

Research Agenda 2025-2028



sano

**Centre for Computational
Personalised Medicine
International Research
Foundation**

Maciej Malawski

Marian Bubak

Jose Sousa

Przemysław Korzeniowski

Jan K. Argasiński

Tomasz Kościółek

Tomasz Gubała

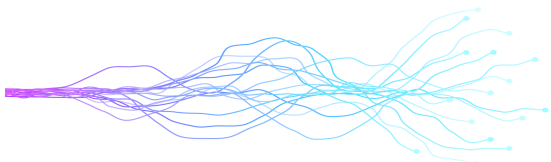
Piotr Nowakowski

ISBN 978-83-976637-1-8

Sano – Centre for Computational Personalised Medicine
International Research Foundation
Research Agenda 2025-2028

15 October 2025

Maciej Malawski, Marian Bubak, Jose Sousa, Przemysław Korzeniowski, Jan Argasiński,
Tomasz Kościółek, Tomasz Gubała, Piotr Nowakowski



Acknowledgments

We extend our gratitude to the Sano International Scientific Committee (ISC), including Professor Alfons Hoekstra (ISC Chair), for their valuable discussions and for providing critical and constructive feedback, all of which contributed significantly to shaping this Research Agenda.

This work was created within the project of the Ministry of Science and Higher Education “Support for the activity of Centers of Excellence established in Poland under Horizon 2020” on the basis of the contract number MEiN/2023/DIR/3796. This work has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 857533. This work is supported by Sano project carried out within the International Research Agendas programme of the Foundation for Polish Science, co-financed by the European Union under the European Regional Development Fund.



This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 857533 and from the International Research Agendas Programme of the Foundation for Polish Science No MAB PLUS/2019/13.



Republic
of Poland



Foundation for
Polish Science

European Union
European Regional
Development Fund



Ministry of Science and Higher Education
Republic of Poland

Funded by the initiative of the Minister of Science and Higher Education
“Support for the activities of Centers of Excellence established under the Horizon 2020 program”

Table of Contents

Mission Statement.....	4
Mission and objectives	4
Positioning of Sano in the International Landscape.....	4
Research Agenda	5
Global Challenges of Healthcare Systems	5
Computations for Individualised Medicine: AI and Simulation Approaches.....	7
Strategy for Success	9
Vision of Scientific Breakthrough.....	9
Research Teams	12
Computational Intelligence	13
Medical Imaging and Robotics.....	15
Computational Neuroscience	16
Structural and Functional Genomics	18
Extreme-Scale Data and Computing.....	21
Scientific Programmers Team	22
Interactions and Synergies between Research Strands	23
Summary.....	24
References	25

Mission Statement

Mission and objectives

We are developing sophisticated computer methods for the prevention, diagnosis and assistance of the treatment of diseases, to meet the overarching worldwide need for efficient, effective and streamlined healthcare. Our aim is to help clinicians to take better care of patients and to become one of the best Centres for Computational Medicine in Europe.

Sano aims to realise the Mission Statement by focusing on the following Objectives:

1. **Academia:** To become Central Eastern Europe's foremost academic institution for the identification, development and implementation of techniques in Computational Medicine
2. **Translation:** To combine academic, industry and clinical perspectives to inform innovative R&D processes, delivering competitive products and services to the marketplace, creating sustainability
3. **Education:** Deliver internal and external training programmes to provide the next generation of healthcare technology innovators with the unique skills profile required by Computational Medicine
4. **Digital Health and Care:** Make a significant contribution to digitising healthcare, meeting health challenges, improving wellbeing and meeting expectations for data utilisation and treatment efficacy
5. **Entrepreneurship:** Foster an entrepreneurial culture within the Centre to promote translation of research and enhance the innovation potential.

Positioning of Sano in the International Landscape

Positioning Sano within the international landscape requires a clear understanding of how the institute distinguishes itself from others who reside within the same domain of research. Sano uniqueness comes from the combination of its focus, vision and the comprehensive set of approaches it employs. Unlike centres focused narrowly on genomics, bioinformatics or computational biology, Sano sees advancement in this respect as elements of a broader, or more complete, approach to modelling human health and wellbeing. In contrary to organisations focused on bringing AI's newest techniques to clinics, Sano's emphasis lies in crafting integrative technologies that advance healthcare through simulation, AI, and digital health innovation, ensuring that its efforts remain aligned with the evolving demands of modern medicine. Furthermore, in comparison with institutes devoted to robotics and XR in healthcare, Sano pursues promising avenues that apply results of AI and physics-based techniques to this rapidly advancing area of research. While Sano recognises and embraces all these technological advancements in its Research Agenda, our uniqueness comes from holistic approach to modelling, simulating and knowledge generation along health and clinical pathways. By cultivating collaborations with leading institutions such as INSIGNEO and VPH Institute, Sano aims to situate itself as a global leader in Computational Medicine, prioritising software-driven solutions that bridge academia, industry, and clinical practice.

Research Agenda

Global Challenges of Healthcare Systems

The whole world today is becoming increasingly digital, from using computers and AI in everyday life, to advancing all research disciplines, leading to new computational methodologies which result in scientific breakthroughs and innovative technologies. Medical research is the single largest destination for R&D funding across the world, with an average of around 10% of all research expenditure targeted at this topic [1]. This leads to the emergence of Computational Medicine: a new technology which applies computing and engineering methods to medical research, ensuring highest standards of safety and requiring the high level of quality and trust in adopting new research findings.

Their natural desire to live healthy lives has inspired humans to accumulate medical knowledge at an ever-increasing rate, and to develop a multiplicity of technologies for patient data acquisition that can inform possible clinical interventions. Whilst this process has yielded many societal benefits, the vast increase in the extent, and particularly the complexity, of available information means that individual physicians no longer feel confident they can make optimum use of the data [2]. This natural human limitation on information processing has been the key factor in development of computational medicine, which relies on computers to harness the new wealth of clinical information effectively by fusing accumulated knowledge, enormous data volumes and human expertise to meet increasingly complex demand [3].

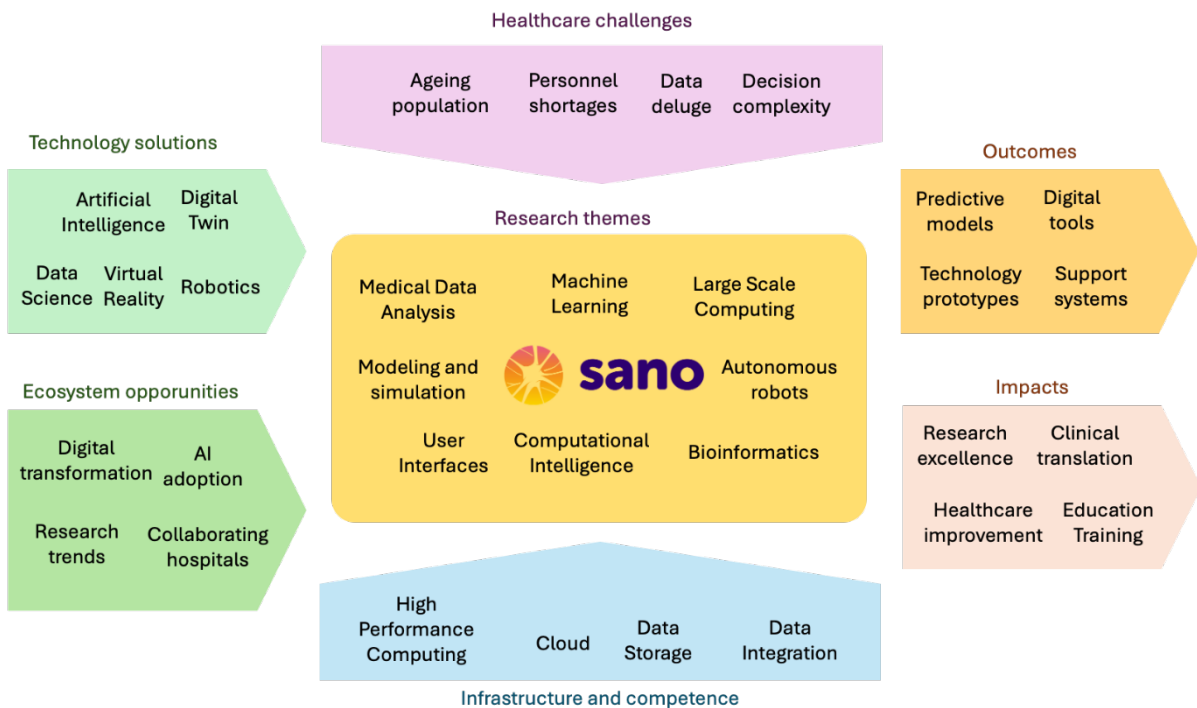


Figure 1 Positioning of Sano with respect to the external challenges, opportunities, technology trends, infrastructure and competences, as well as the major outcomes and impacts

Human health being the highest value, can benefit from developments of novel solutions and technologies that significantly enhance clinical success which can be measured e.g., by healthy life expectancy (HALE). According to WHO, HALE has increased by 8% extending from 58.3 to 63.7 years, while in the same time life expectancy has increased from 66.8 to 73.4 years [4]. The augmentation of HALE has been primarily attributed to the reduction in mortality rates, rather than a mere reduction in the duration of illness. Yet, while we have attained partial success, our focus must not solely rest on prolonging human existence. It is imperative to enhance the quality of life experienced during this extended period with the integration of staying healthy and sustaining optimal health conditions linked directly to quality of life (QoL).

Despite the excellent progress in sustaining healthy life, modern aging societies face enormous challenges in maintaining their healthcare systems efficient in meeting the increasing demands. This is caused by such factors as the lack of medical practitioners, who are overloaded with the volume of patients, often with considerable co-morbid diseases and polypharmacy and the available data, which often leads to phenomenon of burnout syndrome, decreasing the quality of medical decisions and also preventing the establishment of a positive patient-physician relationship based on trust.

