschungszentrum Jülich, Germany**

Contact: `m.wagner@fz-juelich.de`

Keywords: *Swimming; Soft Matter; Hydrodynamics; Thermophoresis.*

Thermophoresis refers to the drift motion experienced by particles immersed in a fluid with an in- trinsic gradient of temperature. In thermophoretic swimmers a local temperature gradient is generated due to the existence of a material that can quickly absorb heat from a heating source such as irradiating light. An asymmetric distribution of the heated material on the particle surface translates into a persistent particle motion [1]. The motion direction is determined by the thermophoretic character of the particle, whether thermophobic or thermophilic [2]. Experimentally, these particles have been synthesized as Janus spherical particles being half coated with gold [1]. Other shapes such as dimer swimmers have already been investigated resulting in a significantly different hydrodynamic behaviour [3, 4]. In this work, we first study the effect of the swimmer shape by means of computer simulations. We employ a well-established mesoscale simulation technique that couples multi-particle collision dynam- ics (MPC) as a coarse-grained description of the fluid with molecular dynamics for an adequate resolu- tion of fluid-colloid interactions [5]. This methodology offers an efficient inclusion of hydrodynamics, thermal fluctuations, and the sustainability of temperature gradients. Moreover, the tunable fluid-solvent interactions allow us to explore various thermophoretic behaviors. We characterize the swimming be- havior as a function of the swimmer shape, e.g. self-propelled dimers with asymmetric sizes, or rod-like swimmers with parallel and perpendicular propulsion. Interaction between pairs of swimmers is investigated as well. Thermophoretic self-propelled particles interact with each other not only through direct pair interactions, but they will react as well to each other's temperature gradients and to their hydrodynamically induced flow fields. Whether and how pairs of swimmers form persistent geometric structures, or swim independently, will determine the collective behavior of large assemblies of these swimmers.

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Computing the nucleon Dirac radius directly at zero momentum transfer

Nesreen Hasan[1,2], Stefan Meinel[4], Jeremy Green[7], Michael Engelhardt[3], Stefan Krieg[1,2], John Negele[5], Andrew Pochinsky[5], Sergey Syritsyn[6], Thomas Lippert[1,2]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Bergische Universität Wuppertal, Wuppertal**

[3] **New Mexico State University, Las Cruces, USA**

[4] **University of Arizona, Tucson, USA**

[5] **Center for Theoretical Physics, MIT, Cambridge, USA**

[6] **Thomas Jefferson National Accelerator Facility, Newport News, USA**

[7] **Institut für Kernphysik, Johannes Gutenberg-Universität Mainz, Mainz**

Contact: `n.hasan@fz-juelich.de`

Keywords: *Lattice QCD.*

We describe a lattice approach for directly computing momentum derivatives of nucleon matrix elements using the Rome method, which we apply to obtain the isovector magnetic moment and Dirac radius. We present preliminary results calculated at the physical pion mass using a 2HEX-smeared Wilson-clover action from the Budapest-Marseille-Wuppertal collaboration. For removing the effects of excited-states contamination, the calculations were done at three source-sink separations and the summation method was used.

Neutron-proton Scattering at NNLO in Nuclear Lattice Effective Field Theory

Ning Li[1], **Ulf-G Meißner**[2,1,3]

[1] **Institute for Advanced Simulation (IAS-4)**

[2] **Helmholtz-Institute für Strahlen- und Kernphysik and Bethe Center for Theoretical Physics, Universityät Bonn, D-53115 Bonn, Germany**

[3] **JARA - High Performance Computing, Forschungszentrum Jülich, D-52425 Jülich, Germany**

Contact: `n.li@fz-juelich.de`

Keywords: *np scattering; nuclear lattice effective field theory; two-pion-exchange potential.*

We present a systematic study of neutron-proton scattering in Nuclear Lattice Effective Field Theory (NLEFT), in terms of the computationally efficient radial transfer matrix method. We consider the chiral expansion with explicit inclusion of two-pion exchange terms up to next-to-next-to-leading order (NNLO). Our leading-order (LO) interaction consists of smeared, local contact terms and static one-pion exchange. For the first time, we explore how our results depend on the lattice spacing a, and estimate the uncertainties in the determination of the NLO coupling constants. We present results ranging from $a = 1.97$ fm to $a = 0.98$ fm, which allows us to assess the effects of lattice artifacts on the scattering phase shifts. We find that lattice artifacts are largely eliminated at $a = 0.98$ fm, provided that the lattice momenta in the pion-nucleon coupling are taken to coincide with the continuum dispersion relation. With these improvements, we find good agreement at NNLO with the Nijmegen S- and P-wave scattering phase shifts. We expect higher partial waves to be equally well described once higher-order (N3LO) contributions are included.

Evaluation of spike sorting results

Nicole Voges[1], **Jeyathevy Sukiban**[2], **Robin Pauli**[1], **Michael Denker**[1], **Lars Timmermann**[2], **Sonja Grün**[1,3]

[1] **Institute of Neuroscience and Medicine (INM-6) and Institute for Advanced Simulation (IAS-6) and JARA BRAIN Institute I, Jülich Research Centre, Germany**

