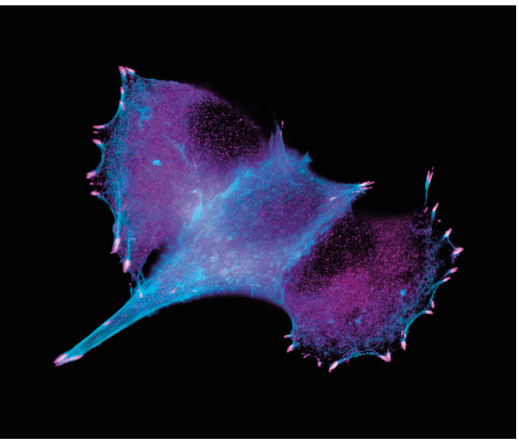
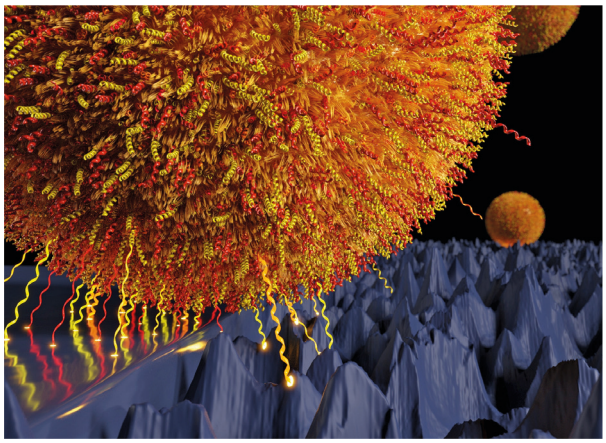
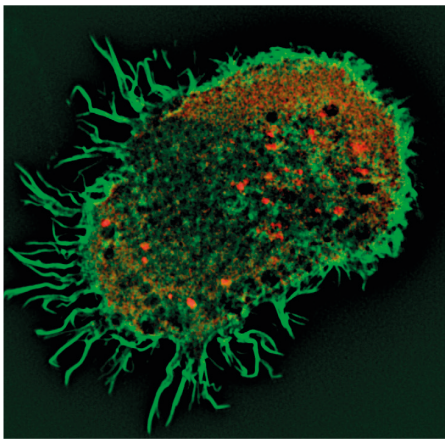
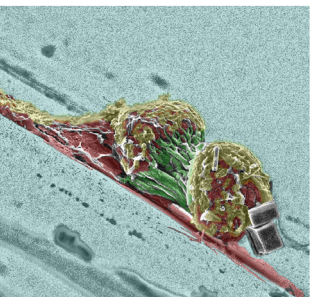
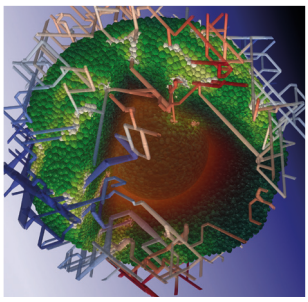
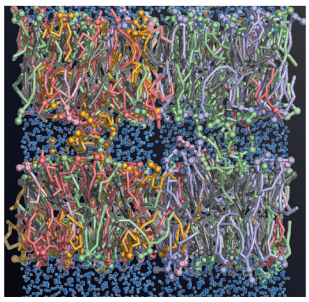
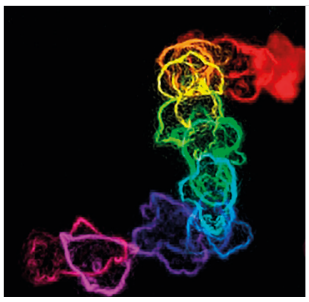
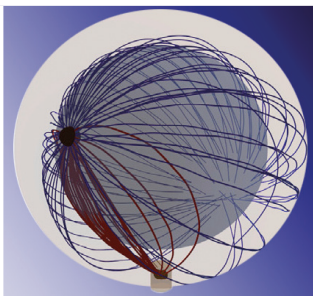
SFB 1027

Collaborative Research Centre 1027

Physical modeling of non-equilibrium processes in biological systems

UNIVERSITÄT DES SAARLANDES

Final Report | 2013-2024

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FINAL REPORT

DFG reference number:

SFB 1027

Project number:

200049484

Title of the Collaborative Research Centre:

Physical modeling of non-equilibrium processes in biological systems

Applicant university/universities:

Universität des Saarlandes

Name of the spokesperson:

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Reporting period (entire funding period):

1.1.2013 – 31.12.2024

1. Summary

English: The central topic of this Collaborative Research Centre (CRC) was the theoretical and experimental modeling of non-equilibrium processes in biological and in particular cellular systems. Its major goal was to reveal and understand basic physical principles governing the active, energy dissipating dynamics of many interacting molecular or cellular agents leading to emergent forms and functions in living matter. Prominent examples of such active processes, taking place far away from thermodynamic equilibrium, include intracellular signaling and transport, cell migration and polarization, and others. Studies over the past three decades on the molecular level have revealed that these physiological phenomena are regulated by complex networks of molecular interactions, but also that this complexity often defies immediate or intuitive understanding. Dynamics is particularly interesting in this context, since in multi-component systems no simple and general link exists to the structure and the properties of the single elements. Consequently, as a quest to gain this understanding, the research topic is currently receiving enormous interest from different fields bearing high future potential.

From a physical point of view, the non-equilibrium processes of interest here go beyond the non-linear and collective phenomena studied in conventional soft-condensed matter systems like complex fluids, colloids and polymers, because cellular processes dissipate energy in a highly organized manner and are internally driven active matter. Thus, the long-term perspective of our initiative was to develop novel theoretical frameworks and new experimental setups that lead to a description level and mechanistic understanding of cellular processes comparable with dynamical phenomena in non-living passive matter.

Among the manifold non-equilibrium processes occurring in cellular systems, the focus of this CRC was placed on self-organization, transport, migration, aggregation, and molecular cooperativity. Emphasis was put on the analysis of emergent phenomena in multi-molecular ensembles in space and in time. This analysis combines the observation and quantification of the spatiotemporal interactions of proteins, organelles and cells with the subsequent theoretical analysis using concepts from statistical physics and bioinformatics. The CRC1027 assembled a highly interdisciplinary team of scientists from Saarland University, Leibniz Institute for New Materials and the Universities of Göttingen and Dresden, to address these timely and complex questions and to contribute to the common goal to integrate - via the identification of individual molecular and subcellular agents - spatiotemporal interactions into functional active processes. Examples included cytoskeleton dynamics and mechanics, intracellular transport, cell migration and polarization, exocytosis at immunological and neural synapses, membrane organization and biofilm formation.

The quantitative analysis of non-equilibrium processes emerging in many-particle systems falls into the realm of physics. The urgent need for the application of established, as well as the development of new, physical methods adapted to understanding cellular systems has been realized by many scientists nationally and internationally. The success of this approach, however, necessitated an efficient integration of biological, medical and physical expertise. In this respect the CRC 1027 offered a unique research environment.

Deutsch: Das zentrale Thema dieses Sonderforschungsbereichs (SFB) war die theoretische und experimentelle Modellierung von Nichtgleichgewichtsprozessen in biologischen, insbesondere zellulären Systemen. Sein Hauptziel war die Aufdeckung und das Verständnis grundlegender physikalischer Prinzipien, die die aktive, energiedissipierende Dynamik vieler interagierender molekularer oder zellulärer Agentien bestimmen und zu emergenten Formen und Funktionen in lebender Materie führen. Prominente Beispiele für solche aktiven Prozesse, die weit entfernt vom thermodynamischen Gleichgewicht stattfinden, sind unter anderem intrazelluläre Signalgebung und Transport, Zellmigration und -polarisation. Studien der letzten drei Jahrzehnte auf molekularer Ebene haben gezeigt, dass diese physiologischen Phänomene durch komplexe Netzwerke molekularer Interaktionen reguliert werden, sich diese Komplexität jedoch oft einem unmittelbaren oder intuitiven Verständnis entzieht. Die Dynamik ist in diesem Zusammenhang besonders interessant, da in Mehrkomponentensystemen keine einfache und allgemeine Verbindung zur Struktur und den Eigenschaften der einzelnen Elemente besteht. Im Bestreben, dieses Verständnis zu erlangen, stößt das Forschungsthema derzeit auf großes Interesse aus verschiedenen Bereichen mit hohem Zukunftspotenzial.

Aus physikalischer Sicht gehen die hier interessierenden Nichtgleichgewichtsprozesse über die nichtlinearen und kollektiven Phänomene hinaus, die in konventionellen Systemen weicher kondensierter Materie wie komplexen Fluiden, Kolloiden und Polymeren untersucht werden, da zelluläre Prozesse Energie hochorganisiert dissipieren und von intern getriebener aktiver Materie angetrieben werden. Die langfristige Perspektive unserer Initiative bestand daher darin, neuartige theoretische Rahmen und neue experimentelle Aufbauten zu entwickeln, die zu einem Beschreibungsniveau und mechanistischen Verständnis zellulärer Prozesse führen, das mit dynamischen Phänomenen in unbelebter passiver Materie vergleichbar ist.

Unter den vielfältigen Nichtgleichgewichtsprozessen in zellulären Systemen lag der Schwerpunkt dieses SFB auf Selbstorganisation, Transport, Migration, Aggregation und molekularer Kooperativität. Der Schwerpunkt lag auf der Analyse emergenter Phänomene in multimolekularen Ensembles in Raum und Zeit. Diese Analyse kombiniert die Beobachtung und Quantifizierung der räumlich-zeitlichen Interaktionen von Proteinen, Organellen und Zellen mit der anschließenden theoretischen Analyse unter Verwendung von Konzepten der statistischen Physik und Bioinformatik. Der SFB 1027 versammelte ein hoch interdisziplinäres Team von Wissenschaftlerinnen und Wissenschaftlern der Universität des Saarlandes, des Leibniz-Instituts für Neue Materialien sowie der Universitäten Göttingen und Dresden, um diese aktuellen und komplexen Fragen zu bearbeiten und zum gemeinsamen Ziel beizutragen, räumlich-zeitliche Interaktionen durch die Identifizierung einzelner molekularer und subzellulärer Wirkstoffe in funktionelle aktive Prozesse zu integrieren. Beispiele hierfür waren die Dynamik und Mechanik des Zytoskeletts, intrazellulärer Transport, Zellmigration und -polarisation, Exozytose an immunologischen und neuronalen Synapsen, Membranorganisation und Biofilmbildung.

Die quantitative Analyse von Nichtgleichgewichtsprozessen in Vielteilchensystemen fällt in den Bereich der Physik. Viele Wissenschaftlerinnen und Wissenschaftler national und international haben den dringenden Bedarf an der Anwendung etablierter sowie der Entwicklung neuer physikalischer Methoden zum Verständnis zellulärer Systeme erkannt. Der Erfolg dieses Ansatzes erforderte jedoch eine effiziente Integration biologischer, medizinischer und physikalischer Expertise. In dieser Hinsicht bot der SFB 1027 ein einzigartiges Forschungsumfeld.