The recent emergence of usable Artificial Intelligence (AI) systems made connections that were previously out of reach, possible. The clinical community is simultaneously excited and challenged by this process as, whilst it certainly wishes to embrace the benefits, it is very much concerned that all processes employed to treat patients should be end-to-end explicable, and considerable effort is now being directed to providing this enabling characterisation. This focus on trustworthiness is building human-centred AI, which follows a 'human-in-the-loop' approach, supported by and facilitating human cognitive abilities [5,6]. The so-called human-centred AI provides reliability, security, traceability, and trustworthiness to such systems.

In summary, advancing the frontier in computational medicine will equip us with the means to gather, process, and analyse a myriad of data pertaining to human functioning and empowerment. The challenge at hand lies in unifying all biopsychosocial dimensions into a single digital staying healthy model of human health (Human Digital Twin) while upholding the right to privacy for patients and the right to work for physicians. To embrace all these factors, a broad, interdisciplinary, and unified approach is imperative to truly comprehend the intricacies of this complex issue, without falling prey to oversimplification.

By developing a unified approach to data husbandry, Sano's goal is the unrestricted benefit across all society that will follow from its comprehensive approach to acquisition, allowing knowledge to be built universally from all patient data, including historical, environmental, genetic and self-monitored information. Sano's core techniques of data science, multi-scale modelling and simulation, and artificial intelligence combine with its in-house supercomputing expertise and facilities to provide uninterrupted coverage of the computational landscape.

Sano's dedicated approach to Computational Medicine builds on the currently underused power of data to push the boundaries of healthcare and research, maximizing the effectiveness of well-targeted advances for the betterment of all members of society. This updated Research Agenda gives the directions for future development of Sano – already successful as a Centre of Excellence in Computational Medicine – to extend its set of competences, enabling the creation of unrestricted solutions that expand the understanding of every patient's condition beyond its narrow biological diagnostic frame, to encompass clinical co-morbidities, psychology, lifestyle, environment, and more. Sano will leverage multi-modal data to break down historical information silos and facilitate a 360-degree holistic view of health conditions, fulfilling the promise of personalized, precision care.

Recognizing that the adoption of these technologies in medicine brings both opportunities and threats, Sano, as a non-profit, independent research institute, pledges to create trustworthy, explicable, reliable and human-centered healthcare solutions, and to serve as a trusted and mission-focused reviewer and advocate [5,6].

Computations for Individualised Medicine: AI and Simulation Approaches

An individual's (perceived) health is one of the major factors for his/her well-being and quality of life. Progress in our understanding of human physiology and pathology is crucial to understand the multitude of factors inside and outside the skin that determine our health, and not only contributes to prevention of disease, but also to diagnosis, optimised precision treatments, and revalidation. One of the most transformative developments in this domain is the rise of **digital twins**—high-fidelity virtual replicas of biological systems. While widely established in engineering, digital twins are now gaining traction in biomedical research, where they offer promising avenues for disease detection, progress prediction, diagnosis, and personalized treatment. As defined in European EDITH Roadmap, The Virtual Human Twin (VHT) is an “integrated multi-level, multi-time, and multi-discipline representation of quantitative human physiology and pathology” [7].

Historically, biomedical modelling has been grounded in simulation-based, physics-driven approaches [8]. More recently, **AI and data-driven techniques** have emerged as powerful tools to analyse large-scale, multimodal biomedical data [9]. The convergence of these two paradigms is where the most exciting innovations are happening today—such as **physics-informed neural networks** [10] and **AI-based surrogate modelling** [11], which combine the interpretability of mechanistic models with the adaptability and scalability of AI. Sano is a unique centre which combines and innovates in these two paradigms for medicine.

Digital twins in healthcare are inherently multiscale and multidisciplinary, requiring models that integrate diverse data types—ranging from molecular profiles to imaging and physiological signals. The updated research agenda of Sano focuses on development of such hybrid approaches to create VHT models for three relevant clinical domains: **cardiovascular diseases**, **neurological disorders**, and **gastrointestinal conditions**, as well as **interactions** between them. These three domains were strategically selected based on their clinical importance, existing experience of Sano in modelling and AI techniques that can be applied to them, availability of excellent clinical collaborators with access to data, as well as translation potential and impact. Each domain presents unique modelling challenges and clinical needs, but at the same time there are deep connections between them. For example, gastrointestinal dysfunction can impact neurological health via the gut-brain axis [12], and cardiovascular issues often co-occur with both gastrointestinal and neurological symptoms [13]. Understanding these interdependencies requires integrated, multimodal modelling frameworks.

Our digital twin models will simulate key physiological processes **within and across** cardiovascular, neurological, and gastrointestinal systems, aiming to support personalised diagnostics, disease progression forecasting, and therapeutic planning. Realising this vision requires substantial **computing infrastructure**, capable of supporting data-intensive AI pipelines, high-resolution simulations, and real-time updates based on patient-specific inputs. By **bridging simulation-based and data-driven approaches** and applying them to interconnected biomedical domains, this research will considerably advance scientific understanding and accelerate the translation of research into clinical impact.

Building on the strong foundation of the **Sano Centre for Computational Medicine**, a Centre of Excellence uniquely dedicated to VHT methods, high-performance computing (HPC) and artificial intelligence (AI) for medical applications, this updated research agenda aims to deliver a **new generation of digital twin solutions**. Our deep understanding of this field will result in significant research record and create robust, lasting USP (*deep tech*), with a clear path toward **clinical translation**,

particularly in the domains of **cardiovascular**, **neurology**, and **gastroenterology** and their **interactions** along the increasingly important **heart-brain-gut axis**. This translation will be conducted in collaboration with clinicians from Poland and Europe, with the support of committed industrial partners.

Established Excellence in Digital Twin Components

Sano has a **unique interdisciplinary environment**, bringing together international (10 countries of origin) expertise in HPC, VHT, AI, biomedical modelling, and human-centred design. It is the **only single institution in Poland** with demonstrated capabilities across the full spectrum of these key digital twin components. The team that created Sano has **over two decades of experience** in designing and operating computing infrastructures specifically tailored for biomedical applications, starting in 2002 from CrossGrid EU FP5 project, through ViroLab, VPH-Share, EurValve and InSilicoWorld (2024), and ongoing 5 projects. Current research teams have demonstrated excellence in pioneering **AI-driven techniques** for medical image and signal processing, including advanced generative AI (Gen-AI) for **creating realistic synthetic images**, efficient **leveraging GPU-based computing clusters**, development of **physics-based realistic surgical simulators**, and development of **intuitive interfaces for patients and clinicians**, including **web, mobile, and immersive VR platforms**—essential for the usability of clinical digital twins. This convergence of technological capabilities and domain expertise under one institutional roof is **exceptionally rare** and offers a unique opportunity to build a truly integrated, clinically relevant digital twin ecosystem.

Embedded in European Digital Twin Initiatives

Sano is **deeply embedded in major European efforts** to build the digital twin ecosystem:

- An active member of the **Virtual Physiological Human (VPH) Institute**, which plays a leading role in advancing personalized medicine through in silico modelling.
- An active contributor to the **EDITH CSA** (European Virtual Human Twin), shaping the roadmap for the European Health Data Space and digital twin frameworks.
- Key contributor to the **In Silico World** and **GEMINI** projects, both dedicated to bringing digital twins into real-world clinical and regulatory use.
- Partner of MSCA doctoral training networks **ThromboRisk** (full partner) **InSilicoHealth** (associated), ensuring a robust pipeline of early-career researchers.
- A member of **Avicenna Alliance** — an association of industry, academia and healthcare organisations co-developing in silico medicine.

Through these, Sano has direct access to **state-of-the-art methodologies, regulatory frameworks, and collaborative networks** across Europe, ensuring alignment with the broader EU VHT Initiative.

Strategic Need for a Dedicated Unit Given the **complexity and scope** of digital twin development—requiring tight integration of modelling, data, AI, computing, and user interaction—a **dedicated institution such as Sano** is essential to consolidate and expand existing efforts. This unit will act as a focal point for international collaboration, translational research, and workforce development, ensuring sustained impact across research, clinical, and industrial domains.

Sano already possesses **critical scientific** (5 teams, 10 senior & 42 junior researchers, 153 papers & 400 conf. contributions in 4 years, 4.62 avg. IF), **technological** (9 software developers, compute: access to LUMI – 380 PFLOPS 8. fastest world system, and Helios – 90k GPUcore, licences, own background IP at TRL 4-5), and **organizational capabilities** (22 support specialists, 536 m2 of fully equipped labs, data & expertise from 15+ collaborating clinics, 8 industrial contracts, 6 EU grants, €24M grant budget, 700k+ patient data analysed, currently accessing further 2M+ cases) that directly align with the goals of the proposed digital twin research agenda.



With its proven track record, comprehensive technical ecosystem, and active international collaborations, **Sano represents the ideal environment** to house such a unit and lead the next frontier in digital twin research.

Strategy for Success

Vision of Scientific Breakthrough

The Virtual Human Twin (VHT) is an “integrated multi-level, multi-time, and multi-discipline representation of quantitative human physiology and pathology” [7]. VHT builds on top of 15 years of development of Virtual Physiological Human (VPH) methods, and already started to deliver models (“digital twins”) for clinically-exploited diagnosis and treatment assistance [8]. Paired with explainable computational intelligence techniques, VHT is leading medicine into the territory of rigorously tested, evidence-based technologies and processes [9]. This poses a research challenge of great importance: building digital twins for specific pathologies. Artificial Intelligence (AI), recently experienced remarkable growth (doubled in 4 years to ~\$200b), primarily through deep learning (DL) approaches based on big data. While its application to medicine is also growing (\$15b, 25% CAGR), severe limitations negatively impact the adoption: opaqueness, bias, and privacy concerns. In high-risk healthcare environments, where trustworthiness is critical, the current AI techniques add to insecurity, while their development consumes outstanding resources. These limitations are grounded in the underlying connectionist approach, which equates learning associations from data (with limited prior knowledge) with continuous learning to build intelligence [14]. Our ambition is to address these challenges, by proposing a research agenda for Sano.

The overarching objective will be to develop, test, and validate a computational digital twin platform for assessment, prevention, diagnosis, intervention and recovery, which can be applied to a broad spectrum of medical challenges, with the focus on three relevant clinical domains: **cardiovascular diseases**, **neurological disorders**, and **gastrointestinal conditions**, as well as **interactions** between them. The platform, based on the results and experience of all of Sano research teams, aims to combine the concepts of virtual human twin with the novel approaches to machine learning that enhances today’s AI technology in terms of explainability, trustworthiness and robustness.