[2] **Department of Neurology, University Hospital Cologne, Germany**

[3] **Theoretical Systems Neurobiology, RWTH Aachen University, Germany**

Contact: `n.voges@fz-juelich.de`

Keywords: *spike sorting; Parkinson's desease; STN; data analysis.*

n Parkinson's disease (PD) the STN plays an important role in the formation of pathological oscillatory activity within the basal ganglia-cortex loop. The primary measure to reveal such oscillations is the local field potential (LFP). While it is assumed that the LFP reflects synaptic input to groups of neurons, the relationship between this population signal and the single neuron activity is still a matter of debate [1, 2]. Our long-term goals are to investigate the spike-LFP relationship in STN recordings obtained during deep brain stimulation surgery, as well as to assess the amount of synchrony between individual neurons in order to elucidate how oscillations on the population level translate to neuronal synchrony. A critical step to achieve this goal is to correctly isolate the spiking activity of single units in extracellular STN recordings from Parkinson patients measured with a Ben Gun five channel micro-marcro-electrode holder. We employed a number of spike sorting algorithms [e.g., 3] and found that different spike sorting methods yield inconsistent results. We quantify these differences by the number of detected single units and the individual assignment of spikes to the detected units. Our long-term goal critically depends on the spike sorting quality [4], as, e.g., spike synchrony evaluation depends on the percentage of correctly identified spikes [5]. Hence, we introduced two additional approaches. Firstly, we developed a set of tools that estimates the isolation quality of single units [6]. These tools calculate the similarity of the spike shapes within one unit compared to other units. Secondly, we generated synthetic ground truth spike data of mixed units with the statistical features of the STN recordings: We selected the two most different spike shapes which we combined linearly to obtain pairs of spikes with a controlled dissimilarity. Assuming Poisson spike rates we generated spike trains by inserting such spike pairs into a noisy background obtained by phase shifting the original noise. These data enable us to calibrate and verify our spike sorting results, i.e., to check if the number of extracted units and the spike-to-unit assignment is correct. By use of these two approaches, we compare and evaluate various spike sorting methods to finally select and apply the most appropriate one for the analysis of our STN recordings.

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Behavior specific spike patterns in macaque motor cortex during an instructed-delay reach-to-grasp task

Pietro Quaglio[1,5], Emiliano Torre[1,5], Michael Denker[1,5], Thomas Brochier[2], Alexa Riehle[2,1,4,5], Sonja Grün[1,3,4,5]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **Institut de Neurosciences de la Timone (INT), UMR 7289, CNRS, Aix-Marseille Universite, Marseille, France**

[3] **Theoretical Systems Neurobiology, RWTH Aachen University, Aachen, Germany**

[4] **RIKEN Brain Science Institute, Wako-Shi, Japan**

[5] **Institute of Neuroscience and Medicine (INM-6) and JARA BRAIN Institute I, Jülich Research Centre, Germany**

Contact: **p.quaglio@fz-juelich.de**

Keywords: *spike synchrony; massively parallel spike trains; higher-order correlations; motor behavior.*

Cell assemblies [1] exhibiting neuronal interactions at the millisecond time scale were suggested as building blocks of information processing in the brain [2,3]. Significant patterns of synchronous spikes in electrophysiological recordings are considered as a signature of an active assembly. We recently developed a statistical method - the Spike Pattern Detection and Evaluation (SPADE) analysis [4] - to detect synchronous spike patterns in massively parallel spike data (MPST) on the order of 100 or more neurons. The method deals with a) the combinatorial explosion of the number of patterns to consider by employing a variant of the frequent item set mining technique [5, 6], and with b) the challenge of statistically assessing these patterns due to the multiple testing problem by using Monte-Carlo techniques.

We applied the SPADE analysis to electrophysiological data recorded from the motor cortex of two monkeys while they executed a delayed reach-to-grasp task. MPST were recorded by using a 100-electrode Utah array chronically implanted at the MI/PMd border [7]. We hypothesized that different classes of spike patterns occur depending on the behavioral conditions and periods in the trial. To investigate this, we analyzed and compared data from the same set of neurons recorded during the 4 different behavioral conditions (combinations of object load and grip type), and during 6 time epochs of different stages of the task protocol.

We found [8] a variety of significant patterns in specific time epochs and behavioral conditions in both monkeys. We then analyzed the spatial organization of these patterns on the recording array with respect to its cortical location, and found that pairs of neurons involved in synchronous patterns were preferentially aligned along the medio-lateral orientation. We also assessed the specificity of the neuronal composition of patterns to different behavioral contexts and found a strong specificity to the grip type and the specfic behavioral epoch. These findings provide evidence for the existence of higher-order spike patterns occurring in relation to behavior.

Acknowledgements. *Acknowledgements. Supported by Helmholtz Portfolio Theme Supercomputing and Modeling for the Human Brain (SMHB), EU grant 604102 (Human Brain Project, HBP),ANR GRASP France.*

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Superparamagnetism-induced mesoscopic electron focusing in topological insulators

Philipp Rüßmann[1,2], **Nguyen H. Long**[1,2], **Phivos Mavropoulos**[1,2], **Stefan Blügel**[1,2]

[1] **Peter Grünberg Institut (PGI-1)**

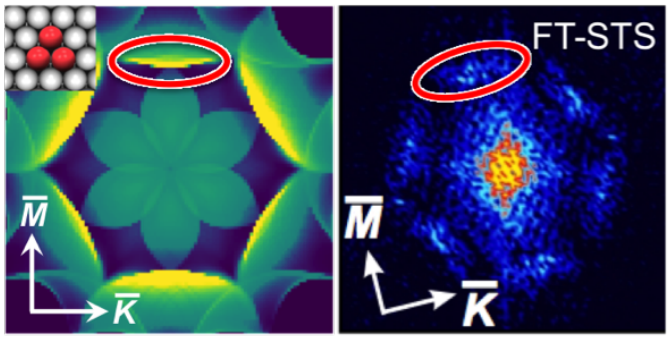
[2] **Institute for Advanced Simulation (IAS-1)**

Contact: `p.ruessmann@fz-juelich.de`

Keywords: *density functional theory; ab-initio simulation; electronic structure; topological insulators; scanning tunneling microscopy; electron scattering.*