2. Selection of the most important published results

2.1 Publications with scientific quality assurance

1. **Hairpin protein partitioning from the ER to lipid droplets involves major structural rearrangements.** R. Dhiman, R.S. Perera, C.S. Poojari, H.T.A. Wiedemann, R. Kappl, C.W.M. Kay, J.S. Hub, B. Schrul, *Nat. Commun.* **15**, 4504 (2024). https://doi.org/10.1038/s41467-024-48843-8
2. **The structure and mechanics of the cell cortex depend on the location and adhesion state**. D.A.D. Flormann, L. Kainka, G. Montalvo, C. Anton, J. Rheinlaender, D. Thalla, D. Vesperini, M.O. Pohland, K.H. Kaub, M. Schu, F. Pezzano, V. Ruprecht, E. Terriac, R.J. Hawkins, F. Lautenschläger, *Proc. Natl. Acad. Sci. U.S.A*. **121**, e2320372121 (2024). https://doi.org/10.1073/pnas.2320372121
3. **PIEZO1-mediated mechano-sensing governs NK-cell killing efficiency and infiltration in three-dimensional matrices.** A.K. Yanamandra, J. Zhang, G. Montalvo, X. Zhou, D. Biedenweg, R. Zhao, S. Sharma, M. Hoth, F. Lautenschläger, O. Otto, A. del Campo, B. Qu. *Eur. J. Immunol*. 54, e2350693 (2024). https://doi.org/10.1002/eji.202350693
4. **MemPrep, a new technology for isolating organellar membranes provides fingerprints of lipid bilayer stress.** J. Reinhard, L. Starke, C. Klose, P. Haberkant, H. Hammarén, F. Stein, O. Klein, C. Berhorst, H. Stumpf, J.P. Sáenz, J. Hub, M. Schuldiner, R. Ernst, *EMBO J*. 43, 1653 (2024). https://doi.org/10.1038/s44318-024-00063-y
5. **Molecular Simulations Reveal the Free Energy Landscape and Transition State of Membrane Electroporation.** G. Kasparyan, J.S. Hub, *Phys. Rev. Lett.* **132**, 148401 (2024). https://doi.org/10.1103/PhysRevLett.132.148401
6. **Vesicles driven by dynein and kinesin exhibit directional reversals without regulators.** D'Souza, A.I., Grover, R., Monzon, G.A., L. Santen, S. Diez, *Nat. Commun.* **14**, 7532 (2023). https://doi.org/10.1038/s41467-023-42605-8
7. **Regulating Bacterial Behavior within Hydrogels of Tunable Viscoelasticity**. S. Bhusari, S. Sankaran, A. del Campo, *Adv. Sci.* **9**, 2106026 (2022). https://doi.org/10.1002/advs.202106026
8. **Cytotoxic Efficiency of Human $CD8^+$ T Cell Memory Subtypes**. A. Knörck, G. Schäfer, D. Alansary, J. Richter, L. Thurner, M. Hoth, E.C. Schwarz. *Front. Immun.* **13**, 838484 (2022). https://doi.org/10.3389/fimmu.2022.838484
9. **Lipid Droplets Embedded in a Model Cell Membrane Create a Phospholipid Diffusion Barrier**. S. Puza, S. Caesar, C. Poojari, M. Jung, R. Seemann, J. S. Hub, B. Schrul, J.-B. Fleury. *Small* **18**, 2106524 (2022). https://doi.org/10.1002/smll.202106524
10. **Optimal non-Markovian search strategies with n-step memory**. H. Meyer and H. Rieger, *Phys. Rev. Lett.* **127**, 070601 (2021). https://doi.org/10.1103/PhysRevLett.127.070601
11. **Free energies of membrane stalk formation from a lipidomics perspective**. C.S. Poojari, K.C. Scherer, J.S. Hub. *Nat. Commun.* **12**, 6594 (2021). https://doi.org/10.1038/s41467-021-26924-2
12. **Engineered living biomaterials**. A. Rodrigo-Navarro, S. Sankaran, M.J. Dalby, A. del Campo, M. Salmeron-Sanchez. *Nat. Rev. Mater.* **6**, 1175 (2021). https://doi.org/10.1038/s41578-021-00350-8
13. **Optoregulated force application to cellular receptors using molecular motors**. Y. Zheng, K.L.M. Han, R. Zhao, J. Blass, J. Zhang, D.W. Zhou, J.-R. Colard-Itté, D. Dattler, A. Çolak, M.

Hoth, A.J. García, B. Qu, R. Bennewitz, N. Giuseppone, A. del Campo, *Nat. Commun.* **12**, 3580 (2021). https://doi.org/10.1038/s41467-021-23815-4

14. **Nascent fusion pore opening monitored at single-SNAREpin resolution**. P. Heo, J. Coleman, J.-B. Fleury, J.E. Rothman, F. Pincet, *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2024922118 (2021) https://doi.org/10.1073/pnas.2024922118
15. **Computational models for active matter**. M.R. Shaebani, A. Wysocki, R.G. Winkler, G. Gompper, H. Rieger, *Nat. Rev. Phys.* **2**, 181 (2020) https://doi.org/10.1038/s42254-020-0152-1
16. **Capillary Action in Scalar Active Matter**. A. Wysocki, H. Rieger, *Phys. Rev. Lett.* **124**, 048001 (2020). https://doi.org/10.1103/PhysRevLett.124.048001
17. **Persistence-Speed Coupling Enhances the Search Efficiency of Migrating Immune Cells**. M.R. Shaebani, R. Jose, L. Santen, L. Stankevicins, F. Lautenschläger, Phys. Rev. Lett. **125**, 268102 (2020). https://doi.org/10.1103/PhysRevLett.125.268102
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20. **Stable tug-of-war between kinesin-1 and cytoplasmic dynein upon different ATP and roadblock concentrations**. G.A. Monzon, L. Scharrel, A. D'Souza, V. Henrichs, L. Santen, S. Diez, *J. Cell. Sci.* **133**, jcs249938 (2020). https://doi.org/10.1242/jcs.249938
21. **Different binding mechanisms of Staphylococcus aureus to hydrophobic and hydrophilic surfaces**. E. Maikranz, C. Spengler, N. Thewes, A. Thewes, F. Nolle, P. Jung, M. Bischoff, L. Santen, K. Jacobs, *Nanoscale* **12**, 19267 (2020). https://doi.org/10.1039/D0NR03134H
22. **Self-Organized Lane Formation in Bidirectional Transport by Molecular Motors**. R. Jose, L. Santen. *Phys. Rev. Lett*. **124**, 198103 (2020). https://doi.org/10.1103/PhysRevLett.124.198103
23. **Migration of Cytotoxic T Lymphocytes in 3D Collagen Matrices**. Z. Sadjadi, R. Zhao, M. Hoth, B. Qu , H. Rieger, *Biophys. J.* **119**, 2141 (2020). https://doi.org/10.1016/j.bpj.2020.10.020
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25. **Stepping out of the shadow: STIM2 promotes IL-3–induced cytokine release**. D. Alansary, B.A. Niemeyer, *Sci. Signal.* **12**, eaax0210 (2019). https://doi.org/10.1126/scisignal.aax0210
26. **Optoregulated Drug Release from an Engineered Living Material: Self-Replenishing Drug Depots for Long-Term, Light-Regulated Delivery**. S. Sankaran, J. Becker, C. Wittmann, A. del Campo, *Small* **15**, 1804717 (2019). https://doi.org/10.1002/smll.201804717
27. **Positional Information Readout in Ca2+ Signaling**. V.H. Wasnik, P. Lipp, K. Kruse, *Phys. Rev. Lett.* **123**, 058102 (2019). https://doi.org/10.1103/PhysRevLett.123.058102
28. **Highly Reproducible Physiological Asymmetric Membrane with Freely Diffusing Embedded Proteins in a 3D-Printed Microfluidic Setup**. P. Heo, S. Ramakrishnan, J. Coleman, J.E. Rothman, J.-B. Fleury, F. Pincet, *Small* **15**, 1900725 (2019). https://doi.org/10.1002/smll.201900725
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Friedmann, S. Mang, A. Knörck, M. Hoth, C. Kummerow. *J Biol Chem*. **293**, 16348 (2018). https://doi.org/10.1074/jbc.RA118.004549

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31. **Active superelasticity in three-dimensional epithelia of controlled shape.** Latorre, E., Kale, S., Casares, L., M. Gómez-González, M. Uroz, L. Valon, R.V. Nair, H. Garreta, N. Montserrat, A. del Campo, B. Ladoux, M. Arroyo, X. Trepat, *Nature* **563**, 203 (2018). https://doi.org/10.1038/s41586-018-0671-4
32. **A calcium optimum for cytotoxic T lymphocyte and natural killer cell cytotoxicity.** X. Zhou X, K.S. Friedmann, H. Lyrmann, Y. Zhou, R. Schoppmeyer, A. Knörck, S. Mang, C. Hoxha, A. Angenendt, C.S. Backes, C. Mangerich, R. Zhao, S. Cappello, G. Schwär, C. Hässig, M. Neef, B. Bufe, F. Zufall, K. Kruse, B.A. Niemeyer, A. Lis, B. Qu, C. Kummerow, E.C. Schwarz, M. Hoth, *J. Physiol.* **596**, 2681 (2018). https://doi.org/10.1113/JP274964
33. **Toward Light-Regulated Living Biomaterials**. S. Sankaran, S. Zhao, C. Muth, J. Paez, A. del Campo, *Adv. Sci.* **5**, 1800383 (2018). https://doi.org/10.1002/advs.201800383
34. **Pure Protein Bilayers and Vesicles from Native Fungal Hydrophobins**. H. Hähl, J. N. Vargas, A. Griffo, P. Laaksonen, G. Szilvay, M. Lienemann, K. Jacobs, R. Seemann, J.-B. Fleury, *Adv. Mater.* **29**, 1602888 (2017). https://doi.org/10.1002/adma.201602888
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36. **Actin kinetics shapes cortical network structure and mechanics**. M. Fritzsche, C. Erlenkämper, E. Moeendarbary, G. Charras, K. Kruse, *Sci Adv.* **2**, e1501337 (2016). https://doi.org/10.1126/sciadv.1501337
37. **A calcium-redox feedback loop controls human monocyte immune responses: The role of ORAI Ca2+ channels.** S. Saul, C.S. Gibhardt, B. Schmidt, A. Lis, B. Pasieka, D. Conrad, P. Jung, R. Gaupp, B. Wonnenberg, E. Diler, H. Stanisz, T. Vogt, E.C. Schwarz, M. Bischoff, M. Herrmann, T. Tschernig, R. Kappl, H. Rieger, B.A. Niemeyer, I. Bogeski, *Sci Signal.* **9**, ra26 (2016). https://doi.org/10.1126/scisignal.aaf1639
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46. **Interstitial fluid flow and drug delivery in vascularized tumors: a computational model.** M. Welter, H. Rieger. PLoS One. **8**, e70395 (2013). https://doi.org10.1371/journal.pone.0070395
47. **Membrane binding of MinE allows for a comprehensive description of Min-protein pattern formation.** M. Bonny, E. Fischer-Friedrich, M. Loose, P. Schwille, K. Kruse, *PLoS Comput Biol*. **9**, e1003347 (2013). https://doi.org/10.1371/journal.pcbi.1003347

2.2 Other publications and published results

48. **Multiple clustered centrosomes in antigen-presenting cells foster T cell activation without MTOC polarization**. I. Stötzel, A.-K. Weier, A. Sarkar, S. Som, P. Konopka, E. Miková, J. Böthling, M. Homrich, L. Schaedel, U. Kazmaier, K. Symeonidis, Z. Abdullah, S. Uderhardt, M. Hons, R. Paul, H. Rieger, E. Kiermaier, bioRxiv 2024.07.18.604057 (2024). https://doi.org/10.1101/2024.07.18.604057
49. **Tau accelerates tubulin exchange in the microtubule lattice.** S. Biswas, R. Grover, C. Reuther, C.S. Poojari, M.R. Shaebani, M. Grünewald, A. Zablotsky, J.S. Hub, S. Diez, K. John, L. Schaedel. bioRxiv 2024.10.05.616777 (2024); https://doi.org/10.1101/2024.10.05.616777
50. **The mechanism how Pretubulysin-induced microtubule disassembly improves T cell search efficiency.** G. Montalvo, M.R. Shaebani, S. Nandakumar, N. Cowley, R. Zhao, R. Hawkins, M. Hoth, M.A. Lauterbach, L. Schaedel, B. Qu, F. Lautenschläger, bioRxiv 2025.02.24.639827 (2025); https://doi.org/https://doi.org/10.1101/2025.02.24.639827