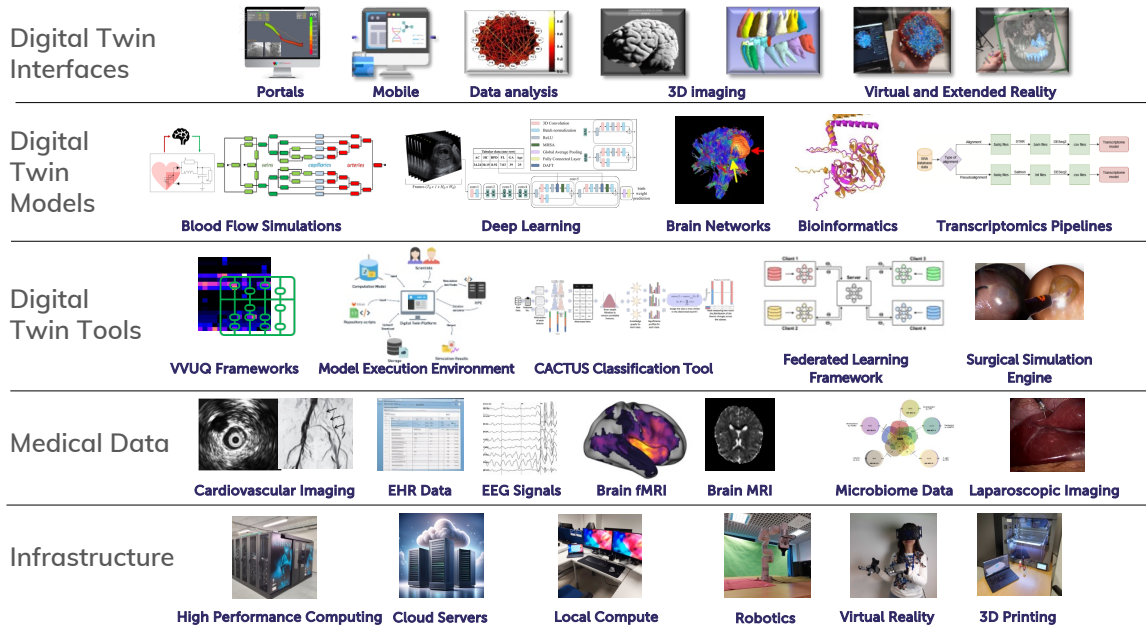


Figure 2 Overview of the integrated Digital Twin Platform under development at Sano

The efficiency and potential of the new computational platform will be demonstrated on a societally important challenges, based on the collaborations with clinicians through our Polish and European networks.

Sano, by developing a new digital twin platform, will reach an important milestone in this challenging research and technological problem of great importance, enabling the entire new development avenue of building trustable, clinically-applicable digital twins for specific pathologies. Sano, a non-profit research foundation completely devoted to the research in computational medicine, is ready to address this challenge, as five research teams will combine skills, methodologies, available infrastructure, and existing IP to achieve this ambitious goal. The resulting solution will combine methods of simulation, artificial intelligence, computational biology, virtual reality technologies, and high-performance computing, to deliver an integrated computational platform covering the full pathway of prevention, diagnosis, intervention and recovery in human diseases.

The key research directions for the Sano Digital Twin platform are based on the experience of Sano research and development so far.

Sano's Digital Twin Platform will be capable of integrating diverse digital twin models across spatial and temporal scales. This platform will support model orchestration, simulation, and real-time feedback from clinical data, providing scalability and efficiency thanks to the convergence of HPC, cloud and AI infrastructures. It will also provide standardised APIs and data exchange protocols to enable seamless communication and interoperability between models operating at different biological scales and within different organ systems. It will be based on the experience of Sano team in scientific workflow management and optimisation on emerging computing infrastructures [15], production-grade MEE platform [16], experience in virtual and containerised environments [17,18], and HPC-Whisk technology for combining HPC and Cloud [19].

A Hybrid Modelling Methodology combines deterministic (simulation-based) models with data-driven AI techniques to enable adaptive and accurate modelling of complex biological systems. **Competences** Sano has already demonstrated the capability and experience in developing physics-based simulation models for cardiovascular system, including Deep Vein Thrombosis (DVT) [20,21] and baroregulation of

the heart rate by the nervous system [22], as well as in physics-based real-time simulations for virtual surgery [23]. This is coupled by the vast experience of developing novel AI-based methods for medical image analysis [24], brain surgery planning [25], including applications in diagnostics and patient monitoring (applied to SAH, DVT, PAH, AD, allergies and many others) [26,27]. Sano has experts in generative AI methods for realistic image synthesis (quoted by NVIDIA in their Surgical AI 2025 keynote as the current state of the art) [28]. Hybrid modelling methods have been applied to Alzheimer's disease prognosis [29]. Special attention will be given to physics-informed AI and surrogate modelling approaches, with the use of generative AI.

Multimodal Data Integration Technology incorporates heterogeneous data types (e.g., genomics, imaging, physiological signals, electronic health records) to ensure personalised, high-fidelity digital twin construction and calibration. This will be based on Sano experience in medical data analysis, including small and missing data [30], mixing tabular and imaging data [27], federated learning [31] and analysis of genomics and proteomics datasets [32], as well as platforms for cloud-based secure data storage and sharing [33,34]. Based on that, we will develop a unified data integration technology within the digital twin platform, employing such security features as federated learning and hardware-assisted trusted execution environments (TEE) in modern processors and GPUs.

Agentic AI for Research Automation that implement intelligent, autonomous agents to support and partially automate critical research processes—such as model development, validation, and parameter tuning—thus accelerating scientific discovery and increasing reproducibility. This will be built on Sano experience in development of solutions for science automation, such as MEE platform [16], but will be further expanded with the recent advances in agentic AI solutions, where multiple specialised agents collaborate on a common goal, using recent developments in multi-agent AI technologies, such as CrewAI, LangGraph or BeeAI open source solutions [35], as well as open protocols such as model context protocol (MCP). As a further step we envision the use the coordinated AI agents for advancing the healthcare decisions, as proposed by [36].

Immersive Interfaces for Clinicians, Patients and Researchers. That integrate VR/XR-enhanced visualisation tools to facilitate intuitive exploration and interaction with digital twins, improving clinical interpretability, research usability and patient empowerment. **Competences** Sano has the technology and experience in realistic VR surgical simulations [23], virtual environments [37] and user interactions in VR [38]. This showcases the ability to blend rigorous modelling with real-time interaction (high-TRL prototypes already created for Spina Bifida, cholecystectomy, and CV stenting simulator, recently deployed at a CMUJ curriculum) [39]. Here we will employ these techniques for providing interactive user interfaces for researchers, clinicians and medical students, as well as patients, to enable next level of interactions with DT in real-time realistic VR environments.

This agenda balances scientific innovation with translational ambition and ensures the active synergy of all research groups involved through tightly coordinated implementation and shared objectives.

Originality of the Approach

The proposed research agenda is grounded in a framework that merges **physical modelling** and **AI-based approaches** to create powerful, interpretable, and scalable digital twins for biomedical applications. The core novelty lies in the **synergistic integration** of these two traditionally distinct paradigms—where each complements and enhances the other.

On one hand, **physics-based simulations** offer a deep, mechanistic understanding of biological processes, grounded in validated scientific theory [21,22]. On the other, **AI and machine learning** excel at recognising complex patterns and generalising from data, even in high-dimensional or noisy settings

[30]. By **enhancing simulation models with AI**, we aim to accelerate computation (e.g., through surrogate models), fill gaps in knowledge, and enable real-time interactivity [40]. Conversely, **embedding physics into machine learning models** improves their accuracy, robustness, and interpretability by “making AI more scientific” — key qualities for clinical trust and adoption [41,42].

Innovation also lies in the use of **explainable AI (XAI)** techniques informed by physics-based simulations. Unlike black-box approaches, this hybrid methodology will enable clinicians and researchers to **trace model predictions back to physiological mechanisms**, enhancing credibility and supporting clinical decision-making.

The above combined finally enables the **transformative approach of leveraging agentic AI systems**—autonomous software agents that collaboratively assist patients, caregivers, clinicians and researchers, with inbuilt explainability. For **researchers**, these agents will construct and automate complex workflows based on high-level natural language prompts, such as: *“Given this folder of patient datasets, preprocess them, launch simulations on the HPC cluster, analyse results, and generate visual reports.”* This represents a significant leap beyond current tooling and parallels emerging paradigms like **Model Execution Environment (MEE)** by enhancing them with **powerful LLM-driven interfaces**.

For **clinicians**, our **“Digital Twin of a Doctor”** assistant will be capable of interpreting patient-specific digital twin simulations, suggesting hypotheses, and supporting personalised treatment planning. While still in its infancy, this concept lays the groundwork for future breakthroughs in human-AI collaboration in medicine.

The same assistant will empower **patients and their caregivers**, with visualisation of the decision process and the clinical pathway, and a clear indication of where and how they can act to (i) enhance the outcome (right-on-time precise information reporting [43]) and (ii) select from the available treatment strategies.

Understanding the energy-related challenges of modern era computing, we apply our original, state-of-the-art methods of **efficient use of emerging computing infrastructures** [15]. We aim to harness the **convergence of HPC and AI hardware**—including the latest GPU-accelerated solvers (e.g., Ansys for CFD), serverless computing [19,17], and AI Factories (through close collaboration with Cyfronet – GAIA AI project)—to support data-driven and simulation-based components combined. This unified hardware/software environment ensures scalability, sustainability, and readiness for real-time clinical applications.

Such **deep integration of simulation, AI, automation, and advanced computing**, applied cohesively to three critical medical domains, has never been realised at scale before, and represents a significant advancement over existing methodologies in biomedical digital twin research.

Research Teams

Sano's scientific teams are formed in a transparent process involving the International Scientific Committee (ISC), which co-creates and approves Sano's long-term research agenda and strategic development plan. The ISC has the final say in the international recruitment and leadership of Sano's scientific teams.