In topological insulators the spin-momentum locking in the topological surface state and the existence or absence of time-reversal symmetry (TRS) (magnetic or non-magnetic defects, respectively) has severe consequences on the scattering properties. We study the prototypical topological insulator Bi2Te3 and show the interplay between the warping of the Fermi surface and the breaking of TRS by different Mn defects on the surface. The breaking of TRS by the magnetic defects leads to standing wave patterns observable with Scanning Tunneling Spectroscopy (STS). STS scans combined with Fourier transformed STS images at different energies reveal that a strong signal with standing wave pattern having a coherence length of more than 30nm can only be seen in a small energy window [1]. Our calculations demonstrate that two ingredients are needed to observe a strong backscattering signal; (i) the Fermi surface needs to support nesting and (ii) the TRS breaking scattering center needs to show a strong enough magnetic moment which can be realized by small cluster of Mn that couple ferromagnetically. The excellent agreement of experimentally measured FT-STS image and theoretical calculation for a Mn trimer on Bi2Te3 can be seen in Figure 1 on the right and left, respectively.

In our calculations we employ the full potential relativistic Korringa-Kohn-Rostoker Green function method within density functional theory for the electronic structure and scattering properties at defects [2,3].



Comparison of simulated (left) and experimental image (right) of the Fourier transformed STS spectrum [1] for a Mn trimer (shown in inset) on Bi2Te3.

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Decision-specific sequences of neural activity in balanced random networks driven by structured sensory input

Philipp Weidel[1], **Renato Duarte**[1,4,5], **Abigail Morrison**[1,2,3,4]

[1] **Institute of Advanced Simulation (IAS-6) & Institute of Neuroscience and Medicine (INM-6) & JARA BRAIN Institute I, Jülich Research Center, 52425 Jülich, Germany**

[2] **Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr-University Bochum, 44801 Bochum, Germany**

[3] **Simulation Laboratory Neuroscience – Bernstein Facility for Simulation and Database Technology, Institute for Advanced Simulation, Jülich Aachen Research Alliance, Jülich Research Center, Jülich, Germany**

[4] **Bernstein Center Freiburg, Albert-Ludwig University of Freiburg, Freiburg im Breisgau, 79104, Germany**

[5] **Institute for Adaptive and Neural Computation, School of Informatics, University of Edinburgh, EH8 9AB, UK**

Contact: `p.weidel@fz-juelich.de`

Keywords: *spiking neural network; plasticity; robotics; ROS; MUSIC.*

Perceptual decision-making is an intricate process implicating the coordinated activity of multiple brain areas [1,2]. Recent experimental studies demonstrate the existence of a complex interplay between decision-related neural events and transient working memory processes [1], implemented by distributed circuits where specific sub-populations appear to be differentially involved in the evidence accumulation process and subsequent behavioral outcomes [2]. This results in observable divergences in choice-specific neuronal dynamics, unfolding as reproducible trajectories throughout the network's state-space [1] and hinting at the dissipative nature of the underlying dynamical system, which executes cognitively relevant processing through transient trajectories. Despite this evidence, the majority of modeling studies addressing reward-modulated decision-making tend to simplify the formalization of environmental representations in the cortex as stable, attractor states corresponding to discrete environmental states [3]. Even models involving transient-based computations often simplify sensory stimuli to a discrete set of inputs transduced as stochastic point processes [4]. These simplifications potentially draw an incomplete picture of neural dynamics and therefore provide limited insights into the true nature of computation in neural circuits. To overcome this issue, we take one step towards realistic in silico experimental settings by using structured virtual environments to obtain rich sensory input to drive model neural systems using the ROS-MUSIC toolchain [5]. It allows us to simulate robotic agents in virtual 3D environments performing a realistic perceptual decision task, which can be directly equated to experimental data. The robotic simulation generates realistic and structured sensory data which is encoded to spiking neural activity using a nonlinear encoding process, as formalized in [6]. The encoded sensory data is then used as input to a balance recurrent neural circuit. In this study, we investigate the emergent dynamical features of neural activity when the agent is navigating a virtual T-maze. We observe decision-specific sequences of neural activity akin to experimental evidence [1], revealing possible processing strategies employed by the neural substrate. Furthermore, we investigate the role of different adaptation/plasticity mechanisms in shaping the system's dynamics. In order to equate our results with those of other studies, we attempt to partition the network state-space into discrete activity clusters, which carry relevant information that could potentially be used to drive reinforcement learning algorithms.

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Role of the extracellular loop ECL2 and membrane lipids for ligand recognition in GPCRs.

Ruyin Cao[1,2], **Giulia Rossetti**[1,2,3], **Dirk Bier**[4], **Paolo Carloni**[1,2]

[1] **Institute for Advanced Simulation (IAS-5)**

[2] **Institute of Neuroscience and Medicine INM-9, Forschungszentrum Jülich, Wilhelm-Johnen-Straße, D-52428, Jülich, Germany**

[3] **Jülich Supercomputing Centre (JSC)**

[4] **Institute of Neuroscience and Medicine INM-5, Forschungszentrum Jülich, Wilhelm-Johnen-Straße, D-52428, Jülich, Germany**

Contact: `r.cao@grs-sim.de`

Keywords: *metadynamics; GPCR; ligand binding.*

Extracellular loops (ECLs) of GPCRs are very diverse in lengths and sequence compositions, and increasing evidence suggests their key role in early stages of ligand recognition. By using metadynamics simulations [1] we uncover the role of the extracellular loops in the multi-step dissociation pathways of the high affinity antagonist ZM241385 [2] from the orthosteric binding site of human adenosine receptor type 2A ($hA_{2A}R$) [3]. We discover two precedently undecribed vestibular binding sites, where ECL1 and ECL2 use lipid-specific interaction patterns to stabilize the ligand. Moreover, we also showed that these two vestibular binding sites are evolutionally correlated to the deep orthosteric binding site, strongly suggesting the presence of an allosteric pathway connecting these topologically distinct regions of the receptor. We further found a solvent-exposed binding site on the ECL2, whose existence is confirmed by mutagenesis experiments, pointing toward a role of ECL2 in early ligand recognition step. By extending our analysis to other human GPCRs for which structural information are available, we found that the evolutionary coupling between ECLs and orthosteric binding site also exists for 22 human GPCRs, in 18 of which, the ECL2 is involved. Our finding uncover a potentential allosteric modulation of the extracellular loops, ECL2 being the key player, on to the deep orthosteric binding site.