3. Overview of Projects

TP	Title	Research area	Principal investigator(s), institution(s), location(s)	Period
A1	Cytoskeletal self-organization and cell signaling	Biological Physics Theoretical Physics	**Kruse, Karsten, Prof. Dr.** Dept. of Biochemistry, University of Geneva	2013-2020
A2	Dynamics of polarization of T cells	Biophysics, Cell Biology, Immunology	**Qu, Bin, Dr.** CIPMM & Dept. of Biophysics, Saarland University, Homburg **Hoth, Markus, Prof. Dr.** CIPMM & Dept. of Biophysics, Saarland University, Homburg	2013-2024 2013-2020
A3	Physical processes during T cell search, polarization, and killing	Biological Physics, Theoretical Physics, Statistical Physics	**Rieger, Heiko, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2013-2024
A4	Spontaneous activity in the developing cochlea	Biophysics, Cell Biology, Immunology	**Engel, Jutta, Prof. Dr.** CIPMM & Dept. of Biophysics, Saarland University, Homburg	2013-2016
A5	Local cPKC-translocation as a mechanism for localized cell response	Biophysics, Cell Biology	**Lipp, Peter, Prof. Dr.** Molecular Cell Biology Saarland University, Homburg **Kruse, Karsten, Prof. Dr.** Dept. of Biochemistry, University of Geneva	2013-2016
A6	Dissecting KDEL receptor clustering at the mammalian cell surface in response to cargo binding, internalization and compartmental transport	Molecular and Cell Biology	**Schmitt, Manfred, Prof. Dr.** Dept. of Biosciences, Saarland University, Saarbrücken	2013-2020
A7	Stochastic approach to active processes and diffusive dynamics in biological environments	Theoretical Biophysics, Statistical Physics	**Shaebani, M. Reza, Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2013-2024
A8	Motor-driven transport of intracellular cargo: Cooperativity and control	Experimental and Theoretical Biophysics	**Diez, Stefan, Prof. Dr.** B CUBE, TU Dresden **Santen, Ludger, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2017-2024
A10	The actin cortex during transitions of cellular states	Experimental Physics, Biological Physics	**Lautenschläger, Franziska, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2017-2024
A11	Killing efficiency of cytotoxic T lymphocytes and natural killer cells against cancer cells	Biophysics, Cell Biology, Immunology	**Hoth, Markus, Prof. Dr.** CIPMM & Dept. of Biophysics, Saarland University, Homburg	2021-2024
A12	Environmental control of melanocyte differentiation and transformation through cell adhesion & mechanics	Molecular Cell Biology, Biophysicss	**Iden, Sandra, Prof. Dr.** Dept. of Cell and Developmental Biology, Saarland University, Homburg	2021-2024

A13	The role of MAPs in microtubule lattice dynamics	Experimental physics, Biophysics	**Aradilla-Zapata, Laura, Jun.-Prof. Dr.,** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2021-2024
B1	Modeling biofilms - proteins and bacteria	Experimental Physics, Biological Physics, Theoretical and Statistical Physics	**Jacobs, Karin, Prof. Dr.** **Hähl, Hendrik, Dr.** **Santen, Ludger, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2013-2024
B2	Bacterial adhesion and biofilm formation: Physical processes at interfaces	Experimental Physics, Biophysics, Microbiology	**Jacobs, Karin, Prof. Dr.** ZBP & Dept. of Physics, Saarbrücken **Bischoff, Markus, PD Dr.** Dept. of Infection Medicine, Saarland University, Homburg	2013-2024
B3	Bioinspired control of biofilms on soft and hard oral tissues	Preventive Dentistry	**Hannig, Matthias, Prof. Dr**. Dept. of Dentistry, Saarland University, Homburg	2013-2024
B4	Microfluidic platform to study the transport properties of model cell membranes	Experimental Physics, Biological Physics	**Fleury, Jean-Baptiste, Dr.** **Seemann, Ralf, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2013-2024
B5	Aggregation of red blood cells in flow	Experimental Physics	**Wagner, Christian, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2013-2016
B6	Dynamics of ligands and forces in T cell activation	Biophysics, Biochemistry	**del Campo, Aránzazu**, **Prof. Dr.** Leibniz Institut for New Materials (INM), Saarland University, Saarbrücken	2017-2024
B7	MD simulation of large-scale transitions at membranes and interfaces	Biological Physics, Theoretical Physics	**Hub, Jochen, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2021-2024
B8	Studying bacterial behavioral dynamics in artificial biofilms	Microbiology, Biochemistry, Biophysics, Materials Science	**Sankaran, Shrikrishnan, Dr.** Leibniz Institute for New Materials (INM), Saarland University, Saarbrücken	2021-2024
C1	Fluctuations and cooperativity in molecular recognition and development	Biological Physics	**Ott, Albrecht, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2013-2024
C2	DNA-methylation pattern formation: mechanistic analysis, and mathematical modelling of epigenetic control	Epigenetics, Epigenomics, Molecular Genetics, Mathematical Modelling	**Walter, Jörn, Prof. Dr.** Dep. of Biosciences Saarland University, Saarbrücken **Wolf, Verena, Prof. Dr.** Dept. of Informatics, Saarland University, Saarbrücken	2013-2016
C3	Cellular reorganization upon state transitions	Bioinformatics	**Helms, Volkhard, Prof. Dr.** ZBI & Dept. of Biosciences, Saarland University, Saarbrücken	2013-2024

C4	Decoding the functional relevance of compartmentally controlled calcium and redox signaling	Biology, Medicine, Biophysics, Physiology	**Niemeyer, Barbara, Prof. Dr.** CIPMM & Dept. of Biophysics, Saarland University, Homburg **Bogeski, Ivan, Prof. Dr.** Institute of Cardiovascular Physiology, University of Göttingen	2013-2024
C5	The role of protein-lipid interactions in fast Ca^{2+}-triggered exocytosis	Biophysics, Neurophysiology	**Schwarz, Yvonne, Dr.** **Bruns, Dieter, Prof. Dr.** CIPMM & Dept. of Physiology, Saarland University, Homburg	2013-2024
C6	Cooperative action of SNARE peptides in fusion	Biophysics	**Böckmann, Rainer A., Prof. Dr.** Dept. of Biology, University of Erlangen-Nürnberg	2017-2020
C7	Membrane protein organization studied at the single molecule level using liquid-phase electron microscopy	Biophysics, Electron Microscopy	**de Jonge, Niels, Prof. Dr.** Leibniz Institute for New Materials (INM), Saarland University, Saarbrücken	2017-2021
C9	Lipid Droplet Formation: Cooperative processes governing protein partitioning between membranes of distinct physicochemical properties	Biochemistry, Cell Biology	**Schrul, Bianca, Jun.-Prof. Dr.** PZMS & Dept. of Medical Biochemistry, Saarland University, Homburg	2019-2024
C10	A kinetic proofreading mechanism for sensing lipid saturation	Biochemistry, Cell Biology	**Ernst, Robert, Prof. Dr.** PZMS & Dep. of Medical Biochemistry, Saarland University, Homburg	2021-2024
MGK	Integrated Research Training Group		**Jacobs, Karin, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2013-2024
ZX	Bioinformatics service project	Bioinformatics	**Helms, Volkhard, Prof. Dr.** ZBI & Dept. of Biosciences, Dept. for Biosciences, Saarland University, Saarbrücken	2021-2024
Z	Central tasks of the CRC		**Rieger, Heiko, Prof. Dr.** ZBP & Dept. of Physics, Saarland University, Saarbrücken	2013-2024

4. Research Achievements of the CRC

The overall aim of this CRC was to bring fundamental physics to biomedical systems to understand and solve biological questions and ultimately translate these findings to medicine. Within its three funding periods, the CRC 1027 succeeded to establish specific systems and platforms to reach its overall research goal: 1) Tailor made killing assays for the study of immune cells, in particular killer cells, as among the fastest migrators. 2) Engineered collagen matrices and programmable surfaces were established as platforms to study migration and search, cell polarization and mechano-sensation. 3) Artificial lipid membranes and lipid bilayers were established to study functions of membrane proteins like SNAREs and hairpin proteins. 4) Specific models to analyze, for instance, migration data of immune cells and their search processes, or to understand mechanical processes during the formation of the immunological synapse. A clear goal was to unfold the full power of the stablished platforms and to extend our arsenal of methods and systems by integrating new investigators devoted to contributing to the overall aim of our CRC. Many of them (Hub, Schrul, Ernst, Iden, Aradilla-Zapata) were hired by the University during the second funding period of the CRC, explicitly with the aim to strengthen the CRC 1027 which is why their expertise and research field fitted quite naturally into the CRCs research program. The most successful strategy of the CRC 1027 was to build on the combination of complementary theoretical, experimental and clinical expertise. To concretize this scientific development we summarize in the following briefly some of the main research achievements of the individual projects:

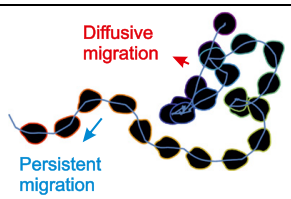
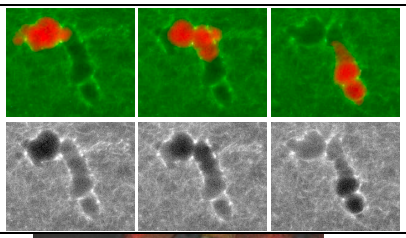
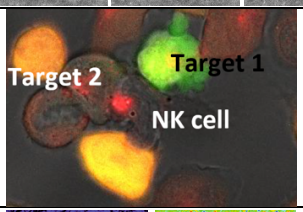
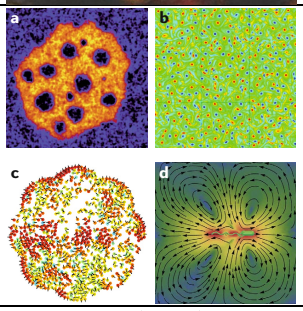
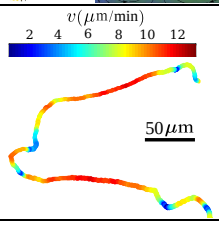
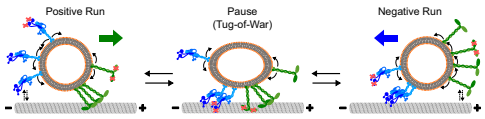
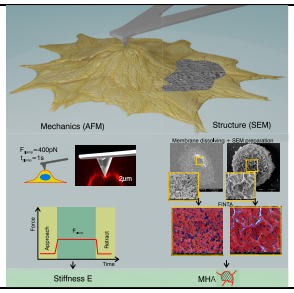
Project A2 (B. Qu) performed pioneering work in systematically characterizing the impact of extracellular and intracellular physical properties on the functionality of immune cells, in particular T and natural killer (NK) cells, as well as elucidating the underlying mechanisms [3,13,24,45,50]. Project A3 (H. Rieger) developed a quantitative model to understand centrosome relocation during the formation of the immunological synapse during target cell killing [48], which laid the foundation for future work on the centrosome relocation during cell migration. Furthermore, they studied broadly stochastic search processes, with applications to immune cells, and a focus on search strategies with memory and collective search processes [10,24,40]. Project A10 (F. Lautenschläger) revealed a clear correlation between the structure (cortical thickness, cortex mesh size, actin bundling) and the stiffness of the acto-myosin cortex and was able to understand this correlation with the help of a theoretical model [2]. Project A11 (M. Hoth) established a simple, economic, time-resolved killing assay [45] with which they could, over the years, systematically study T and NK cells killing target cells in a well-controlled environment [3,8,24,30,33]. Among many other things they found that, bystander cells can improve killing efficiency and that killing of cancer cells by T cells and NK cells is not independent of each other [8]. Project A12 (S. Iden) used reductionist cell models to delineate the role of environmental factors such as extracellular matrix (ECM) proteins and substrate stiffness for the differentiation and function of skin pigment cells (melanocytes).