Teams working together towards a common goal

The development of a robust, multi-scale, and clinically applicable digital twin platform at Sano is made possible by the combined strengths of five interdisciplinary research teams. Each brings deep,

complementary expertise that, when integrated, enables innovation across the full digital twin development pipeline—from data collection and modelling to simulation, validation, and deployment in clinical environments.

All Sano research teams will work together towards the common goal of a digital twin platform.

The Extreme-scale Data and Computing team (ExC) will contribute to the platform architecture, provide models and data for cardiovascular and neuroscience, and the HPC expertise will be used to train AI models by all the teams and to process big data by others. The Medical Imaging and Robotics (MIR) team will develop solutions based on data and models acquired and/or developed by the other teams (CN, ExC) and these will be closely integrated with the platform being developed. The Computational Intelligence team will provide key methods, abstractions and tools related to explainable AI and continuous machine learning for the platform, which will be used by the other teams. The Computational Neuroscience (CN) team will provide platform-wide data and methods related to neuroimaging and neurological signal analysis, which will be integrated into the platform in a continuous learning mode. Similarly, the Structural and Functional Genomics (SFG) team will be responsible for bioinformatics analyses and development of microbiome-based data and models integrated with the platform.

Computational Intelligence

Research scope and objectives

The team research agenda aims to evolve and explore the development of artificial intelligence (AI) systems capable of continuous learning by mimicking human tacit knowledge acquisition mechanisms, unlike conventional deep learning (DL) models, which depend on large amounts of labelled data. The team will explore the development of intelligent agents that can autonomously sense their environment, generate beliefs, and learn from experience without predefined goals.

The proposed research builds on a complex adaptive system (CAS) framework, specifically an adaptive spiking neural network (aSNN). It focuses on the dynamic interactions of intelligent agents that collaborate to solve problems and enhance their learning capabilities through system-emergent tacit knowledge.

The agenda is grounded in three key objectives: (1) Enabling the emergence of tacit knowledge by building intelligent agents capable of sensing the world through abstractions, models, and inference to generate beliefs without training/validation approaches. Our previous research [30, 43] using abstractions without training/validation achieved better results than explainable ML methods. (2) Modelling an aSNN of intelligent agents to generate emergent tacit knowledge by building theory and architecture of interconnected agents that interact dynamically to solve problems collaboratively. (3) Develop an AI continuous learning theory by creating a framework demonstrating the systems development of tacit knowledge.

Tacit knowledge encompasses context-specific, experiential, and embodied knowledge that resists codification and is acquired through intuition, practice, and personal experience [44]. We will argue that a CAS [45] modelled as aSNN [46] is the proper framework for the study of tacit knowledge as an emergent property of the behaviour of intelligent agents as it provides several advantages, such as sparse coding, precise spike timing encoding, and local plasticity rules, which allow for efficient information representation and adaptive learning mechanisms. We will use at least three years of longitudinal data from an ongoing clinical project enrolling nine clinicians diagnosing allergies, providing a unique setting for exploring my assumptions. This data allowed for the development of agents replicating the classification process of each clinician as data-driven explicit knowledge using

my team-developed CACTUS (Comprehensive Abstraction and Classification Tool for Uncovering Structures) agent [43]. The development of the proposed AI architecture will generate tacit knowledge emergent from the self-organisation process of the multi-agent CAS, allowing the development of agents' continuous learning towards a better agreement with the clinicians.

The research agenda is not focused solely on developing AI tools but on AI modelling genuine human ways of acquiring knowledge, as, in this way, we are proposing to build artificial intelligence that can tell us something true of human intelligence rather than a kind of, however helpful, 'alien' intelligence.

Research projects and directions

To achieve this, we aim to develop three projects addressing three fundamental questions:

How can we build intelligent agents that can autonomously sense and adapt to their context by mimicking human learning mechanisms? We hypothesise that intelligent agents can autonomously develop a sense of the world by abstracting raw data and building fully connected graphs, extracting statistically significant rules and making inferences to overcome variability [47, 48, 49], something not yet tested. My team's research [30, 43, 50] on learning from abstractions without training/validation data allowed us to develop an agent (software tool), CACTUS - that uses probabilistic and PageRank approaches to classify events, influencing state-of-the-art by demonstrating how data abstractions maintain feature stability under missing data. Our recent research is focused on extracting automatic models of the world from fully connected graphs under time constraints, aiming for improved knowledge synthesis and inference under data variability. The team's ongoing research aims to integrate sensing and adaptation in agents to build agents' beliefs by unifying abstractions, models of the world informed by tacit knowledge and inference as Bayesian models. These methods often incorporate intrinsic goals or subgoal discovery, enabling agents to structure their belief hierarchies autonomously [51]. My team is already running experiments using *Prolog* [52] to structure beliefs independently from the available data based on models of the world.

Can a spiking neural network of intelligent agents build tacit knowledge from shared beliefs? The development of tacit knowledge is particularly relevant in dynamic, decentralised, and open-ended problems, where agents interact through beliefs built on noisy, incomplete and small data. **We hypothesise that learning happens actively without intentional prompts and is grounded in the unintentional development of tacit knowledge resulting from spiking neural network self-organisation.** Other teams' research [53,54] collectively highlights the utility of dynamic networks, feedback loops, and learning-based frameworks in producing emergent adaptive behaviours, but none explicitly address the emergence of tacit knowledge. For the last three years, the team has been working [30, 43, 50] on fully connected networks to develop ML algorithms with better classification balanced accuracy over existing explainable ML methods when using noisy and small data. **The fully connected network results from raw data discretisation using ROC distributions to classify the data features independently into Up and Down [30, 43]. This discretisation relates directly to SNNs being a crucial step in SNN information processing.** The diffusion of tacit knowledge has been modelled extensively in networked systems, with many works utilising weighted-edge and small-world network approaches. Evolutionary game-theoretic (EGT) models [55] can provide further insights by capturing non-relational behaviour and long-term dynamics, providing strategies for facilitating the effective transfer of tacit knowledge in complex, competitive environments. This can be a methodological approach that recognises what an Up and Down parameter implies.

Will an AI framework of intelligent agents go beyond explicit knowledge towards continuous learning? The self-organisation of spiking neural networks (SNNs) and their transition from fully

connected to scale-free topologies is a prominent area of research in computational neuroscience, with investigations often focusing on the role of activity-dependent plasticity and spiking dynamics. **We hypothesise that shared beliefs can shape the development of tacit knowledge from the self-organisation system [56, 57] from possible fully connected network agents to a scale-free network.** Tacit knowledge does not rely on an explicit representation but emerges in conjunction with the environment, such as the way a pocket calculator embodies mathematics, hydrodynamic principles are embodied in the movement of a fish and walking, or perceptual patterns emerge from the interaction of neural control and the kinematic interaction of body, senses and environment. This tacit knowledge depends on feedback between the system and its world, and it is fundamental to building mental representations of the environment. Combining the principles of CAS with belief-sharing agents makes it possible to create systems that adapt, evolve, and exhibit emergent continuous learning [58]. The measurement of the beliefs of each agent from the input spike train to the output will allow for the evidence of emergent tacit knowledge resulting from the self-organisation into a scale-free network.

The novelty of using intelligent agents capable of inference on a model of the world, supervised by tacit knowledge captured from the emergent self-organisation of an aSNN, is innovative and presents high feasibility challenges. A contingency plan to overcome risks will focus on minimising the impact of the inability to simulate the self-organising nature of complex adaptive systems, as it is central to the inference of the existence of tacit knowledge.

Towards products and translation

CACTUS is already at TRL 6, undergoing testing at both hospital and industry levels. The team expects that by July 2026, parts two and three of the agent, models of the world, and inference will be at least on TRL4 and ready to be tested in real-world environments. The next years of planned research are built on the cornerstone of the ongoing collaboration with Ameryka Children's Hospital in Poland, which will enable the development of conceptual AI continuous learning using allergies and ageing as proof of concept.

Medical Imaging and Robotics

Research scope and objectives

Medical Imaging and Robotics group focuses on pioneering interdisciplinary solutions at the intersection of medical imaging, surgical technologies, artificial intelligence, and robotics. We strive to significantly enhance diagnostic precision, surgical effectiveness, and patient outcomes through advanced computational methods and innovative robotic systems. Our scope spans algorithm development, surgical simulation, synthetic data generation, and autonomous robotics, integrated tightly with clinical validation and real-world application.

Research projects and directions

Advanced Medical Image Analysis Our team develops sophisticated algorithms for detailed analysis and interpretation of medical images from Ultrasound, CT, and MRI modalities. The specific projects include automatic fetal birth weight estimation from ultrasound, precise segmentation of vessels in fetal surgery, teeth segmentation from CT scans, and pulmonary hypertension diagnosis from MRI. Utilizing state-of-the-art deep learning and image processing techniques, we aim to enhance diagnostic accuracy, improve disease characterization, and support therapeutic planning and monitoring.

Surgical Simulation and Training Technologies Our group develops advanced simulation tools aimed at enhancing surgical education and proficiency. We create realistic, high-performance laparoscopic,

endoscopic, and fetoscopic simulation platforms using GPU-accelerated physics engines. These systems support surgical training, robot learning, and validation through collaborations with clinical partners like Imperial College London.

Interactive AI and Decision Support We are exploring interactive AI-driven decision support systems designed to augment medical and surgical precision and efficiency. By combining multimodal imaging data, deep learning-based predictive analytics, and intuitive visualization techniques, our research facilitates real-time surgical decision-making support, enhancing both safety and outcomes in complex medical procedures.

Synthetic Data Generation and Clinical Validation Focusing on bridging the gap between simulation and clinical practice, we generate highly realistic synthetic surgical data using advanced machine learning models. Our approach includes meticulous integration of real surgical datasets for model training and validation, ensuring realistic and clinically relevant synthetic outputs. Rigorous testing protocols involve collaboration with expert surgeons to evaluate realism and applicability, informing continuous refinement and clinical acceptance of our tools.