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Spin Disorder Effect on the Electronic Properties of NiMnSb

Roman Kováčik[1], **Phivos Mavropoulos**[1], **Stefan Blügel**[1]

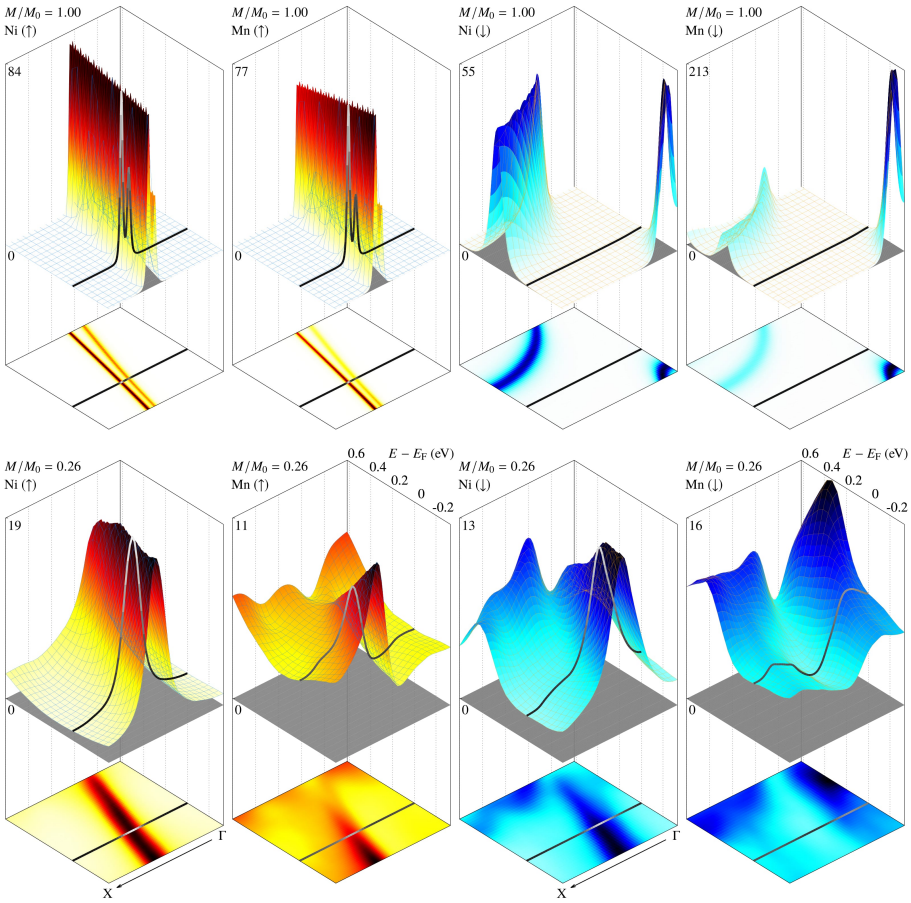
[1] **Institute for Advanced Simulation (IAS-1)**

Contact: `r.kovacik@fz-juelich.de`

Keywords: *KKR; spin disorder; spectral function; NiMnSb.*

An important contribution to the spin-caloric transport properties in magnetic materials at elevated temperatures is the formation of a spin-disordered state due to the local moment fluctuations. We investigate how the spin disordered state affects the spectral function, self energy and transport properties of NiMnSb, a prototypical half-metallic ferromagnet. The electronic structure of NiMnSb is calculated within the full-potential Korringa-Kohn-Rostoker Green function framework [1]. The Monte-Carlo methodology is employed to simulate the effect of temperature induced spin disorder and the set of spin-disordered configurations is used to obtain statistical averages of the relevant material properties [2-4].

As an example of our results, we point out qualitative differences between the spectral function projected on Ni and Mn sites (depicted in the figure). In comparison to T = 0 K (top panel), the spin up spectral function at around the Curie temperature (bottom panel) only broadens in case of Ni whereas it acquires rather rich landscape in case of Mn. In the spin down, the most interesting outcome is the shift of the prominent peak: away from the Γ-point in case of Ni and to a higher energy across the Fermi level in case of Mn.



Spectral function of NiMnSb at T = 0 K (top) and around Curie temperature (bottom) projected on Ni and Mn sites.