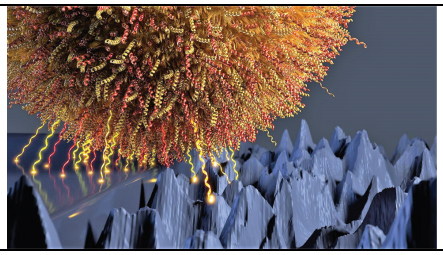
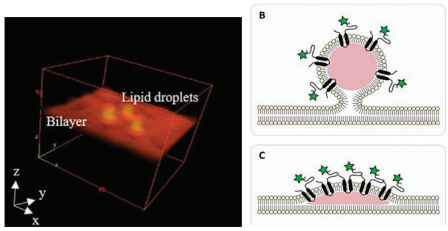
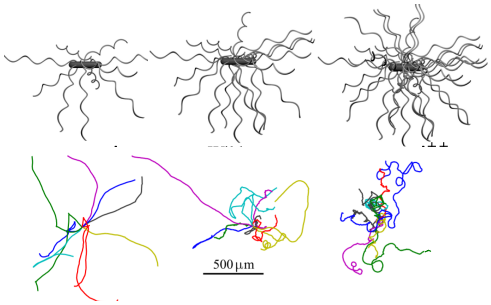
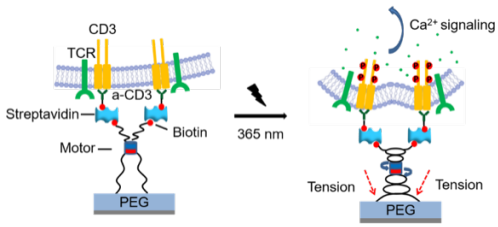
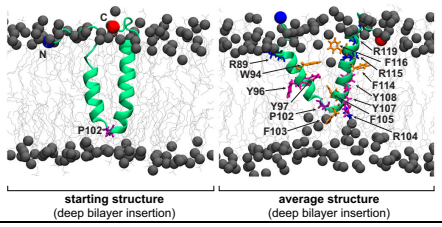
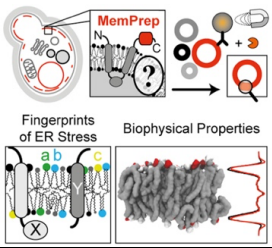
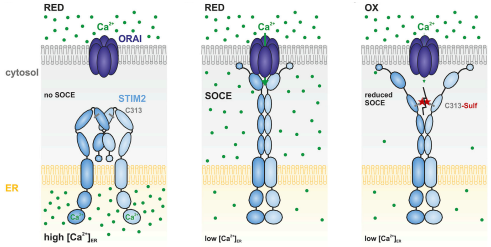
B1, B2 (K. Jacobs, L. Santen M. Bischoff, H. Hähl) studied in a combined experimental / computational approach the adhesion of the pathogenic bacterium *Staphylococcus aureus* to hydrophilic and hydrophobic surfaces and revealed that binding to both types of surfaces is mediated by thermally fluctuating cell wall macromolecules that behave differently on each type of substrate [22]. Project B4 (R. Seemann, J.-B. Fleury) developed a microfluidic system that enables the formation, observation and manipulation of artificial cell membranes. This system has been successfully used to understand the interaction of nano- and microparticles with such a membrane [29,39], to investigate protein mediated membrane fusion [14] and to study the behavior of lipid droplets in the presence of proteins and peptides [9]. In project B6 (A. del Campo) T cell activation by forces

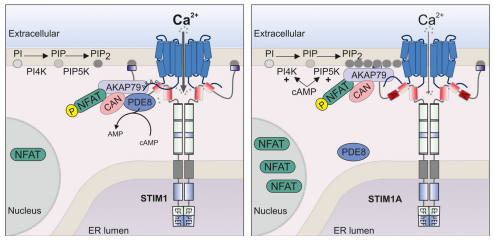
was examined using a synthetic mechanoactuated interface with molecular machines [13], which was only possible by joining expertise in synthetic biomaterials (B6) and T cell biology (A2). Project B7 (J. Hub) found that membrane fusion proteins are by far more than mechanical springs equipped with hydrophobic membrane anchors. Instead, fusion proteins may actively remodel the membrane by locally enriching certain lipids and by increasing membrane disorder, thereby shaping the free energy landscape of membrane fusion [1,5,9,11]. Project B8 (S. Sankaran) has shown major ways in which bacterial growth and metabolism are influenced by confinement in mechanically restrictive environments with different viscoelastic properties. These provide key insights into their behavioral changes within specific domains of natural biofilms [7].

Project C9 (B. Schrul), in a major interdisciplinary collaboration with B4 and B7, uncovered a novel mechanism underlying the protein partitioning from phospholipid bilayer membranes of the endoplasmic reticulum (ER) to the lipid droplet (LD) phospholipid monolayer [1]. ER/LD proteins can adopt distinct and stable conformations in these two different types membranes and must undergo unexpected major structural rearrangements during ER-to-LD partitioning; a finding that challenges previous models that suggested a simple passive diffusion mechanism underlying this partitioning. Project C10 (R. Ernst) modeled and biochemically reconstituted the mechanism of signal amplification by a lipid saturation sensor and has developed new protocols for isolating organelle derived membranes for studying biophysical membrane homeostasis in complex biomembranes [4]. Project C4 (B. Niemeyer, I. Bogeski) identified several molecular mechanisms and key players involved in the redox-calcium interplay at the subcellular level and determined their functional impact in immune and cancer cells [26,38,42]. Finally project C3 (V. Helms) developed the webservers TFmiR and PPIXpress/PPICompare to characterize the rewiring of gene-regulatory and protein-protein interaction networks between two cellular conditions.

In the following we provide a graphical overview of these main achievements.

	**A1/A2/A10: Deterministic actin waves as generators of cell polarization cues.** L. Stankevicins, N. Ecker, E. Terriac, P. Maiuri, R. Schoppmeyer, P. Vargas, A.-M. Lennon-Duménil, M. Piel, **B. Qu, M. Hoth, K. Kruse, F. Lautenschläger**, *Proc. Nat. Acad. Sci. U.S.A. 117, 826 (2020).*
	**A2/A3: Migration of Cytotoxic T Lymphocytes in 3D Collagen Matrices.** Z. Sadjadi, R. Zhao, **M. Hoth**, **B. Qu**, **H. Rieger**, *Biophys. J. 119, 2141 (2020).*
	**A2** (later **A11**)**: Natural killer cells induce distinct modes of cancer cell death: Discrimination, quantification, and modulation of apoptosis, necrosis, and mixed forms.** C.S. Backes, K.S. Friedmann, S. Mang, A. Knörck, **M. Hoth**, C. Kummerow, *J. Biol. Chem. 293, 16348 (2018).*
	**A3/A7: Computational models for active matter.** **M. R. Shaebani**, A. Wysocki, R. G. Winkler, G. Gompper, **H. Rieger**, *Nat. Rev. Phy. 2, 181 (2020).*
	**A7/A8/A10: Persistence-speed coupling enhances the search efficiency of migrating immune cells.** **M. R. Shaebani**, R. Jose, **L. Santen**, L. Stankevicins, **F. Lautenschläger**, *Phys. Rev. Lett., 125, 268102 (2020).*
	**Vesicles driven by dynein and kinesin exhibit directional reversals without regulators.** D'Souza, A.I., Grover, R., Monzon, G.A., L. Santen, S. Diez, *Nat. Commun.* **14**, 7532 (2023).
	**A10: The structure and mechanics of the cell cortex depend on the location and adhesion state.** D.A.D. Flormann, L. Kainka, G. Montalvo, C. Anton, J. Rheinlaender, D. Thalla, D. Vesperini, M.O. Pohland, K.H. Kaub, M. Schu, F. Pezzano, V. Ruprecht, E. Terriac, R.J. Hawkins, **F. Lautenschläger**, *Proc. Natl. Acad. Sci. U.S.A. 121, e2320372121 (2024).*

	**B1/B2: Strength of bacterial adhesion on nanostructured surfaces quantified by substrate morphometry.** C. Spengler, F. Nolle, J. Mischo, T. Faidt, S. Grandthyll, N. Thewes, M. Koch, F. Müller, **M. Bischoff**, M.A. Klatt, **K. Jacobs**, *Nanoscale* 11, 19713 (2019).
	**B4/B7/C9: Lipid Droplets Embedded in a Model Cell Membrane Create a Phospholipid Diffusion Barrier.** S. Puza, S. Caesar, C. Poojari, M. Jung, **R. Seemann**, **J. S. Hub**, **B. Schrul**, **J.-B. Fleury**. *Small* 18, 2106524 (2022).
	**B5/A7: Flagellar number governs bacterial spreading and transport efficiency.** J. Najafi, **M.R. Shaebani**, T. John, F. Altegoer, G. Bange, **C. Wagner**. *Sci Adv*. 4, eaar6425 (2018).
	**B6/A2: Optoregulated force application to cellular receptors using molecular motors**. Y. Zheng, K.L.M. Han, R. Zhao, J. Blass, J. Zhang, D.W. Zhou, J.-R. Collard-Itté, D. Dattler, A. Çolak, **M. Hoth**, A.J. García, **B. Qu** , R. Bennewitz, N. Giuseppone, **A. del Campo**, *Nat. Commun.* 12, 3580 (2021).
	**C9/B7: Hairpin protein partitioning from the ER to lipid droplets involves major structural rearrangements.** R. Dhiman, R.S. Perera, C.S. Poojari, H.T.A. Wiedemann, R. Kappl, C.W.M. Kay, **J.S. Hub**, **B. Schrul**, *Nat. Commun.* 15, 4504 (2024).
	**C10/B7: MemPrep, a new technology for isolating organellar membranes provides fingerprints of lipid bilayer stress.** J. Reinhard, L. Starke, C. Klose, P. Haberkant, H. Hammarén, F. Stein, O. Klein, C. Berhorst, H. Stumpf, J.P. Sáenz , **J. Hub**, M. Schuldiner, **R. Ernst**, *EMBO J.* 43, 1653 (2024).
	**C4/C6/A2: Oxidative Stress-Induced Stim2 Cysteine Modifications Suppress Store-Operated Calcium Entry.** C.S. Gibhardt, S. Cappello, R. Bhardwaj, R. Schober, S.A. Kirsch, Z. Bonilla Del Rio, S. Gahbauer, A. Bochicchio, M. Sumanska, C. Ickes, I. Stejerean-Todoran, M. Mitkovski, D. Alansary, X. Zhang, A. Revazian, M. Fahrner, V. Lunz, I. Frischauf, T. Luo, D. Ezerina, J. Messen, V.V. Belousov, **M. Hoth**, **R.A. Böckmann**, M.A. Hediger, R. Schindl, **I. Bogeski**, *Cell Rep. 33, 108292 (2020).*

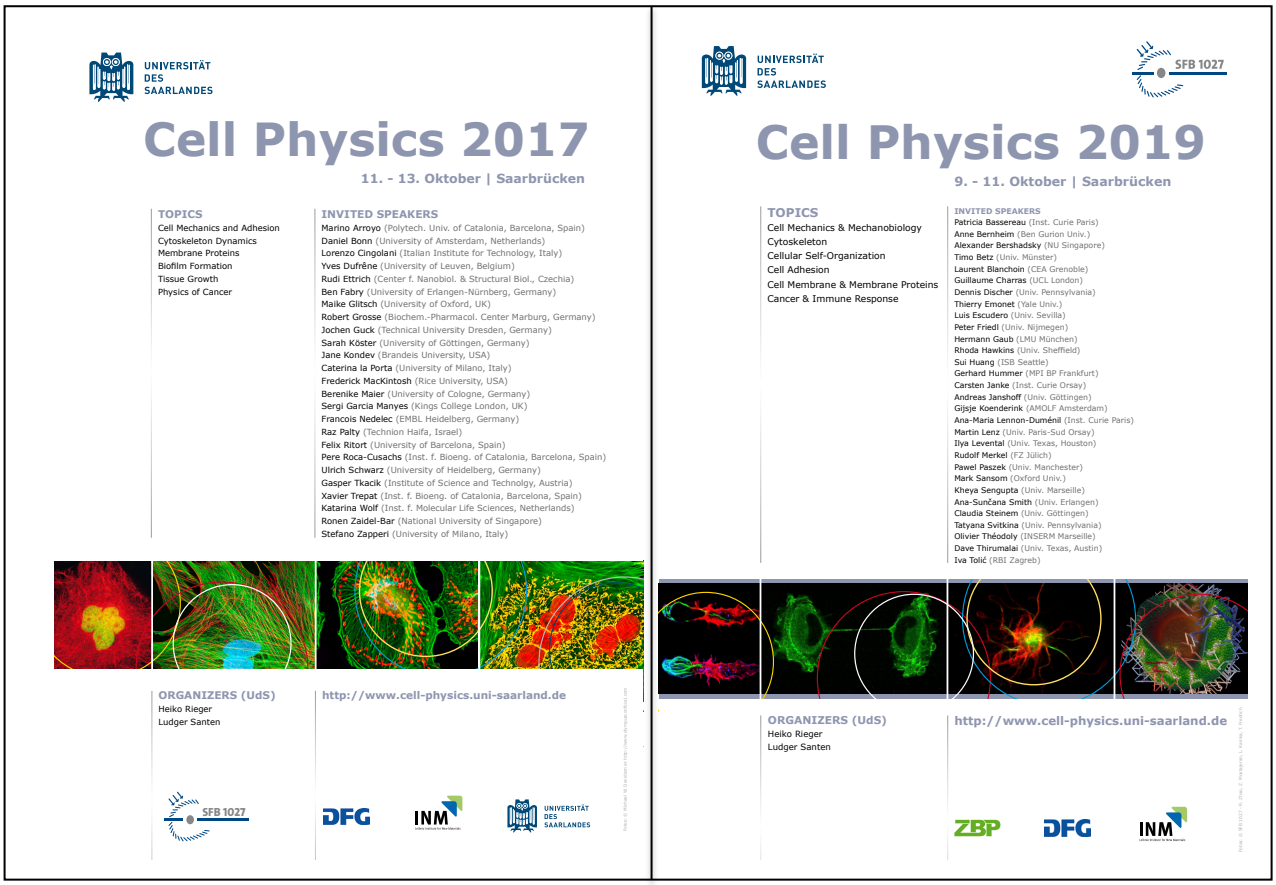
	**C4/C3/C5: A longer isoform of Stim1 is a negative SOCE regulator but increases cAMP-modulated NFAT signaling.** M.L. Knapp, D. Alansary, V. Poth, K. Förderer, F. Sommer, D. Zimmer, **Y. Schwarz**, N. Künzel, A. Kless, K. Machaca, **V. Helms**, T. Mühlhaus, M. Schroda, A. Lis, **B.A. Niemeyer**, *EMBO reports 23, e53135 (2022).*