Autonomous and Assistive Robotic Systems Our research encompasses the development of autonomous and assistive robotic solutions for both surgical and caregiving applications. We integrate state-of-the-art computer vision methods with robotic control strategies, developing Vision-Action Models (VAM) to enable autonomous and semi-autonomous medical robots. Our research includes training neural networks to interpret complex scenes, predict precise actions, and enhance robotic dexterity and decision-making capabilities, thereby improving outcomes. Projects include remote and autonomous robotic ultrasound systems that increase diagnostic accessibility and precision, and assistive caregiving robots equipped with advanced sensory and cognitive functionalities designed to aid mobility-impaired individuals. These robots are developed and refined through pilot studies and clinical feedback to ensure seamless integration into healthcare workflows.

Towards products and translation

Our research group is deeply committed to transforming innovative AI and robotic technologies from laboratory settings into practical, clinically validated products. By closely collaborating with healthcare providers and industry partners, we are actively translating advanced simulation tools, autonomous robotic systems, and sophisticated diagnostic algorithms into user-friendly solutions. For instance, our automatic fetal weight estimation and virtual reality surgical simulators demonstrate clear pathways to clinical adoption, directly addressing unmet clinical needs and improving patient care. Additionally, our generative AI methodologies facilitate broader access to reliable, realistic datasets, essential for product development and regulatory approval. Emphasizing rigorous clinical validation, regulatory compliance, and ethical frameworks, we ensure our research outputs not only achieve technological excellence but also gain practical acceptance and utility in healthcare markets.

Computational Neuroscience

Research scope and objectives

The Computer Vision Data Science group at Sano – Centre for Computational Medicine will progressively transition towards a primary focus on Computational Neuroscience. This shift will emphasize the application of advanced computational techniques to model and understand complex neural processes, aligning with the group's evolving research priorities. The group will expand its efforts in Computer Vision, a field of artificial intelligence and computer science aimed at developing methods for machines to interpret and analyse visual data, such as images and videos. Data Science will continue

to play a central role, focusing on extracting insights from data through statistical models, computational algorithms, and domain-specific expertise. Future work will prioritize the development of rigorous theoretical frameworks and statistical methods capable of addressing the complexity of nonlinear brain functions, where human intuition may fall short. The increasing volume and complexity of data will drive the need for innovative analytical strategies, leading to interdisciplinary collaborations with experts in neuroscience, mathematics, physics, engineering, and computer science.

Computational Neuroscience will become a key research focus, emphasizing the use of mathematical models, algorithms, and simulations to explore the nervous system's mechanisms, particularly the brain's information processing capabilities and their influence on behaviour. The group's agenda will centre on developing models that explain how neural circuits encode, process, and respond to information, positioning the team at the intersection of neuroscience, data science, artificial intelligence, and computer science.

The group's research will focus on the following core domains in the coming years.

Research projects and directions

Data Analysis Future projects will explore advanced mathematical techniques for medical imaging and brain data interpretation, with planned studies including quaternion-based CT image conversion and whole-brain MRI analysis of grey matter atrophy across neurodegenerative conditions such as Alzheimer's disease and frontotemporal dementia.

Image Segmentation and Classification The group will focus on developing methods for brain structure analysis and pathology detection using imaging techniques and deep learning approaches. Planned projects will include the use of functional connectivity gradients in ischemic stroke, deep learning protocols for glioma grading, and the application of graph convolutional networks for traumatic brain injury classification.

Predictive Modeling The research agenda will emphasize machine learning models for forecasting neurological states and conditions. Efforts will focus on the application of explainable graph neural networks for epilepsy detection and prediction in EEG recordings.

Biologically Inspired Artificial Intelligence The group will further develop neuromorphic computing approaches, with a focus on spiking neural networks (SNNs) to simulate neuronal activity and model complex neurobiological processes.

The group's short-term objective is to support PhD candidates in successfully completing their doctoral research. Current PhD students include Rosmary Blanco, Monika Pytlarz, Joan Falco Roget, and Mahmoud Nasr. To enhance international collaboration and knowledge exchange, the group engages with leading institutions such as the Children's Hospital of Philadelphia, the University of Amsterdam, and the University of Messina, through research internships.

Towards products and translation

The team will focus on ensuring long-term financial sustainability through a diversified funding strategy. This will involve pursuing both individual and collaborative grants, with a National Science Centre (NCN) Preludium grant already secured and further proposals submitted, including NCN Sonata, FNP First Team, and NCN Weave-UNISONO. The group will also continue efforts toward commercialization, with two stroke-related projects undergoing patenting processes for key technological innovations.

Structural and Functional Genomics

Research scope and objectives

The gut microbiome plays a significant role in shaping health and is an area of active research at the interface of computational biology and medicine. Due to its potential – as a biomarker – it is an important element of preventive measures (e.g. supplementation, personalized diet, etc.), diagnostics (biomarker studies), and therapeutics (intestinal microbiota transplants; FMT, biotherapy, stratification of interventions, etc.). The Structural and Functional Genomics (SFG) team at Sano develops computational methods to extract actionable knowledge from human metagenomics data, with a particular focus on the gut microbiome. Our core mission is to provide excellence in microbiome bioinformatics to enable a transformation in healthcare. We achieve this by developing robust biomarkers, predictive models, and diagnostic tools designed for clinicians, biomedical researchers, and public health experts.

Our work spans fundamental questions of protein structure and function, as well as translational goals such as digital twin technologies to enable microbiome-based precision medicine. At present, rather than focusing on individual patient–doctor interactions, we emphasize broader biomedical applications—including diagnostics, therapeutics, and public health interventions.

Collaborations with clinical and cohort-based research groups, including the [Jagiellonian University Medical College](#), [Malopolska Centre of Biotechnology](#), and the [Estonian Microbiome Cohort \(EstMB\)](#), allow us to align our research with clinically relevant needs, bridging the gap between metagenomic discovery and real-world healthcare applications.

Research projects and directions

Our research portfolio integrates deep learning, structural bioinformatics, molecular modelling, and large-scale metagenomics to tackle critical challenges in microbiome science. We focus on building computational frameworks and predictive models that are scalable, reproducible, and clinically relevant. Each project contributes to our overarching goal: translating complex microbiome data into actionable biomedical knowledge – spanning diagnostics, treatment personalization, and digital twin development. Across different projects the SFG Team is collaborating with different teams across Sano. With the [Extreme Scale Data and Computing](#) team we collaborate on computing, scalability and digital twin technology implementation; with the [Computational Neuroscience](#) team on all gut-brain axis research challenges; with the [Computational Intelligence](#) team on integrating clinical data with omics analyses, in particular in studying the relationships between microbiome and human health; [Scientific Programmers](#) team contributes their expertise in creating high-quality, scalable software to be shared with other researchers, used in pre-clinical and clinical studies, or to be commercialized with Sano industry partners.

The current portfolio of SFG team projects include:

MicrobiomeGPT and microbiome Digital Twins MicrobiomeGPT is a deep neural network trained on large cross-sectional and longitudinal human gut metagenomic datasets. It learns embedded representations of individuals based on both taxonomic composition and functional potential. The model captures shared functionality across individuals, handles high-dimensional, sparse, and variable data, and enables tasks such as age, BMI, or disease status prediction. It inherently serves as a microbiome foundation model which may be fine-tuned to reflect individual microbiome characteristics and dynamics. The intent behind digital microbiome twins is to achieve personalized, dynamic models to forecast microbiome trajectories and inform microbiome-based therapies. This

project is done in collaboration with [Institute of AI for Health, Helmholtz Munich](#); [Institute of Genomics, University of Tartu](#); and the diagnostics company [Diagnostyka S. A.](#)

deepFRI2 deep learning-based high-quality and high-coverage biomolecular function prediction

deepFRI is our protein 3D structure-based machine learning model which predicts protein functions by combining sequence and structural embeddings. Its successor, deepFRI2, integrates additional layers: conserved genomic context, AlphaFold-predicted structures, and evolutionary information. It improves interpretability and extends functional coverage, especially for microbial proteins without homologs. This framework enables us to distinguish between truly unknown versus unannotated functions, which is critical for understanding microbial ecology, evolution, and biochemical diversity. Once finalized, the resulting predictions will feed into metagenomic analyses and reference databases for community use.

Mapping the protein universe of the human gut We explore large-scale protein structure space using models from AlphaFold Protein Structure Database (AFDB), ESMAtlas, and the Microbiome Immunity Project (MIP). By clustering and embedding microbial protein structures, we generate a unified, low-dimensional map of structural and functional diversity in the gut microbiome. This project enables large-scale visualization, search, and annotation of novel proteins, supports functional genomics, and lays the foundation for understanding remote homology and protein innovation across microbial taxa. This project is done in collaboration with [Biozentrum, University of Basel](#), Switzerland and with [VIB.AI Center for AI & Computational Biology](#), Leuven, Belgium partly funded by NCN Weave-UNISONO program.

Reproducible pipelines and gut protein annotation We develop scalable pipelines and a comprehensive reference catalogue of human gut proteins. Objectives include: (1) revising functional annotations; (2) building 3D structural models for proteins lacking homologs; (3) analyzing sequence and structure diversity of "dark" proteins; (4) tracing their evolutionary history and (5) predicting function using structural and genomic context. These tools support meta-analyses and clinician-facing applications. Work done in collaboration with the [Extreme Scale Data and Computing Team](#).

Host-microbiome protein-protein interactions The impact of the microbiome on human health may occur through a variety of mechanisms, one of the most under-studied being interactions of surface or secreted bacterial proteins with human proteins, in particular with the human immune system. The team, through our expertise in structural bioinformatics and AI, is exploring techniques to study host-microbe protein-protein interactions to: (1) better define biomolecular function; (2) establish plausible mechanisms of impact of the microbiome on the phenotype; (3) design interventions modulating those interactions.

Antibiotic synergy prediction and mechanistic interpretability Based on the data on the E. coli bacteria interactome and information on connections between drugs and proteins, we develop a predictive model to identify optimal antibiotic synergies. The aim of the project is to develop appropriate input features for drug pairs to achieve the best possible results of the prediction model. We assume that features reflecting biological mechanisms, extracted from the above databases, will contribute to higher model efficiency. Interpretability of results is also a key element - analysis using methods such as SHAP and assessment of feature importance are to confirm the principles of drug synergy by considering different mechanisms of action. Project done in collaboration with [Łukasiewicz – Krakowski Instytut Technologiczny](#).