Acknowledgements. *Support from the DFG (SPP 1538) is gratefully acknowledged.*

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Short time dynamics of crowded protein solution

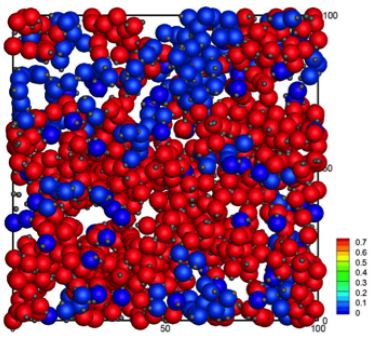
Shibananda Das[1], Jin Suk Myung[1], Gerrit Vligenthart[1], Roland G. Winkler[1], Gerhard Gompper[1]

[1] **Institute for Advanced Simulation (IAS-2)**

Contact: `sh.das@fz-juelich.de`

Keywords: *Mesoscale simulation; Multiparticle collision dynamics; Patchy colloid; Short time dynamics.*

Proteins in aqueous solution can organize into complex structures which effect the diffusive behaviour of the protein. For example, mammalian eye-lens proteins can form gel-like structures when suspended in water and exhibit dynamical arrest in crowded conditions [1]. We investigate the static and dynamical properties of such attractive globular proteins using a hybrid coarse-grained simulation approach. The proteins are modelled as colloidal particles and treated by molecular dynamics simulations. The surrounding fluid is described by the multiparticle collision dynamics method, a mesoscale hydrodynamic technique [2-5]. Colloids with isotropic interaction are studied, as well as colloids with additional attractive patchy interactions. We observe a space-spanning percolating network of the patchy colloids with a considerable influence on their dynamics. We analyze the properties of the network-like arrangement to get insight into the structure of the colloidal aggregates. Thus, we conclude that the complex “patchy” interactions of proteins give rise to a dynamic behaviour in crowded environments which differs drastically from that of spherical colloids.



Configuration of colloids with patch attraction for volume fraction φ=0.1. The color code indicates the cluster size distribution.

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Electron-Transport Calculation Method and its Application for Molecular Electronics

Shigeru Tsukamoto[1], **Stefan Blügel**[1]

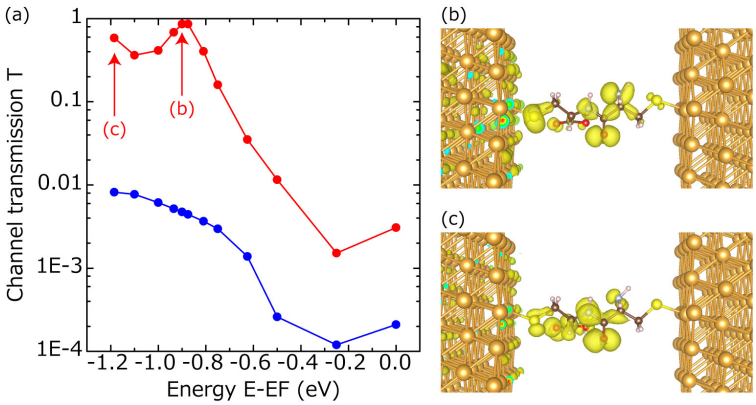
[1] **Institute for Advanced Simulation (IAS-1)**
Contact: `s.tsukamoto@fz-juelich.de`

Keywords: *electron transport; molecular electronics; real-space finite-difference method.*

Introduction. In general, electron transport calculations require relatively large computing unit cells which include many atoms in comparison to the calculations for conventional bulk systems. This is because they contain not only scattering objects but also parts of electrodes, whose effective potential asymptotically approaches to bulk one toward the unit-cell boundaries. In comparison to bulk interface systems, molecular junction systems tend to require large computing unit cells, especially in the directions perpendicular to electron flow. For such large-scale systems, the real-space finite-difference (RSFD) formalism [1] and pseudopotential methods are well known to be suitable in terms of computational efficiency in massively parallel computers. So far, we have developed an electron transport calculation method, called juTrans, based on the RSFD formalism and the projector-augmented wave (PAW) pseudopotentials [2]. As compared to other electron transport calculation methods using localized-orbital basis sets, our method is completely free from choosing basis functions, but still expensive because of the large degree of freedom in solving the Kohn-Sham equation for scattering wave functions.

Method. Our approach to the problem on the computational cost is to reduce the degree of freedom to the requisite minimum without any approximation and losing accuracy. We have found that a block of the Hamiltonian matrix is rank-deficient due to the separable form of the PAW pseudopotentials, and can be transformed into a size-reduced and regular matrix by using the singular value decomposition. As the consequence of the matrix transformation, the overbridging boundary matching formula [3] for scattering wave functions is expressed as smaller linear equations. The reduction of the matrix size turned out to be more than 60%, and the memory consumption for storing the coefficient matrices is reduced by more than 80%.

Application. In the presentation, we are going to show some transport calculation results for molecular junction systems as well as the development of the method. The figure below shows the channel transmission spectra of the molecular junction composed of a dipeptide molecule attached to a couple of Au(111) electrode surfaces. By comparing the spatial distributions of the transmission channels [see Figs. (b) and (c)] with those of an isolated dipeptide molecule, it is turned out that the third and fourth highest occupied molecular orbital (HOMO-2 and HOMO-3) contribute to the transmission peaks and the HOMO and HOMO-1 do not. This can be understood from the fact that the HOMO and HOMO-1 are both localized at either end of the molecule. Therefore, these molecular orbitals do not carry electrons from one side to another side of the molecule.



(a): Transmission spectra of the dipeptide molecular junction with gold electrodes. (b) and (c): Spatial distributions of the transmission channels at the energies indicated by arrows in (a). In (a), the red and blue curves correspond to the first and second channel transmissions, respectively.