4.1 Scientific Events and Science Communication

- **Cell Physics 2014, 2016, 2017, 2019, 2021, 2023**: To gain international visibility the CRC established and organized the biannual international conference "**Cell Physics**" on the campus of the Saarland University in 2014, 2016, 2017, 2019, 2021 and 2023 with more than 20 invited world leading experts in the field and ca. 200 participants, invited talks, contributed talks, poster sessions, and social events. 2023 the Cell Physics was jointly organized with the German Society for Cell Biology (DGZ), thereby further increasing the audience, with many national and international speakers and participants of the fields of cell biology, biophysics and related fields. The six "Cell Physics" conferences between 2014 and 2023 have thus put the Saarland University on the map as one of thriving hot-spots for Biophysics in Europe (see posters and pictures below). The conference series "Cell Physics" continues in 2025 and is then organized by the ZBP, Saarbrücken, see https://www.cell-physics.uni-saarland.de/ For more information on the Cell Physics conferences during the CRC funding period see https://www.cell-physics.uni-saarland.de/#archive
- The **Yeast Lipid Conference 2024** in Homburg was organized by R. Ernst (C10) and partially sponsored by the CRC 1027, see https://www.yeastlipidconference.com/ylc2024-homburg.html
- The **EMBO Workshop "Lipid Droplets: Metabolic Hubs in Health and Disease"**, Sant Feliu de Guixols, Spain was organized by B. Schrul C11 and sponsored by CRC1027, see https://meetings.embo.org/event/23-lipid-droplets
- **Physical Biology Circle Meeting 2019:** The Circle Meeting is a meeting for students and postdocs. Seniors are allowed to listen during Q&A in between presentations but are not allowed to ask questions or give presentations. 2019 it was held the Saarland University. Participation in Circle meetings is restricted to a few European Institutions: MPI PKS Dresden, IST Austria, EMBL Heidelberg, AMOLF Amsterdam, Francis Crick Institute London, Institute Curie Paris, IBEC Barcelona, University of Bologna and Saarland University
- **CECAM-Workshop on "Computational models for active matter":** 2019 M.R. Shaebani (A7), A. Wysocki and H. Rieger (A3) were invited to organize a workshop on "Recent advances in computational methods for active matter" in the renowned CECAM workshop series in Lausanne, see https://www.cecam.org/workshop-details/87
- Since 2021, the CRC 1027 is also well-presented in a monthly webinar organized by the DGZ (**DGZ Focus Workshop**, framework coordination by S. Iden; 12 DGZ workgroups with different topics, each workgroup managed by two workgroup speakers). In this format, topics including cell mechanics, cytoskeleton, imaging, physics of the cell and others are covered. F. Lautenschläger serves as workgroup speaker of the DGZ Workgroup "Cytoskeleton and Molecular Motors", and various PIs have presented their

science in previous focus workshops as invited speakers (L. Aradilla-Zapata, S. Diez, O. Stauffer, S. Iden). More info: https://www.zellbiologie.de/workgroups/

- **Weekly CRC seminar** with external guest and status reports of CRC members. For a list of external speakers see the event calendar on http://www.sfb1027.uni-saarland.de/ and below.



Conference posters of the international conferences organized by the CRC 1027

Participants of the Cell Physics 2019 conference organized by the CRC 1027

Partial list of CRC 1027 seminar guest:

Speaker / Affiliation	Seminar title
Dr. Amos Korman, IRIF, Paris Diderot University	Crazy ants are not so crazy
Dr. David Cheung, School of Chemistry, National University of Ireland, Galway	Proteins at interfaces and surfaces: insights from molecular simulation
Prof. Dr. Roland Wedlich-Söldner, Inst. Cell Dyn. & Imaging, Universität Münster	Calcium-mediated actin reset (CaAR) drives acute cell adaptations
Dr. Aleksandra Walczak, Laboratoire de Physique Théorique, ENS Paris	Diversity of immune receptor repertoires
Prof. Edoardo Milotti, Physics Department, University of Trieste	Computational and analytical models of the tumor microenvironment
Dr. Elisabeth Fischer-Friedrich, BIOTEC, Technische Universität Dresden	Understanding Cells as an active material
Dr. François Nedelec, EMBL, Heidelberg	Predictive Theory of Cytoskeleton Dynamics
Dr. Vasily Zaburdaev, MPI-PKS Dresden	Fission yeast pulls chromosome loops to facilitate
Prof. Dr. Robert Endres, Department of Life Sciences, Imperial College London	Physical principles in sensing and signaling
Dr. Claus Heußinger, Institut für Theoretische Physik, Universität Göttingen	Out-of-equilibrium response of soft and biological matter to forces and deformation
Dr. Karen Alim, MPI DS Göttingen	Physical forces shaping morphology
Dr. Dmitry Fedosov, Institute of Complex Systems, FZ Jülich	Non-equilibrium processes in biosystems: membrane-cytoskeleton interactions and the formation of cell aggregates
Prof. Michael Feig, Michigan State University	From simulations of biomolecules to biological function
Prof. Samuel Safran, Dpt. Materials & Interfaces, Weizman Institute, Israel	Mechanical synchronization of beating within and between cardiomyocytes
Prof. Dr. Georg Conrads, Dep. Op. & Prev. Dentistry & Periodontology, RWTH Aachen	Bioactive NanoCoat - Controlling biofilm by functional coatings
Dr. Olivia du Roure, ESPCI, Paris	Actin networks' mechanics and growth assessed by a magnetic colloids technique
Prof. Ned Wingreen, Lewis-Sigler Institute & Department of Mol. Biol., Princeton	Protein phase transitions in and out of cells
Prof. Dr. Sebastian Hahnel, Universitätsklinikum Regensburg	Biofilms on polymeric dental materials
Prof. Dr. Markus Lill, Purdue University, USA	From Water to Fibrils - The Many Faces of Computer-Aided Drug Discovery
Prof. Kazuhiro Nagata, Laboratory of Mol. Biology, Kyoto Sangyo University	Maintenance of ER homeostasis by ER redox network
Prof. Chia-en A. Chang, University of California, Riverside	Modeling ligand-protein binding kinetics using molecular simulations and a novel pathway search method
Prof. Dr. Tim Foster, Trinity College Dublin, Irland	Role of Surface Proteins in Biofilm formation by Staphylococci
Prof. Dr. Irene Wagner-Döbler, Helmholtz Centre for Infection Research, Braunschw.	The secret life of the microbiota in periodontal pockets

Prof. Thomas M. Magin, Institute of Biology & SIKT, University of Leipzig	Intermediate filament proteins – guardians of tissue integrity
Prof. Dr. Roberto Mulet, Physics Faculty, University of Havana, Cuba	Characterizing steady states of genome-scale metabolic networks in continuous cell cultures
Prof. Dr. Carien Niessen, University of Cologne	Making, maintaining and breaking epithelial barriers: the importance of integrating mechanical and chemical signals
Dr. Peter Loskill, Fraunhofer-Institut f. Grenzfl.- und Bioverfahrenstechnik IGB, Stuttgart	Stem cell based microphysiological Organ-on-a-Chip systems as in vitro models of human tissue
Prof. Dr. Gleb Oshanin, LPTMC, University Pierre & Marie Curie / CNRS, Paris	Active microrheology in confined systems: from superdiffusive to giant diffusive fluctuations
Prof. Dr. Holger Kress, Biological Physics Group, University of Bayreuth	Size-dependent organelle transport during phagocytosis
Dr. Daiki Matsunaga, Rudolf Peierls Center for Theoretical Physics, Oxford University	Position control of magnetic particles/swimmers under flow
Prof. Dr. Anne Le Goff, Laboratoire Biomécanique et Bioingénierie, Université de technologie de Compiègne, France	Biomechanics of platelet production
Dr. Pavel Paszek, Division of Infection, Immunity & Respiratory Medicine, University of Manchester, UK	Dynamics and heterogeneity of inflammatory signaling in single cells
Prof. Dr. Huan-Xiang Zhou, Department of Chemistry and Department of Physics, University of Illinois at Chicago	Physical basis of protein liquid-liquid phase separation
Prof. Dr. Rongxi Yang, Department of Molecular Epidemiology, Nanjing Medical University, P. R.China	he study of in-intro epigenetic biomarker for the early diagnosis and prognosis of breast cancer
Dr. Kelly Aubertin, CRCHUM, Université de Montréal Canada	Mechanical and optical properties of biological systems
Dr. Dorothea Brüggemann, Institute for Biophysics, University Bremen	Nanobiophysics of cells
Dr. Jörg Schnauß, Dep. Physics, Universität Leipzig	Driving Life's Engine: from semiflexible components to cell migration
Prof. Dr. Manuel Salmeron-Sanchez, Centre for the Cellular Microenvironment, University of Glasgow, UK	Engineering the cellular microenvironment – materials, growth factors and beyond
Dr. José Alvarado, Massachusetts Institute of Technology, Cambridge	Molecular motors robustly drive active gels to a critically connected state
Dr. Siddharth Deshpande, Kavli Institute of Nanoscience, Delft University	Synthetic Cells: Make-Grow-Divide
Dr. Cornelia Monzel, Experimental Medical Physics, University Düsseldorf	Magnetic Manipulation of Molecular Activity in Model Membranes and Cells
Dr. Anna Taubenberger, TU Dresden Biotec	Studying cell-microenvironment interactions from single cells to 3D in vitro model
Prof. Dr. Nicolai Miosge, Universität Göttingen	Manipulating co-regulators of RUNX and SOX9 to enhance the chondrogenic potential of chondrogenic progenitor cells in osteoarthritis
Prof. Dr. Ali Al-Ahmad, Dep. Op. Dentistry & Periodontology, Uni. Freiburg,	Oral biofilm - Current research topics
Prof. Dr. Benedikt Berninger, Center f. Dev. Neurobiol., King's College London	Engineering neurogenesis for the postnatal brain
Prof. Dr. Dr. Hans-Robert Kalbitzer, Inst. Biophys.,Phys. Chem., Uni. Regensburg	Detection of Rare Conformational States of Proteins by High Pressure NMR Spectroscopy