Drug discovery and repurposing of compounds inducing re-replication In the project, we are looking for small chemical molecules that induce overexpression of the CDT1 protein, leading to re-replication and cytotoxicity in cancer cells. This strategy uses differences in the functioning of cancer and healthy

cells, which allows for selective action of the drug. We developed a predictive model, a ML transformer with an attention mechanism, to identify patterns in the experimental data and test new chemical compounds that induce a similar effect in vitro. We compared the results of this model with the results of traditional machine learning methods, assessing the effectiveness using metrics such as ROC-AUC, precision and recall. Project done in collaboration with [Łukasiewicz – Krakowski Instytut Technologiczny](#).

Microbiome spread and interactions in analog space missions In collaboration with the [Jagiellonian University Medical College](#) and [Space Technology Centre AGH](#) we are designing and analyzing the data from analog astronauts taking part in analog space missions (simulated closed environment on Earth). By collecting and analyzing health, activity and microbiome data from the astronauts we aim to build a set of models and recommendations facilitating future space missions and long-term human activity outside of Earth. This project is also a promising avenue for future Digital Twins development.

Sinonasal microbiome We analyze longitudinal sinonasal microbiome data from healthy individuals and patients with chronic rhinosinusitis (CRS) to evaluate the effects of off-target systemic antibiotic use. We study changes in taxonomic composition, dysbiosis risk, and the spread of antibiotic resistance, aiming to assess the sinonasal cavity as a reservoir for resistant organisms. The result of this project is likely to change the current clinical practice regarding the use of antibiotics in CRS. The project is done in collaboration with the [Jagiellonian University Medical College](#).

The gut-brain axis in neurological and psychiatric disorders We investigate functional amyloid proteins produced by gut bacteria and their potential roles in neurological disorders. Our analyses focus on their bioinformatic identification and on potential mechanistic links to diseases such as Parkinson's or Alzheimer's, offering a microbiome-centric perspective on the gut-brain axis and neurodegeneration. We are also expanding our efforts to other neurological (stroke, glioma, etc.) and psychiatric disorders to develop new analytical tools and insights, which in future could result in multi-system digital twins. This work is done in collaboration with the [Computational Neuroscience team](#).

[Towards products and translation](#)

The SFG team is committed to translating computational microbiome research into tools and frameworks that support biomedical innovation. Our ongoing translational efforts include:

- **Digital Twins for Clinical Prediction** – Development of personalized digital twins of the human gut microbiome that can forecast disease risk, therapy response, or post-intervention microbiome trajectories.
- **Microbiome-Based Biomarkers and Diagnostics** – Identification of robust microbial and protein-level biomarkers with clinical utility, developed in collaboration with medical partners and validated using cohort datasets.
- **Drug Discovery Support Tools** – ML-powered prediction platforms for antibiotic combinations and small molecule effects, tailored for cancer biology and infectious disease applications.
- **Open and Reproducible Infrastructure** – Deployment of scalable and user-friendly bioinformatics pipelines, reference databases, and prediction APIs that can be integrated into biomedical research and clinical decision-support systems.

Through strong clinical collaborations, reproducible tooling, and foundational AI models, we aim to bridge the gap between metagenomic discovery and application by bringing microbiome-based precision medicine closer to clinical reality. The primary industry collaborators of the SFG Team are deep-tech biotechnology companies (e.g. [Human Biome Institute](#), [Sanprobi](#), or [Ardigen](#)) or diagnostics

companies (**Diagnostyka**). The team is also working closely with healthcare professionals to eventually bring change also to the clinical practice, as exemplified by the sinonasal microbiome project.

Extreme-Scale Data and Computing

Research scope and objectives

Computational medicine relies on access to computing and data infrastructures in all aspects - from modelling and simulation, training AI models, verification, validation, uncertainty quantification, to data analysis at any scale, or integration with the continuum of computing and data resources – including local machines, high-performance computing (HPC), cloud, edge and internet-of-things (IoT) devices. This calls for expertise in these diverse computing environments, both in usage, integration, but also in development of new tools and methods that are specifically tailored to medical applications.

Extreme-Scale Data and Computing team research focuses on ever-growing computing and data requirements of medical applications, recently expanded by the development in AI techniques. Also, more traditional physics-based models forming the basis of Virtual Human Twins (VHT) initiative require novel computing techniques and approaches for VVUQ processes, crucial in the regulatory and certification pathways.

Our team brings together experts in cardiovascular modeling, brain imaging, and computing technologists, leading to valuable synergies and results. Further, we collaborate with other Sano teams, where computing demands are growing, in particular with the team focusing on functional and structural genomics. Our focus will continue to be on always improving the quality of research, strengthening collaborations, bringing the technologies to higher TRL levels, and facilitating uptake of the software solutions. Specific projects and research directions are described below.

Research projects and directions

Venous modelling to inform treatment of patients presenting with lower limb thrombosis We developed a transient zero-D model to characterise system-scale blood circulation in the lower limb vasculature – as an extension of the steady-state model, and performed a global sensitivity analysis of the model to identify clinically significant parameters for pressure and flow metrics [20]. Additionally, we developed a 3D CFD model of idealised geometries of vein unifications to investigate local flow [21]. Next steps include sensitivity analysis of the 3D model using HPC infrastructures, and application of the model to the clinical data obtained from the collaborating clinicians. The research on modelling will be further developed in the scope of Thromborisk Doctoral Network, and the translation aspects are carried out within the PRIME grant awarded by the FNP.

Development of Quantitative Models of Cardiac Neuro-Regulation We created a zero-dimensional closed-loop model with left ventricle, and zero-dimensional model of four-chamber heart, and attempted to solve the problem of stiffness of set of ordinary differential equations [22]. Next steps involve sensitivity and uncertainty analysis to reveal parametric interactions and model space, which assist in placing them into the appropriate regime of operation limited by physiological boundaries. Appropriate mechanisms to present results to clinical end-users will be developed and assessed at this stage. Coupled models will be applied to either clinical data sourced from the literature, or to existing data on hypovolemia, as appropriate.

Application of federated learning (FL) to medical data at large scale including: medical image classification and segmentation [31], personal mobile/wearable patient data, NGS genomics data. We

have shown that the FL algorithms can be used for analysis of X-Ray data at large scale [59]. Next steps include application to deep learning-based image translation between various MRI imaging modalities [60], and estimation of microstructural parameters from diffusion MRI.

Performance evaluation, prediction and optimization of medical applications on emerging computing infrastructures We analysed the computing requirements of a range of medical applications and are developing a framework for performance monitoring of containerized applications on HPC infrastructures. Next steps include application of the methodology to the large-scale CFD simulations on supercomputers, and developing the performance models to estimate resource consumption and other performance metrics based on configuration of systems and applications.

Application of cloud-native and big-data technologies for genomics pipelines The goal of this research is to extend the transcriptomics atlas pipeline using cloud and HPC technologies [61]. The cloud-native architecture allows us to build the pipeline in a scalable and robust manner, but the complexity of cloud infrastructures makes it hard to optimize the time- and cost-efficiency of the resulting solution [62]. This calls to a methodology for experimental evaluation of various architectural patterns and configuration options, which can be generic and applied to a wide class of large-scale genomics data analysis pipelines. We are exploring the use cases from transcriptomics and functional genomics, which require large-scale data processing capabilities.

Towards products and translation

The research team also collaborates closely with Scientific Programmers Team and contributes to the development of tools supporting research and development. This includes experience in development of solutions for science automation, such as MEE platform [16], which in the future is planned to be further expanded with the recent advances in agentic AI solutions, where multiple specialised agents collaborate on a common goal, using recent developments in multi-agent AI technologies. The team also applies the serverless computing paradigm to selected problems of medical applications, based on our in-house HPC-Whisk framework [19] for running serverless applications on supercomputers, or CloudVVUQ serverless library for VVUQ pipelines [63]. Next steps involve multi-cloud scenarios via application of Lithops open source framework and Kubernetes-based deployments, and the paths towards HPC-AI-Cloud convergence in computing infrastructures, powered by AI Factories and AI Gigafactories initiatives of EU.

Scientific Programmers Team

While the Scientific Programmers Team is not a research team in its own right, its role is to support the research teams of Sano in facilitating access to large-scale computational resources, and ensuring that these resources are used in an efficient manner in the scope of research projects carried out at Sano. To this end, members of the Scientific Programmers Team have a background in IT, and are experienced with developing and operating customized IT solutions for research – including decision support systems, AI platforms, interfaces for scheduling and monitoring jobs submitted to HPC resources, cloud computing platforms and numerous others.

In operational terms, the Scientific Programmers Team works by assigning its members to specific research teams – in collaboration with their respective leaders – and tasking them with development of IT solutions sought by these teams, as well as with troubleshooting IT-related issues which emerge along the way. This is an ongoing concern, and we envision that it will remain relevant during the period covered by this update of the Sano Research Agenda. Recruitment and assignment of scientific

programmers to research teams will be aligned with the available resources, financial and otherwise, and driven by the requirements expressed by research team leaders.

In addition to assisting researchers in their ongoing work, the Scientific Programmers Team also maintains a range of services provided externally by Sano. This includes prototypes of tools which embody the outcomes of research work, services developed and deployed in collaboration with our external partners (including the Advanced Partners from the Sano Teaming consortium), as well as dedicated computing infrastructures, both in-house and external. Furthermore, the Scientific Programming Team is responsible for maintaining the Sano data storage and publication infrastructure, with Sano currently being onboarded as a full member of the RODBUK consortium (bringing together major academic and research institutions interested in publishing and sharing primary research data).

Further activities for the Scientific Programming Team, in addition to handling the ongoing support tasks described above, include establishment of formalized VVUQ (verification, validation and uncertainty quantification) pipelines, in accordance with the V&V standards published by ASME, as a step towards certification and production deployment of computational models developed at Sano.

Interactions and Synergies between Research Strands

Synergies for a Unified Digital Twin Platform What distinguishes Sano is not only the depth of expertise in each domain, but the **cross-cutting collaboration** between these groups. The **ExC** team ensures all models and AI agents are deployed and scaled efficiently. **MIR** and **CN** bridge simulation and clinical practice through visualisation, imaging, and interface design. **HM**, **CILab** and **SFG** drive the platform's intelligence, incorporating data-driven inference and molecular-level personalization. Together, these teams form a cohesive, integrated research ecosystem capable of delivering **next-generation digital twins** for **cardiovascular**, **neurological**, and **gastroenterological** applications. The collaborative model ensures continuous feedback between domains—where computational insights inform clinical pathways, and real-world clinical use refines simulations and AI. This synergy lays a strong foundation for the **Sano Digital Twin Platform**, positioning it to impact both research and clinical practice on a European and global scale.