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Locomotion of Swimming and Swarming Bacteria

Thomas Eisenstecken[1], **Jinglei Hu**[2], **Gerhard Gompper**[1], **Roland G. Winkler**[1]

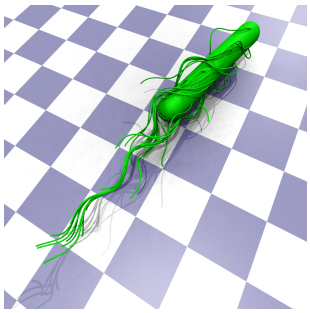
[1] **Institute for Advanced Simulation (IAS-2)**

[2] **Kuang Yaming Honors School, Nanjing University, Nanjing 210023, China**

Contact: `t.eisenstecken@fz-juelich.de`

Keywords: *Microswimmers; Mesoscale Simulation Methods; Multiparticle Collision Dynamics.*

Flagellated microorganisms not only swim as individuals, but exhibit also collective behavior in form of swarming [1]. Swarming has been distinguished from other forms of locomotion near surfaces, e.g., swimming, due to the morphological changes bacteria undergo. During the transition form swimming to swarming cells, the number of flagella increase and the cells often become more elongated. We developed a mechano-elastic model for E.coli cells [2], where a spherocylindrical body is propelled by rotating helical flagella. To take hydrodynamic interactions into account, the bacterium model is coupled to the multiparticle collision dynamics algorithm, a mesoscale hydrodynamic simulation technique [3]. We study the influence of morphological changes on the locomotion of bacteria. We demonstrate that the swimming velocity of individual cells decays as the length of the body and the number of flagella increases. Furthermore, we study how confinement and boundary conditions affect the swimming behavior of planktonic [4] and swarmer cells.



Simulation snapshot of a swarmer cell near a solid surface.

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Correlations in binary networks with time-dependent input

Tobias Kühn[1,2], **Michael Denker**[1,2], **PierGianLuca Mana**[1,2], **Sonja Grün**[1,2,3], **Moritz Helias**[1,2,4]

[1] **Institute for Advanced Simulation (IAS-6)**

[2] **INM-6**

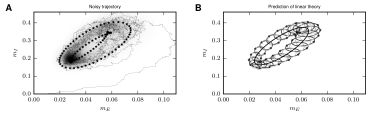
[3] **Theoretical Systems Neurobiology, Faculty I, RWTH Aachen**

[4] **Department of Physics, RWTH Aachen**

Contact: `t.kuehn@fz-juelich.de`

Keywords: *Glauber dynamics; pairwise correlations; Local Field Potential; cortical activity; NEST.*

In [1], it was shown by Unitary Event analysis [2,3] that the occurence of simultaneous spikes is more strongly locked to the phase of the LFP beta-oscillations than the activity of the other neurons, which was related to the existence of cell assemblies. To study the influence of remote brain areas visible in the LFP on the correlated single neuron activity in a small cortical subnetwork, we examine a balanced network of homogeneously connected binary model neurons [4] receiving input from a sinusoidal perturbation [5]. This simple model serves us to capture the main properties and illustrate mechanisms that cause time-modulated correlations. The Glauber dynamics of the network is simulated and approximated by mean-field theory. Treating the periodic input in linear response theory, the cyclostationary first two moments are analytically computed, which agree with their simulated counterparts over a wide parameter range. The zero-time lag correlations consist of two terms, one due to the modulated susceptibility (via external input and recurrent feedback) and one due to the time-varying autocorrelations. For some parameters, this leads to resonant correlations and non-resonant mean activities. Our results can help to answer the salient question how oscillations in mesoscopic signals and spike correlations interact. An interesting extension of our model is to include cell assemblies [6] allowing a closer comparison to experimental findings.



Empirical density of population activity of the E-I network. Gray shading indicates time-averaged occupation of states, stars the theoretically predicted range of probable trajectories.

Acknowledgements. *Supported by the Helmholtz foundation (VH-NG-1028, SMHB); EU Grant 604102 (HBP). Simulations with NEST (nest-simulator.org).*

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Grand canonical simulations for structural predictions of neuronal G protein-coupled receptors in complex with their target ligands

Thomas Tarenzi[1,2], **Vania Calandrini**[3,4], **Raffaello Potestio**[5], **Paolo Carloni**[2,3,4]

[1] **CaSToRC, The Cyprus Institute, Nicosia, Cyprus**

[2] **Department of Physics, RWTH Aachen, Aachen, Germany**

[3] **Institute for Advanced Simulation (IAS-5)**

[4] **INM-9, Computational Biomedicine, Forschungszentrum Jülich, Germany**

[5] **Max Plank Institute for Polymer Research, Mainz, Germany**

Contact: `t.tarenzi@hpc-leap.eu`

Keywords: *GPCRs; Ligand binding; Molecular Mechanics/Coarse-Grained simulation.*

G protein-coupled receptors (GPCRs) are the largest membrane-bound receptor family expressed by humans; in particular, neuronal GPCRs participate in about the 80% of the signaling processes in the brain. Because structural information is lacking for about the 95% of GPCRs, computer-aided structural predictions are the methods of choice for structural insights of most neuronal GPCRs. We have developed a hybrid 'Molecular Mechanics/Coarse-Grained' (MM/CG) scheme, which describes the binding site along with the ligand in full atomistic details, while the rest of the receptor is described at coarse-grained level [1,2]. Hydration is accounted for including around the MM region a droplet of water molecules, confined by a repulsive potential to prevent evaporation. To improve the description of the solvation shell, we are implementing the Hamiltonian Adaptive Resolution Scheme (H-AdResS) [3]. This will allow water molecules to change on the fly their resolution when freely diffusing across the MM and CG regions, in order to simulate a Grand Canonical ensemble that provides a more realistic description of the solvent reservoir.

Acknowledgements. *Supported by the European Union's H2020-MSCA-ITN programme.*

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Hybrid MPI/multithreaded parallelism for the DFT code FLEUR

Uliana Alekseeva[1], **Daniel Wortmann**[1]

[1] **Institute for Advanced Simulation (IAS-1)**

Contact: `u.alekseeva@fz-juelich.de`

Keywords: *DFT; LAPW.*

An accurate and realistic description of materials of scientific or technological interest requires ab-initio methods that are able to handle a variety of phenomena such as non-collinear magnetism, spin-orbit coupling effects, (external) electric fields, correlation effects, low dimensions, etc. The code FLEUR (www.flapw.de) allows to investigate material properties on a quantum mechanical level within the vector spin-density formulation of density functional theory (DFT). This massively parallelized code is based on the full-potential linearized augmented planewave (FLAPW) method for bulk, film and wire geometry. With this method, it is possible to accurately describe a wide variety of systems with open structures and low symmetry.