Dr. Mohamed Hamed, Universität Rostock	Unravelling mechanism of actions of combined drug application via molecular analysis of multi-OMICs datasets
Dr. Chetan Poojari, Tamper University of Technology, Finland	he Unconventional Secretory Pathway of Fibroblast Growth Factor 2: A Direct Gateway Into the Extracellular Space
Dr. Gregory Lavieu, Institut Curie - Paris	Reconstitution of Extracellular Vesicle Content Release in a Cell Free Extract
Dr. Jalal Sarabadani, Dep. Math. Sciences, Loughborough University, UK	Physics of DNA (polymer) translocation through a nanopore
Dr. Andreas Krämer, National Institute of Health, Bethesda MD, USA	Membrane Permeability from Conventional MD Simulations: Counting Transitions vs. Bayesian Analysis
Ass. Prof. Anupam Sengupta, Physics of Living Matter Group, Uni. Luxembourg	Fluctuation induced emergent traits in living matter
Dr. Brandon Harvey, National Institute on Drug Abuse, Baltimore, USA	KDEL receptors are adaptive regulators of the endoplasmic reticulum proteome
Prof. Dr. Andreas Heuer, Universität Münster	Domain formation in lipid membranes as studied via computer simulations
Dr. Sara Jabbari Farouji, Institute of Physics, University of Mainz	Controlling stability and transport of magnetic microswimmers by an external field
Dr. Charisios Tsiairis, Institute for Biomedical Research, Basel, Switzerland	Crosstalk between Mechanical and Biochemical Signals during Hydra Regeneration
Prof. Dr. Rodrigo S. Lacruz, Sackler Institute & NYU College of Dentistry	Pathophysiology of calcium dysregulation in dental enamel cells
Dr. Oliver Otto, Zentrum f. Innovationskompetenz: Universität Greifswald	Virtual fluidic channels: from functional single cell rheology to tissue mechanics
Prof. Dr. Phil Selenko, Weizmann Institute of Science, Rehovot, Israel	Looking at proteins in live cells with atomic resolution: from Science Fiction to Science Reality
Prof. Dr. Anne Kenworthy, School of Med., University of Virginia Charlottesville	Membrane domain biogenesis and function
Prof. Dr. Dora Tang, MPI-CBG, Dresden	Bottom up approaches to synthetic Cellularity
Dr. Johannes Rheinländer, Universität Tübingen	Active and Passive Cell Mechanics with Scanning Probe Microscopy
Prof. Dr. Natalie Thamwattana, School of Math. & Phys. Sci., University of Newcastle, Australia	Modelling neural cells and cell-cell interactions in phagocytosis
Dr. Loisa Reissig, Freie Universität Berlin	Differential Photodetectors: From Photonic Devices to their Use as an Analytical Platform
Jun.-Prof. Dr. Marcel Lauterbach, CIPMM, Saarland University	Optics for Neuroscience
Prof. Dr. Taher Saif, Mechanical Science and Engineering University of Illinois at Urbana-Champaign, USA	Neuronal tension – a new paradigm for understanding memory and learning
Prof. Dr. Jan Lipfert, Department of Physics, LMU München	Regulation and Dynamics of Biological Macromolecules under Forces and Torques
Prof. Dr. Katrin Philippar, ZHMB, Saarland University	Structure and function of FAX/TMEM14 membrane proteins
Dr. Janna Nawroth, Emulate, Inc., Boston, USA	Cilia biomechanics and the link to human airway diseases
Dr. Baeckkyoung Sung, KIST Europe, Saarbrücken	Ordered and disordered phases of biological matter: fundamentals and applications

Dr. Liang Liu, CNRS-Université de Lorraine, Nancy	Scanning Gel Electrochemical Microscopy (SGECM): Looking for Biological Applications
Dr. Rhoda Hawkins, Department of Physics and Astronomy, University of Sheffield, UK	Force generation by cytoskeleton molecules
Dr. Medhavi Vishwakarma, Cellular and Molecular Medicine, University of Bristol	Cooperation and competition within epithelial cells dictate tissue repair, maintenance and tumorigenesis
Dr. Dedy Septiadi, Adolphe Merkle Institute, University of Fribourg	Cell Mechanics and Cell Optics in Biology
Prof. Dr. Gregory Schehr, LPTMS, Université Paris Sud (Orsay), France	First-passage problems in statistical physics
Dr. Hannes Witt, MPI DS & Inst. Organic Biomolecular Chem., Uni Göttingen	From single filaments to many vesicles – understanding collective behavior of biological model systems
Dr. Patrick Rose, Office of Naval Research Global, London, UK	ONR Global: A funding program in search for the next great idea
Prof. Dr. Metin Tolan, Dep, Physics, TU Dortmund	The hydrophobic gap at high pressures
Prof. Dr. Ulf Dittmer, Institut für Virologie, Universität Duisburg-Essen	Seeing is believing: The regulatory T cell response during retroviral infection
Prof. Dr. Wolfgang Schamel, Inst. Molecular Immunology & BIOSS Centre for Biological Signalling Studies, Uni. Freiburg	Optogenetics: Light-controlled activation of the T cell receptor reveals kinetic proofreading

4.2 National and international collaboration

Members of the CRC participated in **DFG priority programs** (e.g. SPP 1710, SPP 1757, SPP 1782, SPP 2171, and SPP 2265), or programs funded by the German Federal Institute of Education and Research – BMBF (e.g. CORDILUX), thus actively cooperating within a network of German groups. National recognition is also visible by three of the PIs previously being elected as “Fachkollegiaten” of the DFG (K. Jacobs until 2020, Soft matter, biological Physics, M. Hoth until 2020 Biophysics; A. del Campo since 2020 Material Sciences), and one PI (K. Jacobs) being member of the “Wissenschaftsrat” (German Council of Science and Humanities) and an Ordinary Member of the Academy of Sciences and Literature, Mainz and Corresponding Member of the Academy of Sciences, Göttingen. K. Jacobs is now also a Vice-President of ther DFG. M. Hoth is a member of the National Academy of Sciences, Leopoldina and S. Iden has been elected in 2020 to the board of the German Society for Cell Biology (DGZ). Two PIs of the CRC are also recipients of ERC grants: R. Ernst (in 2019) and L. Aradilla-Zappata (in 2024).

Other international cooperations of members of the CRC within institutionalized scientific networks are the Max Planck School for “Matter to Life” (K. Jacobs), EU funded networks such as Marie Curie Training networks (e.g. “POLYFILM”), International Graduate Colleges (e.g. IGRK 532, IRTG 1830), ERASMUS Mundus Joint Doctorate Programs, and international study courses (e.g. Saar-Lor-Lux). Furthermore, the international networking is consolidated by e.g. editorial work for international journals (H. Rieger: Divisional Associate Editor for Phys. Rev. Lett., Editor in Chief for Europ. Phys. J. B until 2024; Editor for J. Stat. Mech. and Europhys. Lett. until 2023) and by memberships in international scientific boards etc. by the members of the CRC.

5. Impact on Research Priorities and International Visibility

The CRC 1027 is at the center of the scientific profile of the Saarland University, which are "NanoBioMed", "Computer Sciences", and "Sustainability", the latter of which was just established. Its central topic "Physical modeling of biological systems" is part of the "NanoBioMed" priority area and has experienced substantial support by the Faculty of Natural Science, the Medical School as well as by the University's president's office and the state government, reflected also by the fact that several PIs of the CRC are tightly involved in strategic processes and development at UdS: M. Schmitt, the PI of A6, became the President of the Saarland University in 2016, and L. Santen, PI of A8 and B1, became the President of the Saarland University in 2024. R. Ernst, PI of C11, became Vice President for Research in 2024. M. Hoth, PI of A11 and Co-PI of A2 until 2020, was until 2020 Vice-Dean (Prodekan) of the Medical Faculty; A. del Campo, PI of B6, is coordinator of the new "Leibniz-Wissenschaftscampus". Four PIs, A. del Campo (B6), M. Hoth (A11), J. Hub (B7) and F. Lautenschläger (A10) participate in the proposal for a Cluster of Excellence, „nextAID³", with which new and innovative ways in a AI-driven drug research and development should be explored. The result of the 2nd round will be announced in May 2025.

Over the previous decade, the biophysical research within the CRC 1027 at UdS has been the driving force for the development of successful scientific bridges not only between the campuses Saarbrücken and Homburg, but furthermore between UdS and the Leibnitz Institute for New Materials (INM). To bundle the biophysical research between faculties of natural sciences and medicine the Saarland University established the **Center for Biophysics (ZBP)** involving the members of the CRC 1027 as a nucleus, see https://www.uni-saarland.de/en/faculty-nt/biophysics.html. The ZBP and its new research building (see next point) will continue the research infrastructure established by the CRC 1027 beyond its funding period and extend it by the research areas membrane biophysics and multicellular processes. A proposal for a **new research building for the ZBP** on campus Saarbrücken, was granted in 2018 and involved 37 Mio. € for construction of a 3800 m^2 building, which will be finished in 2026. It will merge the 9 biophysics groups on campus Saarbrücken, all CRC 1027 members, and host 7 key laboratories and lab space for common research activities with the ZBP groups of campus Homburg.

Moreover, in recent years, several key investments in core technologies have been made at both the Saarbrücken and Homburg Campus to strengthen the CRC 1027. All CRC scientists have full access to high-resolution and super-resolution fluorescence microscopy, including spinning-, confocal-, TIRF-microscopy, and STORM. The imaging technologies are complemented by sensitive tools for the characterization of biological samples, including Fluorescent Recovery After Photobleaching (FRAP) to measure the diffusion of fluorescently labelled biomolecules, Atomic Force Microscopy (AFM), and Real-Time Deformation Cytometry (RT-DC) to characterize cell mechanics. These technologies will be integrated into a Microscopy Core Facility to be established within the ZBP, and which will be funded by UdS with permanent scientific and technical staff.

These developments led to a continuously increasing international significance and visibility reflected by an increasing number of high impact publications and invitations to international conferences. Each PI of the CRC 1027 participated each year in at least two, but usually more, international conference on conferences with biophysical or biological background, where they presented the results of the CRC. Many of these biophysical conferences were also organized by PIs of the CRC themselves, as for instance:

- **The Cytoskeleton as Active Matter, 818. Häreus-Seminar**, 30.9.-4.10.2024 in Bad Honnef, was co-orgamized by F. Lautenschläger (A10), see https://www.we-heraeus-stiftung.de/veranstaltungen/the-cytoskeleton-as-active-matter/
- **From Soft Matter to Biophysics,** 16.-21.2.2025 in Les Houches, France, was co-organized by K. Jacobs (B1, B2, IRTG), see https://www.we-heraeus-stiftung.de/veranstaltungen/from-soft-matter-to-biophysics-2025/
- **EMBO Workshop: Physics of Cells - PhysCell2022**, 12.-16.9.2022 in Ein Gedi, Israel, was co-organized by F. Lautenschläger (A10), see https://events.embo.org/22-physics-of-cells/
- Two **Sino-German Symposia on** *Metabolic Disorders and Immunity* (June 17-21, 2024, in Chengdu, China and September 23-27, 2024, Homburg, Germany), co-organized by B. Qu (A2).
- Annual annual **"Workshop on Computer Simulation and Theory of Macromolecules"** in Hünfeld since 2001, co-organized by H. Grubmüller (Göttingen) and V. Helms (C3, ZX).
- **5th Lipid Droplets Workshop**, 9.12.2022, and **4th Lipid Dropled Workshop**, 19.11.2021, virtual meetings, organized by B. Schrul (C9).
- **EMBO Workshop: Cell polarity and membrane dynamics**, 26.-31.5.2019 in Sant Feliu de Guixols, Spain, co-organized by S. Iden (A12), see https://meetings.embo.org/event/19-cell-polarity-dynamics

6. Structural Impact of the Collaborative Research Centre

6.1 Staffing

The UdS strengthened the CRC 1027 by establishing the following research groups during the funding period:

- the appointment of Laura Aradilla-Zapata (A13) as a Junior-Professor for Molecular Cell Biophysics within the WISNA program in 2020. After receiving an ERC Starting Grant in 2023 she was promoted to W2 in 2024.
- the appointment of Bianca Schrul (C9) as a Junior-Professor for Molecular Cell Biology in 2017. She was integrated into the CRC in 2019 with a “Nachantrag”. She was promoted to W2 in 2023.
- the appointment of Sanda Iden (A12) in 2019 as W2 Professor for Cell and Developmental Biology (formerly Dept. of Developmental Biology) involving a denomination of a professorship towards stronger cell biology aspect which strategically supported CRC. After she received an offer from the University of Marburg she was promoted to W3 in 2024.
- the appointment of Jochen Hub in 2018 as a W3-professor for Theoretical Biophysics as successor of Karsten Kruse (A1, discontinued), who is now in Geneva, Switzerland.
- the appointment of Robert Ernst (C10) in 2017 as W3 professor heading the Department of Biochemistry and Molecular Biology.
- the appointment of Franziska Lautenschläger (A10) in 2013 as Junior Professor W1 with tenure track W2. She was promoted in 2020 to a permanent W2 professorship in Physics.
- the general appointment policy of the university: The generation change in the Physics department and the Institute for Biophysics offered a unique opportunity to install research groups that had a sustained interest in establishing a collaborative research center bridging physical and life sciences,
- Saarland University also made great efforts to keep physicists and life scientists at Saarland University when they had offers for professorships from other universities.