Feasibility of the Research Agenda The feasibility of the research agenda is strongly supported by the scientific leadership, advanced infrastructure, and institutional capacity already established at the Sano Centre for Computational Medicine. The project is led by Maciej Malawski, a senior researcher with over two decades of experience in distributed computing, workflow systems, and biomedical applications. His leadership ensures a deep understanding of both the technical and organisational complexities involved in executing interdisciplinary, large-scale research. Sano operates with access to top-tier computing infrastructure, including Cyfronet, one of the largest supercomputing centres in Central Europe, and emerging AI Factories, which provide modern GPU-based systems optimised for both data-driven AI workflows and physics-based simulations. This infrastructure is critical for supporting the demanding compute requirements of digital twins. The Centre has assembled a highly competent and synergistic group of research teams, covering key domains such as biomedical modelling, AI, visualization, and HPC. These scientific groups are supported by strong software development, DevOps, and UI/UX design teams, ensuring the robust engineering and usability of research outputs. Crucially, Sano also houses a dedicated business development and translation team, which actively cultivates partnerships with industry stakeholders and clinical institutions. These connections are vital for ensuring that digital twin technologies move beyond research into practical, real-world deployment. Ongoing collaborations with industry partners position the Centre at the forefront of innovation and technology transfer in medical computing. Altogether, the combination of strong leadership, mature infrastructure, interdisciplinary expertise, and a strategic focus on commercialisation makes the successful implementation of this research agenda not only feasible but exceptionally well-supported.

Summary

Mission & Objectives Sano's mission is to develop advanced computational methods for disease prevention, diagnosis, and treatment, aiming to become a leading Centre for Computational Medicine in Europe. The objectives focus on:

- Academic excellence in computational medicine,
- Translating research into innovative products and services,
- Providing specialized education and training,
- Advancing digital health and care,
- Fostering entrepreneurship within the Centre.

International Positioning Sano distinguishes itself by integrating simulation, AI, and digital health innovation, collaborating with leading institutions (e.g., INSIGNEO, VPH Institute), and focusing on software-driven solutions that bridge academia, industry, and clinical practice.

Research Agenda & Global Healthcare Challenges The agenda addresses the digital transformation of healthcare, emphasizing the need for computational medicine due to the complexity and volume of medical data. Sano aims to unify health data into a comprehensive digital model (the "Virtual Human Twin"), leveraging data science, simulation, and AI to improve healthcare outcomes and quality of life.

Computations for Individualised Medicine A major focus is on **digital twins**—virtual models of biological systems for personalized medicine. Sano combines physics-based simulations with AI/data-driven approaches, targeting three clinical domains: **(1)** Cardiovascular diseases, **(2)** Neurological disorders, **(3)** Gastrointestinal conditions, and their interactions (e.g., heart-brain-gut axis). Sano is deeply involved in European digital twin initiatives and collaborates with clinical and industrial partners to ensure real-world impact.

Strategy for Success & Vision The vision is to develop a robust digital twin platform for assessment, prevention, diagnosis, intervention, and recovery across multiple medical domains. The platform will integrate simulation, AI, and automation, aiming for explainability, trustworthiness, and clinical applicability.

Research Teams & Their Agendas Sano's research is driven by five interdisciplinary teams:

- **Computational Intelligence:** Developing AI systems for continuous learning and tacit knowledge acquisition, focusing on intelligent agents and adaptive spiking neural networks.
- **Medical Imaging and Robotics:** Advancing medical image analysis, surgical simulation, synthetic data generation, and autonomous robotics for diagnostics and therapy.
- **Computational Neuroscience:** Applying computational techniques to model neural processes, focusing on brain imaging, predictive modeling, and neuromorphic AI.
- **Structural and Functional Genomics:** Developing computational methods for microbiome analysis, biomarker discovery, and digital twins for precision medicine.
- **Extreme-Scale Data and Computing:** Providing expertise in HPC, cloud, and big data for medical applications, supporting modeling, simulation, and AI at scale.

Scientific Programmers Team supports all research teams with IT solutions, infrastructure, and software development.

Synergies & Implementation The agenda emphasizes cross-team collaboration to build an integrated digital twin platform, leveraging Sano's leadership, infrastructure, and partnerships for successful implementation and real-world deployment.

Sano's updated research agenda sets a clear direction for advancing computational medicine, focusing on digital twins, interdisciplinary collaboration, and translation of research into clinical and societal impact.

References

1. WHO: Gross domestic R&D expenditure on health (health GERD): <https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/gross-domestic-r-d-expenditure-on-health-as-a-percentage-of-total-gerd-april-2023>
2. Kurt C. Stange: The Annals of Family Medicine March 2009, 7 (2) 100-103; DOI: <https://doi.org/10.1370/afm.971>
3. Peter Coveney and Roger Highfield: Virtual You: How Building Your Digital Twin Will Revolutionize Medicine and Change Your Life Princeton University Press, 2023.
4. WHO: Global Health Estimates Technical Paper WHO/DDI/DNA/GHE/2024.1 <https://www.who.int/publications/m/item/who-methods-and-data-sources-for-life-tables-2000-2021>
5. van Berkel et al. (2022). Human-centred artificial intelligence: a contextual morality perspective. Behaviour & Information Technology, 41(3), 502-518. <https://doi.org/10.1080/0144929X.2020.1818828>
6. Carriço, G. (2018). The EU and artificial intelligence: A human-centred perspective. European View, 17(1), 29-36. <https://doi.org/10.1177/1781685818764821>
7. EDITH consortium, Geris, L., Morley-Fletcher, E., Raouzaïou, A., & Mellone, S. (2025). EDITH VHT roadmap. Zenodo. <https://doi.org/10.5281/zenodo.14645647>
8. Morris, P, van de Vosse, F, Lawford, P. et al. "Virtual" (Computed) Fractional Flow Reserve: Current Challenges and Limitations. J Am Coll Cardiol Intv. 2015 Jul, 8 (8) 1009–1017. <https://doi.org/10.1016/j.jcin.2015.04.006>
9. Marco Viceconti, Luca Emili (eds.) Toward Good Simulation Practice, Springer 2024, <https://doi.org/10.1007/978-3-031-48284-7>
10. M. Raissi, P. Perdikaris, G.E. Karniadakis, Physics-informed neural networks: A deep learning framework for solving forward and inverse problems involving nonlinear partial differential equations, Journal of Computational Physics, Volume 378, 2019, Pages 686-707, <https://doi.org/10.1016/j.jcp.2018.10.045>
11. Peng, G.C.Y., Alber, M., Buganza Tepole, A. et al. Multiscale Modeling Meets Machine Learning: What Can We Learn?. Arch Computat Methods Eng 28, 1017–1037 (2021). <https://doi.org/10.1007/s11831-020-09405-5>
12. Emeran A. Mayer, Karina Nance and Shelley Chen: The Gut–Brain Axis; Annual Review of Medicine, Vol. 73:439-453, pp. 439–453 (15) <https://doi.org/10.1146/annurev-med-042320-014032>
13. Chavira, A., Belda-Ferre, P., Kosciolk, T., Ali, F., Dorrestein, P.C., Knight, R. (2019). The Microbiome and Its Potential for Pharmacology. In: Barrett, J., Page, C., Michel, M. (eds) Concepts and Principles of Pharmacology. Handbook of Experimental Pharmacology, vol 260. Springer, Cham. https://doi.org/10.1007/164_2019_317
14. Goel, Ashok K. 2021. "Looking back, looking ahead: Symbolic versus connectionist AI." AI Magazine 42: 83–85. <https://doi.org/10.1609/aaai.12026>
15. Maciej Malawski, Adam Gajek, Adam Zima, Bartosz Balis, Kamil Figiela: Serverless execution of scientific workflows: Experiments with HyperFlow, AWS Lambda and Google Cloud Functions, Future Generation Computer Systems, Volume 110, 2020, Pages 502-514, <https://doi.org/10.1016/j.future.2017.10.029>
16. Kasztelnik, M. et al. (2023). Digital Twin Simulation Development and Execution on HPC Infrastructures. In: Mikyška, J., de Mulatier, C., Paszynski, M., Krzhizhanovskaya, V.V., Dongarra, J.J., Sloot, P.M. (eds) Computational Science – ICCS 2023. ICCS 2023. Lecture Notes in Computer Science, vol 14074. Springer, Cham. https://doi.org/10.1007/978-3-031-36021-3_2