Modern developments aim at extending the applicability of existing methods by harvesting the power of modern massively parallel computer architectures. We present an efficient hybrid MPI/multithreaded implementation of the code FLEUR, which has been developed by the IAS-1/PGI-1 group in the FZJ in the collaboration with the HPC Group in RWTH. The shared memory parallelization augmenting the existing MPI implementation provides not only high one-node performance but also ensure that current and future supercomputers can be efficiently used to perform large DFT calculations. Besides the discussion of the basic algorithms and their computational challenges, we demonstrate the improved scalability of the code for realistic example setups.

Acknowledgements. *Supported by JARA-HPC Seed Funds*

Graphene on Ir(111): from physisoption to chemisorption via metal intercalation and molecular adsorption

Vasile Caciuc[1], **Nicolae Atodiresei**[1], **Stefan Blügel**[1,2]

[1] **Institute for Advanced Simulation (IAS-1)**

[2] **Peter Grünberg Institut (PGI-1)**

Contact: **v.caciuc@fz-juelich.de**

Keywords: *density functional theory; van der Waals interactions; graphene; metal surface; molecular adsorption; metal intercalation.*

Graphene on Ir(111) is an ideal template two-dimensional (2D) material whose physical properties can be functionalized via molecular adsorption [1] or metal intercalation [2,3]. For instance, in a recent combined experimental and theoretical study we have unveiled that the bonding mechanism of the extended 2D π system graphene on Ir(111) is physisorption with a local chemical modulation [4]. Additionally, in previous theoretical and experimental investigations of the Co [2] and Fe [3] intercalated graphene on Ir(111) we also demonstrated the fascinating possibility to induce magnetism in the graphene layer.

Besides this, in this contribution we will discuss in detail how to tune the strength of the van der Waals (vdW) interactions acting between a finite π-conjugated molecular system such as naphthalene ($C_{10}H_8$) and the graphene/Ir(111) system. Our first principles density functional theory (DFT) calculations employing a non-local correlation vdW-DF functional clearly proved that the key ingredient to tune the strength of the naphthalene-graphene vdW interactions is to modify the spatial extent of the π charge distribution in the graphene layer by doping it via intercalated electropositive (Eu) and electronegative (O) atoms at its interface with Ir(111) [5].

With the prospect of using graphene in spintronics applications as spin valve [6], we will also present in detail how the spin splitting of a π molecular system and graphene's electronic structures are finely tailored by the vdW interactions between naphthalene and 3d Co and 4f Eu intercalated graphene on Ir(111).

Acknowledgements. *Supported by the Deutsche Forschungsgemeinschaft (DFG) and VolkswagenStiftung.*

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Towards a Physical Description of Neural Cascades for Translational Neuroscience: a Pilot Project between INM-9 and ICS-3

Vania Calandrini[1,2], **Jonas Riest**[3], **Nägele Gerhard**[3], **Paolo Carloni**[1,2], **Jan K. G. Dhont**[3]

[1] **Institute for Advanced Simulation (IAS-5)**

[2] **INM-9**

[3] **ICS3**

Contact: `v.calandrini@fz-juelich.de`

Keywords: *stochastic computation; Molecular simulation; Signaling cascades; computational modelling; diffusion; mean-field reduction.*

Neural cascades are involved in neurotransmission and trigger a variety of subcellular processes regulating memory, learning, mood, reward and motivation processes, sensing etc. Dysregulation of these cascades is therefore involved in neurological disorders and psychiatric diseases. Current neurological-pathways models aimed at reproducing the time evolution of some of the species involved in these cascades are mostly based on simple mass-action laws. Hence, they do not explicitly take into account essential physical aspects affecting the kinetics such as diffusive processes, geometrical constraints, concentration inhomogeneities, and the presence of driving forces due to, for example, electric fields that affect molecular transport. The existing simple models based solely on mass-action laws cannot predict effects of disease-linked mutations and of drug binding, essential for translational medicine. Purely atomistic simulations are necessary to describe interactions between the molecular species involved in the cascade. The resulting interaction parameters are used as an input to mesoscopic simulations and analytical theories to describe the temporal and spatial evolution processes in the post synapse. The combination of atomistic and mesoscopic simulations as well as analytical theory covers the vast range of time- and spatial scales involved in these cascades. Here we propose to apply this approach on a specific human cascade regulating memory reward processes [1]. The proposed approach is expected to bridge the gap between elementary atomistic descriptions and macroscopic system neurobiology by a mesoscale modeling of the relevant intracellular signaling events. This will provide a route to improve the understanding of the functioning of post-synapse signal transduction and to improve the predictive performance of the models so far available.

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NEST-MC: A morphologically detailed neural network simulator for many core high performance computer architectures

Wouter Klijn[1], **Ben Cumming**[2], **Vasileios Karakasis**[3], **Alexander Peyser**[1], **Stuart Yates**[2]

[1] **Jülich Supercomputing Centre (JSC)**

[2] **Swiss National Supercomputing Center, Future Systems**

[3] **Swiss National Supercomputing Center, User Engagement & Support**

Contact: `a.peyser@fz-juelich.de`

Keywords: *nest; multicompartment; neurosimulator; many-core; HPC; HBP.*

The nest-mc multicompartment neural network simulator will enable new scales and classes of morphologically detailed network simulations on current and future supercomputing architectures. Nest-mc is being developed as a collaboration between the Neuroscience SimLab at the Forschungszentrum Juelich, Barcelona Supercomputing Center and the Swiss National Supercomputing Center (CSCS) under the aegis of the NEST Initiative. The trend towards "many-core" architectures such as GPU and Intel Xeon Phi based systems demands new approaches in software development and algorithm design. Nest-mc is being written specifically for these architectures; it aims to be a flexible platform for neural network simulation, interoperable with models and workflows of NEST and NEURON.