Several CRC members received offers:

- Franziska Lautenschläger (A10), appointed as Junior Professor with tenure track W2 in Physics in 2013, received an offer from the University of Erlangen and was then promoted in 2020 to a permanent W2 professorship in physics at UdS.
- Bin Qu (A2), who held a permanent position as group leader at the Department of Biophysics, has accepted an offer from the University of Osnabrück for a W2 position in 2025.
- Matthias Hannig (B3) declined an offer as Director and Vice-Dean at Western University, London/Ontario, Canada in 2019. He accepted the competitive counteroffer from UdS and negotiated a new professorship position in the Dentistry Department.
- Markus Hoth (A11) declined an offer as Chair of Physiology at the Medical School of Lübeck (2017). Together with his wife, Barbara Niemeyer (C4), they decided to accept the counteroffer from UdS which also secured some funds used as core support for the CRC.
- Ralf Mohrmann (C5) became W2-Professor for Neuophysiology and Cellular Imaging at the University of Magdeburg in 2018. Yvonne Schwarz took over the responsibility as co-project leader in C5.

- Ivan Bogeski (C4) accepted an offer as W2-Professor for Physiology at Göttingen University (2016) just before the start of the last funding period). Considering his many cooperations with CRC members, he remained an integral part of the CRC.
- Karsten Kruse (A1) accepted an offer from the University Geneva, Switzerland (2016, just before the start of 2nd funding period). He collaborated and published successfully with members of our CRC but discontinued his participation since he cannot apply for DFG grants from outside the EU.

In summary, while several younger project leaders accepted external offers, the structural basis of the CRC was significantly strengthened by recruiting new young faculty members working on biophysical topics and by fending off offers to others. As one key instrument, Saarland University in the past offered possibilities for dual career couples to outperform offers from competing universities. In our CRC we have several dual career couples and it is planned to continue this successful strategy when applicable.

The **Leibniz Institute for New Materials (INM)** on the campus of the Saarland University strengthened its focus on bio-interfaces by appointing Prof. Aránzazu del Campo (B6) as a Co-director and concomitantly installing a major working group in this field. Together with Prof. Niels de Jonge (C7), a research group leader in the INM, the outstanding expertise and resources of the INM were successfully integrated into the CRC in the 2nd funding period. In the last funding period Dr. Shrikrishnan Sankaran (B8) from the INM was integrated into the CRC, and Prof. Niels de Jonge (C7) left the INM and joined a private company, Bruker, to develop a new X-ray microscope. Vice versa, three CRC members, Prof. Karin Jacobs (B1/B2), Bin Qu (A2), and Heiko Rieger (A3), were awarded with a fellowship by the INM in 2014, 2019, and 2021, respectively.

6.2 Researchers in early career phases

The CRC 1027 provided a vibrant environment to attract and to empower early career scientists. The following junior PIs are members of the CRC according to DFG criterium (within 8 years after PhD):

- Jun.-Prof. Laura Aradilla-Zapata (A13, doctorate in 2016, one child) held a W1/tenure-track-W2 position from 2020 to 2024, received an ERC starting grant in 2013 and was then promoted to W2 in 2024.
- Bin Qu (A2, doctorate in 2010, two children) holds a permanent position as group leader at the Department of Biochemistry (group of M. Hoth) and was a member of the CRC executive board since 2013. She has now accepted an offer from the University of Osnabrück for a W2 position and will move there in 2025.
- Hendrik Hähl (B1, doctorate in 2011, two children) has a permanent position (work group of Jacobs) in the Physics Department.
- Shrikrishnan Sankaran (B8, doctorate in 2015, two children) holds an independent Junior Group Leader position at the INM. Since 01/2020 he was the speaker of the Young Researchers in the IRTG.
- Franziska Lautenschläger (A10, doctorate in 2011, two children), was appointed as Junior Professor with tenure track W2) in the Physics Department in 2013 and was promoted in 2020 to a permanent W2 professorship in physics. She also profited from tutoring by CRC PIs and CRC prefunding.
- Bianca Schrul (C9, doctorate in 2010) was appointed as Junior Professor W1 with tenure track W2 in 2023 at the Center for Molecular Signaling in the Department of Molecular Bio-

chemistry, submitted successfully an additional proposal (Nachantrag) within the 2nd funding period, and passed the mid-term evaluation in 2020. She also profited from tutoring by CRC PIs and CRC prefunding.

Further three younger project leaders were supported to go for their next career step: Yvonne Schwarz (C5, doctorate in 2012), who holds a permanent position at Department of Biochemistry (work group of D. Bruns) and 2nd funding period's junior PIs Jean-Baptiste Fleury (B4, doctorate in 2009) and Mohammad Reza Shaebani (A7, doctorate in 2008, both had secured working contracts for all CRC periods). M.R. Shaebani finished his habilitation in 2020 and J.B. Fleury in 2020. All the three are now close to the next career step to a first permanent academic position and have tutors at their side for further career planning. They already submitted applications and were invited for interviews for academic positions.

Ralf Mohrmann (formerly C5) and Ivan Bogeski (C4), both former junior group leaders in our CRC, have meanwhile taken up permanent W2 professorships at other universities. Ivan is still an external member of the CRC. Also other former PhD students of the CRC either made an academic career or are on the verge of it: Examples are Peter Loskill, a PhD student of the first funding period (B2), is now W3 professor in Tübingen and headed before the "Organ-on-a-Chip" group at the Fraunhofer Institute for Interfacial Engineering and Biotechnology (IGB) in Stuttgart, and Philipp Jung, currently postdoc in B2, will soon submit his habilitation in the medical faculty and holds a group leader position at the Institute of Medical Microbiology, headed by Sören Becker. Moreover, Yijun Zheng (postdoc in B6) became Associate Professor at Shanghai Technology University. Alessandra Griffo and Christian Spengler were "rising young PIs", employed as postdocs in CRC projects B1 and B2, respectively, both moved to other places for a second postdoc employment and later took up jobs in research teams in industry.

Snapshots of CRC activities in the framework of the IRTG

To support early careers, especially young researchers (YR), including postdocs and PhD students, an **Integrated Research Training Group (IRTG)** has been established. The IRTG measures were designed to help YRs to a) successfully work on their scientific topic and b) to prepare them for their next career step. The measures are complemented by existing early career support structures of Saarland University and are described in the MGK section. About 50% of our PhD students took up postdoctoral positions, the others moved to industry. After 5 years, about half of the postdocs (i.e., 25% of the PhD students) are still working in academic research, and

about half of the PhD students who directly moved to industry are still working in areas close to research topics (e.g., instrument development). We interpret these numbers as a sign that for a large proportion of our graduates, academic research has very positive connotations and represents an attractive field of work. Many of the PIs also note that companies fight for the best minds and already offer very attractive employment contracts to doctoral candidates, even though the defense of the doctorate has not yet taken place. For our alumni, this is a very convenient situation.

In addition, the biannual international conference "Cell Physics" organized by the CRC has developed as a **career accelerator**. It is a well-suited forum for the **placement of postdoc positions**. Submitted abstracts of excellent work by YRs (members or non-members of the CRC) are selected for short oral presentations by the organizers. Poster awards highlight other outstanding work by YRs. Some of the YR presentations directly led to invitations for a postdoctoral position at other institutes. Informal talks and discussions with internationally renowned speakers offer the YRs as well as all junior (and senior) PIs great networking opportunities.

Concerning the career of young scientists, Saarland University has a solid tenure track history and support of junior professors long before implementation of the WISNA program. For **all junior professorships (JPs)**, appointment guidelines (dito for W2/W3 professorships), a reduced teaching load, target agreements, guidelines for mid-term reviews as well as tenure track regulations are clearly specified. For instance, the timing of the interim evaluation for JPs can be arranged flexibly and can be prolonged due to parental leave. JPs are also entitled to apply for funding of major (Art. 91b and 143c GG) and smaller instrumentation as well as for starting grants (“Anschubfinanzierung”) via the university research panel. JPs have their own accounts at Saarland University to dispose independently. JPs are strongly integrated in relevant decision-making processes (search committees, equal members of faculty metings). Also, postdocs and PhD students striving for a career in academia were encouraged to to sign up as members for appointment committees.

Vertragslaufzeit	Anzahl der wissenschaftlichen Mitarbeitenden insgesamt	Doktoranden/innen und Vergleichbare		Postdoktoranden/innen und Vergleichbare	
		männlich	weiblich	männlich	weiblich
bis 12 Monate	41	17	10	6	8
bis 24 Monate	20	11	5	3	1
bis 36 Monate	24	12	6	2	4
bis 48 Monate	16	4	4	5	3

Teaching at UdS: During the funding period of the CRC 1027 the Faculty for Natural Sciences and Technology (NT) established a B.Sc. and a M. Sc. Course in Biophysics, which now run very successfully. Nearly all graduates joined regularly the groups of one of the PIs of the CRC as PhD students.

6.3 Gender equality for researchers and compatibility of research and family

Gender equality, family-friendliness, internationality, and diversity are among the central principles of Saarland University's policy. A central instrument is the Gender Equality Plan, which defines targets for the proportion of women at all levels. The Gender Equality Office (GEO) implements the DFG's "Research-Oriented Standards on Gender Equality". Thus, all members of this CRC have access to a broad range of equal opportunity and diversity measures that are implemented within the whole governance strategy of Saarland University.

Existing gender equality measures at UdS. As the first German university, UdS successfully participated in the BMBF Women Professors I program after presenting a future-oriented equality concept (2008), UdS was chosen in 2014 for the BMBF Women Professors II as one of the 10 best universities in Germany for fulfilling the equality concept, and was successful for the third time in BMBF Women Professors III. The number of female full professors increased from 26 in 2007 (11%) to 51 in 2021 (20%). In addition, UdS currently has a high proportion (39%) of female junior professors.

The "Exzellenzprogramm für Wissenschaftlerinnen" (a three-year excellence program for female scientists) offers a range of workshops and seminars focusing on women's careers in academia. Since 2017, Saarland University implements a dedicated support program, Young Female Scientists Go Future, for female junior professors (W1). Since its certification with the "Audit Familiengerechte Hochschule" (family-friendly university) in 2004, UdS has been constantly increasing its support for students and employees with families and has been successfully re-audited four times. The last certification process (in 2016) was developed at UdS as a pilot for other universities. Given the role model effect, UdS is the first university with an unlimited certification (in 2016). The latest Dialogue Procedure in 2020 has proved the persistent quality of measures in the field of family friendliness.

Additional measures by the CRC. On top of the rich gender equality measures already available at UdS, the CRC implemented a dedicated program to foster scientific careers of female scientists. Measures included training by professional mentors on topics such as career development, leadership skills, negotiation, team building, and conflict management. Participation of female junior PIs and postdoctoral scientists in coaching and networking programs by the YouGoFuture program is funded by the CRC, as organized by the Gender Equality Office of UdS. Although the measures ere available to all CRC members with family duties, they were particularly critical to foster careers of female individuals since family care duties are still disproportionately carried by women. Furthermore, we were dedicated to attracting the most established or most talented female individuals to the CRC at all levels of career and education. By an active recruitment strategy, we aimed to attract high-profile, established, and internationally most visible female experts to all professor levels W1, W2, and W3, and were successful in the cases F. Lautenschläger (A10), L. Aradilla-Zapata (née Schädel) (A13), B. Schrul (C6) and S. Iden (A11).

The CRC successfully recruited female undergraduate research students to CRC groups not only to bring them into contact with the science of the CRC, but furthermore to enable contact with scientifically successful female role models at all career levels from PhD student to professor. Furthermore, we promoted biophysics among talented female high school students by the involvement of CRC researchers in established frameworks at UdS such as MentoMINT organized by the Gender Equality Office, a mentoring platform between female university and high school students, the one-week UniCamp for Girls, and the university-wide Girls' Day.

Family-friendly university: The UdS recognized early the importance of family-friendly structures to keep and to attract strong individuals with families for proceeding a scientific career at UdS. UdS has been the first German university with an unlimited certification as a family-friendly university. In collaboration with the university's Family Office, various well-established measures for ensuring compatibility of family with scientific carrier were available to all members of the CRC. Our researchers could use two childcare facilities on Saarbrücken's campus as well as a flexible short-term childcare facility (FlexiMedKids) in Homburg, which was partially financed (25%) by the CRC. Supplemental parent-child rooms and flexible offers, such as KidsBox and a mobile children's room, were available. The Family Office at UdS coordinates an online database of babysitters for temporary/flexible childcare, which could be booked on-demand by CRC members to allow unrestricted participation in CRC events. The CRC offered childcare or special support for pregnant women and CRC members with care responsibilities, e.g., flexible working schedules, assistance for lab work and teaching duties, additional allowances for business travel. Also of note is that Saarbrücken has recently opened an international school, which helped attracting international talents and their families. On top of these established and widely used measures at the UdS, the CRC provided additional support to CRC scientists with high family duties, including funding for technical or scientific staff to relieve CRC members from routine tasks, technical equipment to facilitate home office and flexible working hours, as well as funding for babysitter services at external conferences.

New research building of UdS for the Center for Biophysics (ZBP), to be finished in 2026

6.4 Research infrastructure

A proposal for a **new research building** for the **Center of Biophysics (ZBP)** on campus Saarbrücken, based on the research activities of the CRC 1027, was granted in 2018 and involved 37 Mio. € for construction of a 3800 m^2 building, which will be finished in 2026. It will merge the 9 biophysics groups on campus Saarbrücken, all of them CRC 1027 members, and host 6 key laboratories (light microscopy, cell culture, clean room, surface analysis, XPS, high performance computing) and lab space for common research activities with the ZBP groups of campus Homburg. The ZBP was established to bundle the biophysical research between faculties of natural

sciences and medicine of UdS involving the members of the CRC 1027 as a nucleus, see https://www.uni-saarland.de/en/faculty-nt/biophysics.html . The ZBP and its new research building (see next point) will continue the research infrastructure established by the CRC 1027 beyond its funding period and extend it by the research areas membrane biophysics and multicellular processes.

Moreover, in recent years, several key investments in core technologies have been made at both the Saarbrücken and Homburg Campus to strengthen the CRC 1027. All CRC scientists have full access to high-resolution and super-resolution fluorescence microscopy, including spinning-, confocal-, TIRF-microscopy, and STORM. The imaging technologies are complemented by sensitive tools for the characterization of biological samples, including Fluorescent Recovery After Photobleaching (FRAP) to measure the diffusion of fluorescently labelled biomolecules, Atomic Force Microscopy (AFM), and Real-Time Deformation Cytometry (RT-DC) to characterize cell mechanics. These technologies will be integrated into a Microscopy Core Facility to be established within the Center for Biophysics (ZBP), and which will be funded by UdS with permanent scientific and technical staff. Moreover, the new building will offer a common cell culture, a clean room, modern surface analytics (e.g. an imaging photoelectron spectroscopy and microscopy plant) as well as a new biophysical computing center.

Currently (2025) large parts of the research equipment acquired during the CRC funding period together with already existing equipment is being organized in Core Facilities, which will then offer access, measurement time and expertise to all members of UdS.

6.5 Knowledge transfer

CRC measures supporting knowledge transfer and public outreach:

The focus of CRC topics was basic research, yet there were some aspects that may find their way to the market or to patients: In A10, for example, tracking software was developed that can quantify different networks. Although the actual code is open source, they are evaluating how to make a user-friendly product that will allow academic and industrial researchers to quantify any type of network. The team of B1 developed with B2 and B3 hydroxyapatite pellets as versatile model surfaces for systematic studies on enamel that shall be made commercially available. Research findings within B2 and B3 might find synthetic, antibacterial coatings for catheters or suitable mouth rinses for patients. Knowledge generated in B6 and B8 may result into new clinical paradigms and materials for the improvement of immunotherapies, treatment of diseases or removal of dental biofilms. At A10 and B1, KWT and WuT (see below) are currently engaged in identifying appropriate transfer strategies. The CRC supports these transfer activities, e.g. by providing central funds to produce a demonstrator.

To raise a stronger attention to the achievements of the members of the CRC, a number of **press releases** were composed during all funding periods, some were even taken up by German newspapers like *Süddeutsche Zeitung, Saarbrücker Zeitung* or by online media like *Spiegel Online, TAZ online* and *nature podcasts.* The CRC maintained a webpage https://www.sfb1027.uni-saarland.de/ that included a **News page** (tinyurl.com/sfb1027-news) announcing the publication of important CRC papers, press releases, conferences, workshops, distinctions and other CRC related events. The CRC also established a **Twitter** account (@SFB_1027) to increase the visibility and share CRC news, findings, announcements for seminars and meetings organized by the CRC, and other CRC relevant highlights.

In the 2nd funding period the CRC published a **public outreach article** "Cell Physics: Understanding How Biological Matter Self-Organizes – SFB 1027" in the science communication magazine "**Scientia**" (see https://www.scientia.global/) connecting science and society by presenting research in an understandable, informative and enjoyable way: tinyurl.com/scienta-sfb1027

Since 2018 the CRC organized annually a **photo competition** among the CRC members to have a repository of high-resolution pictures illustrating ongoing research activities. These pictures were used for the CRC web site, conference announcements (e.g. the Web page and the poster for the Cell Physics), proposal title pages (like the one of this report), and for posting them in the lab-corridors for external visitors.

Moreover, in January 2020, the CRC produced a **movie about the CRC** 1027 and the Center for Biophysics (ZBP) that was shown on the annual meeting of the American Biophysical Society in February 2020, see tinyurl.com/sfb1027-movie. This movie illustrated the mission and research activities of the CRC and the ZBP to a broad audience and is shown on **public events**, in which CRC member were involved. An example was the annual Open Door of the university or the "Night of the Sciences" (Nacht der Wissenschaften) giving introductory lectures into their research fields. They were also invited to present their scientific results on occasions like the "Wissenschaftssommer", the "Highlights in physics" or – as an ongoing regular seminar series – at the "Wissenschaftsforum St. Ingbert". CRC PIs have further shared their research topics with the local public, e.g. in an open lecture series at a cinema in Saarbrücken (Filmhaus Saarbrücken, Bio-Logisch!)".

Members of the CRC 1027 also engaged in **outreach activities in schools** (2-hour courses for kids, 2 weeks courses for high school graduates) and presented their work in a number of interviews in journals with physical (e.g. DPG), biological (e.g. Journal of Cell Science) or generally academic (e.g. 'Forschung und Lehre') readership. To promote some of the topics covered by the CRC (e.g. 'The physics of adhesion and friction; what holds two things together?', "The physics of light", "The physics of fluids)), **hands-on experiments** have been set up that fit into a large box and that can be transported to schools (www.labinabox.de). These boxes enabled a school class of up to 36 pupils to perform within 90 min 4-6 different experiments in small groups: The box was maintained by a person in a gap year doing voluntary work in the social sector (freiwilliges soziales Jahr, FSJ) and by volunteers. Part of the salary of the FSJ person is taken over by this CRC (25%), by the group of K. Jacobs (25%) and by Saarland University (50%).

During the annual Open Door ("**Tag der offenen Tür**") and the annual "**Girl's Day**" of UdS the CRC presented projects, research groups and guided tours through our laboratories. On the annual "**UniCamp for Girls**" of UdS up to 40 girls (in 2020: 20 girls due to pandemic restrictions) camped at UdS for 5 days and experienced MINT research on Campus Saarbrücken. One afternoon was organized by the physics department and all PIs of Saarbrücken campus were involved.

General structures in the Saarland University:

The **Kontaktstelle für Wissens- und Technologietransfer** (Contact point for knowledge and technology transfer - KWT) at Saarland University points out options to establish successful collaborations between scientific and industrial partners. Founded in 1985, it has been engaged in close relation to the **Wissens- and Technologietransfer GmbH** (Knowledge and Technology Transfer – WuT GmbH) - a 100% subsidiary of Saarland University - in the fields of technology transfer. KWT and WuT GmbH provide support in order to initiate contacts, to establish cooperations, to mediate between national and international research contacts/projects and to assist new business founders by offering founding counselling and qualification measures.

As the University's central contact point and service facility, KWT and WuT GmbH are accessible for every researcher in order to promote and support the professional and specific exchange

of information and experience with enterprises. Members of the CRC contact KWT and WuT to, e.g., set up partnerships with companies, to draft appropriate non-disclosure agreement, to organize conferences (like the Cell Physics) or to plan booths at fairs (e.g., Hannover-Messe).

The Saarland Universities' **Patent Marketing Agency** (PVA) was established in 2002 as a new business segment of WuT GmbH, and is funded by the German Federal Ministry of Economics and Technology as part of the WIPANO program. It is responsible for the proprietary protection and marketing of economically relevant research findings, assesses the patentability and market prospects of disclosed inventions, and is responsible for the proprietary protection and marketing of economically relevant research findings. If a member of the university chooses to claim an invention, the PVA staff works in close collaboration with the inventor throughout the entire process, from contract negotiations and proprietary protection to developing marketing strategies and monitoring.

The office rooms at the WuT's **Start-up Center** are available for future entrepreneurs and company founders of Saarland University that are supported and advised by the KWT staff.

The **public relations department** at Saarland University is the interface between the researchers and the general public. It issues press releases on research results in non-technical language and sends press texts to regional and national papers and scientific publications. In certain cases, journalists are linked to scientists working on a particular topic. They organize the OpenDay and flank all measures to recruit students, especially girls in STEM subjects.

In order to further improve the visibility of the involved institutions in Saarbrücken to the general public and in particular to young academics, several measures have been implemented in the past years. In addition to the workshops in the context of equal opportunity measures discussed earlier, we participate in the "MINToring" program, a mentor program for pupils interested in mathematics, computer science, natural sciences and engineering.

6.6 Internal collaboration and management

The CRC 1024 started in 2013 with 17 projects that were selected in the proposal phase according to two strict criteria: 1) the focus had to fit to the topic "Physical modeling of non-equilibrium processes in biological system" and, more selective, 2) the physical modeling aspect of the project had to be strongly present and, most selective, 3) the project must have comprised one or more collaborations between experimentalists and "modelers", theoretical physicists or a bioinformatician, optimally even across projects. In this way a high degree of cooperativity and coherence was brought into the CRC, in spite of its broad topic and the interdisciplinarity of its members, coming from physics, biology, medicine and informatics. These collaborations were in most cases very successful, and projects that could not achieve the overall goal of having at least one publication with another CRC group – there were three – were discontinued after the 1st funding period. Instead, new projects and new PIs fulfilling the criteria 1-3 were integrated in the 2nd funding period and again in the 3rd period when the CRC reached its maximum size of 22 projects and 28 PIs, which collaborated successfully together as is manifested by several high-impact publications with many PIs of different groups involved.

Thus, the strategy, not only to focus on the topic of a project and the excellence of the PI, but also to insist on preliminary collaborative work, or at least concrete plans for it, turned out to be very successful and was highly valued by the reviewers in all three evaluations. It turned out to be essential to demand collaboration plans in the project proposal that were much more concrete and elaborated than what is usually briefly annotated in the "Role of the project within the CRC" part of

the project proposal, optimally the whole project or at least a sub-project was built on an explicit collaboration between an experimentalist and a theorist.

A strategically very important and fruitful step in the development of the CRC was the integration of three research groups of the Leibniz Institute for New Materials (INM) on the UdS campus into the CRC in the 2nd funding period. After Prof. Aránzazu del Campo (B6) became co-director of the INM she established “Biomaterials” as a major research focus there, which fitted also perfectly into the topic of the CRC 1027. Three CRC projects with PIs from the INM were established (del Campo B6, Sankaran B8, de Jonge C7) and the INM became the main external institution with which the CRC most closely collaborated.

To stimulate and intensify collaborations within the CRC 1027 weekly seminars took place (fiercely interrupted by the Covid pandemic), partly with external speakers, partly as status reports of one or more PIs. In addition, each year a global status seminar day was organized to foster the scientific exchange among all groups of the CRC with short reports of all projects and a lot of room for discussions. In this way new collaborations emerged, on top of those already planned in the individual proposals / work plans. Young researchers, including postdocs and PhD students, of the CRC came together during the summer camps of the IRTG, lasting 2-3 days, explaining their projects to each other, listening to didactic lectures on special topics of the CRC etc., which resulted frequently in new collaborations between groups from different fields. Last not least the biannual international conference Cell Physics, organized and financed by the CRC, provided an excellent platform to display the CRCs corporate identity and growing cooperativity to a broad, internation audience, also initiating new collaborations with external researchers. Thus, over the years a powerful, coherent consortium emerged from the CRC 1027, distinguished by an internationally acknowledged biophysical expertise and high international visibility.

The challenges in this process were manifold: strategic decisions, about distributing available resources but in particular those concerning the discontinuation of projects, could interfere with the plans and hops of the affected PIs, for which reason the CRC established a steering committee with five PIs from physics, biology and medicine, which handled all emerging complications with great care and prudence. Also, the discipline to attend and/or organize common events, could sometimes become a challenge, in particular during the pandemic. But in the end it was enjoyable to see that the interest in enthusiasm in common activities and collaborative work actually increased continuously during the whole funding period of the CRC – as already mentioned: a sustainable corporate identity has emerged.