Improvements in performance and flexibility will enable a variety of novel experiments, but the design isn't finalised, and will be driven by the requirements of the community. This is where you come in! We are very interested in your ideas for features which will make new science possible: we ask you to think outside of the box and build this next generation neurosimulator together with us.

Possible features and use cases include:

* Simulating significantly larger networks over longer time scales: simulate a larger proportion of CNS systems with morphological detail, run longer simulations for slowly developing phenomenon and improve statistical power by leveraging large data sets.

* A well-defined high performance C++ API which allows tight integration with other codes: simulate at multiple scales by coupling with other simulators, perform real-time visualization on HPC resources, run online statistics to avoid scaling bottlenecks and embed networks in physically modeled animals.

* Dynamic data structures which allow the creation of models with a time-varying number of neurons, synapses and compartments: simulate neuronal development, healing after injury and age related neuronal degeneration.

What questions haven't you asked yet?

Anisotropic Thermophoresis: Micro-geometry Matters

Zihan Tan[1], **Marisol Ripoll**[2]

[1] **Institute for Advanced Simulation (IAS-2)**

[2] **Institute of Complex Systems (ICS-2/IAS-2)**

Contact: `z.tan@fz-juelich.de`

Keywords: *anisotropic thermophoresis; rods; mesoscale hydrodynamic simulations; thermal diffusion factor; interfacial force.*

Introduction. When a thermal gradient meets colloid-solvent interface, local pressure gradients around colloid will be generated which result in colloidal migration. This transport phenomenon is referred to as colloidal thermophoresis. In contrast to particles with spherical shape, elongated colloids may have a thermophoretic response depends on colloid orientation, and more interestingly a non-vanishing thermophoretic force can be induced in a direction perpendicular to the temperature gradient.

Methods. By means of mesoscale hydrodynamic simulations, we investigate anisotropic thermophoresis of rod-like colloids.

Results. As an analogy to friction of rods, the anisotropic thermophoresis can be characterized by two orthogonal thermal diffusion factors, which determine the thermal diffusion factor in arbitrary orientation. In dilute limit, this linear combination relation explains that the temperature gradient induces no alignment in the rods, and shows that the thermophoretic force increases linearly with the rod length. Rods are constructed by the so-called 'shish-kebab' model what allows us to vary the surface geometry. Remarkably, the amplitude and direction of anisotropy can be changed by tuning rugosity. This can be understood since both different rugosities and solid-liquid interactions induce various interfacial temperature gradients what result in diverse anisotropic effects. Our study shows that anisotropic thermophoresis may be quantitatively controlled by interfacial tunability. In practical, this anisotropic effect of thermophoresis has shown to be the basic mechanism that allows the construction of thermophoretic turbines, which move in the presence of an external temperature gradient.

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Keywords

Authors

Addenda

Fermi surface of Sr_2RuO_4: Role of anisotropic Coulomb interaction and Coulomb-enhanced spin-orbit coupling

Guoren Zhang[1], **Evgeny Gorelov**[1], **Esmaeel Sarvestani**[1], **and Eva Pavarini**[1,2]

[1] **IAS-3, Institute for Advanced Simulation, Forschungszentrum Jülich, D-52425 Jülich, Germany**

[2] **JARA High-Performance Computing**

Contact: `gu.zhang@fz-juelich.de`

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By using the local-density approximation + dynamical mean field theory method, we show that the Coulomb anisotropy and the correlation-enhanced spin-orbit coupling play a crucial role in determining the Fermi surface of Sr_2RuO_4. We also find a strong spin-orbital entanglement. This suggests that the conventional description of Cooper pairs via factorized spin and orbital two-particle functions might not apply to Sr_2RuO_4.

Self-assembly of thermophoretic swimmers

Martin Wagner[1], **Marisol Ripoll**[1]

[1] **Institute of Complex Systems (ICS-2/IAS-2)**

Contact: `m.ripoll@fz-juelich.de`

Keywords: *Hydrodynamics; Active Matter; Mesoscopic simulations; Colloidal phoresis*

Thermophoresis refers to the directed motion of colloidal particles in the presence of a temperature gradient, which can occur towards cold (thermophobic colloids) or warm areas (thermophilic colloids) [1]. Thermophoretic self-propelled motion can be induced in the cases of Janus or dimers colloidal particles with asymmetric heating capacity [2,3]. The thermophoretic properties of the non-heated part produce then a propulsion against or towards the heated part. Equally sized thermophobic microdimers have shown to hydrodynamically behave like pullers (with lateral repulsion), thermophobic microdimers like pushers (with lateral repulsion), and half-coated janus particles like neutral swimmers [4].

Hydrodynamic simulations of microdimers clearly indicate that these hydrodynamic behaviors can be modified and even reversed for microswimmers of unequal beads. Thermophobic microdimers with small heated beads show for example an important lateral attraction as expected for pusher type of swimmers [5]. The collective behavior of these microdimers exibit then a very interesting behavior, which varies from active arrested crystalization, dynamical moving cristals, to planar swarms.

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Coordinator | Thomas Luu
Institute für Kernphysik (IKP-3/IAS4)
Forschungszentrum Jülich GmbH
in the Helmholz Association
52425 Jülich