17. M. Malawski and B. Balis, "Serverless Computing for Scientific Applications," in IEEE Internet Computing, vol. 26, no. 4, pp. 53-58, 1 July-Aug. 2022 <https://doi.org/10.1109/MIC.2022.3168810>
18. K. Burkat et al., "Serverless Containers – Rising Viable Approach to Scientific Workflows," 2021 IEEE 17th International Conference on eScience (eScience), Innsbruck, Austria, 2021, pp. 40-49 <https://doi.org/10.1109/eScience51609.2021.00014>
19. B. Przybylski, M. Pawlik, P. Żuk, B. Lagosz, M. Malawski and K. Rządca, "Using Unused: Non-Invasive Dynamic FaaS Infrastructure with HPC-Whisk," SC22: International Conference for High Performance Computing, Networking, Storage and Analysis, Dallas, TX, USA, 2022, pp. 1-15, <https://doi.org/10.1109/SC41404.2022.00045>
20. Otta, M., Halliday, I., Tsui, J., Lim, C., Struzik, Z.R., Narracott, A. (2022). Sensitivity Analysis of a Model of Lower Limb Haemodynamics. In: Groen, D., de Mulatier, C., Paszynski, M., Krzhizhanovskaya, V.V., Dongarra, J.J., Sloat, P.M.A. (eds) Computational Science – ICCS 2022. ICCS 2022. Lecture Notes in Computer Science, vol 13352. Springer, Cham. https://doi.org/10.1007/978-3-031-08757-8_7
21. Otta, M. et al. (2025). Towards Sensitivity Analysis: 3D Venous Modelling in the Lower Limb. In: Paszynski, M., Barnard, A.S., Zhang, Y.J. (eds) Computational Science – ICCS 2025 Workshops. ICCS 2025. Lecture Notes in Computer Science, vol 15908. Springer, Cham. https://doi.org/10.1007/978-3-031-97557-8_8
22. Tlałka K, Saxton H, Halliday I, Xu X, Narracott A, et al. (2024) Sensitivity analysis of closed-loop one-chamber and four-chamber models with baroreflex. PLOS Computational Biology 20(12): e1012377. <https://doi.org/10.1371/journal.pcbi.1012377>
23. P. Korzeniowski, S. Płotka, R. Brawura-Biskupski-Samaha and A. Sitek, "Virtual Reality Simulator for Fetoscopic Spina Bifida Repair Surgery," 2022 IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS), Kyoto, Japan, 2022, pp. 401-406, <https://doi.org/10.1109/IROS47612.2022.9981920>
24. Szymon Płotka, Karol Pustelnik, Paula Szenejko, Kinga Żebrowska, Iga Rzucidło-Szymańska, Natalia Szymecka-Samaha, Tomasz Łęgowik, Katarzyna Kosińska-Kaczyńska, Przemysław Korzeniowski, Piotr Biliński, Asma Khalil, Robert Brawura-Biskupski-Samaha, Ivana Išgum, Clara I. Sánchez, Arkadiusz Sitek: Direct estimation of fetal biometry measurements from ultrasound video scans through deep learning, American Journal of Obstetrics & Gynecology MFM, Volume 7, Issue 4, 2025, 101623, <https://doi.org/10.1016/j.ajogmf.2025.101623>
25. Falcó-Roget, J., Cacciola, A., Sambataro, F. et al. Functional and structural reorganization in brain tumors: a machine learning approach using desynchronized functional oscillations. Commun Biol 7, 419 (2024). <https://doi.org/10.1038/s42003-024-06119-3>
26. Drożdż A, Duggan B, Ruddock MW, Reid CN, Kurth MJ, Watt J, Irvine A, Lamont J, Fitzgerald P, O'Rourke D, Curry D, Evans M, Boyd R and Sousa J (2024) Stratifying risk of disease in haematuria patients using machine learning techniques to improve diagnostics. Front. Oncol. 14:1401071. <https://doi.org/10.3389/fonc.2024.1401071>
27. Grzeszczyk, M.K., Korzeniowski, P., Alabed, S., Swift, A.J., Trzciński, T., Sitek, A. (2024). TabMixer: Noninvasive Estimation of the Mean Pulmonary Artery Pressure via Imaging and Tabular Data Mixing. In: Linguraru, M.G., et al. Medical Image Computing and Computer Assisted Intervention – MICCAI 2024. MICCAI 2024. Lecture Notes in Computer Science, vol 15005. Springer, Cham. https://doi.org/10.1007/978-3-031-72086-4_63
28. S. Martyniak, J. Kaleta, D. Dall'Alba, M. Naskręt, S. Płotka and P. Korzeniowski, "SimuScope: Realistic Endoscopic Synthetic Dataset Generation Through Surgical Simulation and Diffusion Models," 2025 IEEE/CVF Winter Conference on Applications of Computer Vision (WACV), Tucson, AZ, USA, 2025, pp. 4268-4278, <https://doi.org/10.1109/WACV61041.2025.00419>
29. Luca Gherardini, Aleksandra Zajdel, Lorenzo Pini, Alessandro Crimi, Prediction of misfolded proteins spreading in Alzheimer's disease using machine learning and spreading models, Cerebral Cortex, Volume 33, Issue 24, 15 December 2023, Pages 11471–11485, <https://doi.org/10.1093/cercor/bhad380>

30. Alfredo Ibias, Varun Ravi Varma, Karol Capała, Luca Gherardini, Jose Sousa, SaNDA: A small and incomplete dataset analyser, *Information Sciences*, Volume 640, 2023, 119078, <https://doi.org/10.1016/j.ins.2023.119078>
31. Dominika Ciupek, Maciej Malawski, Tomasz Pieciak: Federated Learning: A new frontier in the exploration of multi-institutional medical imaging data, 2025 <https://arxiv.org/abs/2503.20107>
32. Koehler Leman, J., Szczerbiak, P., Renfrew, P.D. et al. Sequence-structure-function relationships in the microbial protein universe. *Nat Commun* 14, 2351 (2023). <https://doi.org/10.1038/s41467-023-37896-w>
33. Piotr Nowakowski, Marian Bubak, Tomasz Bartyński, Tomasz Gubała, Daniel Haręźlak, Marek Kasztelnik, Maciej Malawski, Jan Meizner, Cloud computing infrastructure for the VPH community, *Journal of Computational Science*, Volume 24, 2018, Pages 169-179, <https://doi.org/10.1016/j.jocs.2017.06.012>
34. Taras Zhyhulin et al. Seamless Integration of Data Sharing Repositories with High-Performance Computing Simulation Platform, CS3 2024 - Cloud Storage Synchronization and Sharing, CERN 2024, <https://indico.cern.ch/event/1332413/contributions/5748280>
35. Girijesh Prasad: Comparing AI agent frameworks: CrewAI, LangGraph, and BeeAI, IBM, 2025, <https://developer.ibm.com/articles/awb-comparing-ai-agent-frameworks-crewai-langgraph-and-beeai/>
36. Moritz, M., Topol, E. & Rajpurkar, P. Coordinated AI agents for advancing healthcare. *Nat. Biomed. Eng* 9, 432–438 (2025). <https://doi.org/10.1038/s41551-025-01363-2>
37. Natalia Lipp, Paweł Strojny, Agnieszka Strojny, Sławomir Śpiewak, Jan K. Argasiński, and Przemysław Korzeniowski. 2023. Performing Tasks in Virtual Reality. Interplay between Realism and Visual Imagery. In *Proceedings of the 29th ACM Symposium on Virtual Reality Software and Technology (VRST '23)*. Association for Computing Machinery, New York, NY, USA, Article 70, 1–2. <https://doi.org/10.1145/3611659.3617221>
38. Jan K. Argasiński and Natalia Lipp. 2023. Enhancing VR Based Serious Games and Simulations Design: Bayesian Knowledge Tracing and Pattern-Based Approaches. In *Proceedings of the 29th ACM Symposium on Virtual Reality Software and Technology (VRST '23)*. Association for Computing Machinery, New York, NY, USA, Article 58, 1–2. <https://doi.org/10.1145/3611659.3616900>
39. M. Wójcikowski, D. Dall'Alba, S. Martyniaki, R. Szydłak, P. Walecki, A. A. Kononowicz, P. Korzeniowski: Preliminary Evaluation of Virtual Reality Simulator for Surgery Training in International Medical Students, *Krakow Conference on Computational Medicine 2025*, https://events.plgrid.pl/event/89/contributions/745/attachments/195/440/VRSR_for_Marian_2.pdf
40. D. Dall'Alba, M. Naskręt, S. Kamińska and P. Korzeniowski, "FF-SRL: High Performance GPU-Based Surgical Simulation For Robot Learning," 2024 *IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS)*, Abu Dhabi, United Arab Emirates, 2024, pp. 8378-8384, <https://doi.org/10.1109/IROS58592.2024.10801658>
41. Peter V Coveney and Roger Highfield: Artificial Intelligence Must Be Made More Scientific; *Journal of Chemical Information and Modeling* 2024 64 (15), 5739-5741 <https://doi.org/10.1021/acs.jcim.4c01091>
42. M. Sarabian, H. Babae and K. Laksari, "Physics-Informed Neural Networks for Brain Hemodynamic Predictions Using Medical Imaging," in *IEEE Transactions on Medical Imaging*, vol. 41, no. 9, pp. 2285-2303, Sept. 2022, <https://doi.org/10.1109/TMI.2022.3161653>
43. Luca Gherardini, Varun Ravi Varma, Karol Capała, Roger Woods, and Jose Sousa. 2024. CACTUS: A Comprehensive Abstraction and Classification Tool for Uncovering Structures. *ACM Trans. Intell. Syst. Technol.* 15, 3, Article 46 (June 2024), 23 pages. <https://doi.org/10.1145/3649459>
44. Robert Earl Patterson, Byron J. Pierce, Herbert H. Bell, and Gary Klein. 2010. Implicit Learning, Tacit Knowledge, Expertise Development, and Naturalistic Decision Making. *J. Cogn. Eng. Decis. Mak.* 4, 4 (2010), 289–303. <https://doi.org/10.1177/155534341000400403>

45. H Schuster. 2001. Complex adaptive systems. Springer (2001). Retrieved from <http://www.springerlink.com/index/lh66341k2j378421.pdf>
46. Zhuoya Zhao, Feifei Zhao, Yuxuan Zhao, Yi Zeng, and Yinqian Sun. 2023. A brain-inspired theory of mind spiking neural network improves multi-agent cooperation and competition. *Patterns* 4, 8 (2023), 100775. <https://doi.org/10.1016/j.patter.2023.100775>
47. Thomas L. Griffiths. 2020. Understanding Human Intelligence through Human Limitations. *Trends Cogn. Sci.* 24, 11 (2020), 873–883. <https://doi.org/10.1016/j.tics.2020.09.001>
48. Brenden M. Lake, Tomer D. Ullman, Joshua B. Tenenbaum, and Samuel J. Gershman. 2017. Building machines that learn and think like people. *Behav Brain Sci* 40, (2017), e253. <https://doi.org/10.1017/s0140525x16001837>
49. Joshua B. Tenenbaum, Charles Kemp, Thomas L. Griffiths, and Noah D. Goodman. 2011. How to Grow a Mind: Statistics, Structure, and Abstraction. *Science* 331, 6022 (2011), 1279–1285. <https://doi.org/10.1126/science.1192788>
50. K. Capala, P. Tworek and J. Sousa, "Stability of Machine Learning Predictive Features Under Limited Data" in *IEEE Transactions on Knowledge & Data Engineering*, vol. 37, no. 09, pp. 5627-5638, Sept. 2025 <https://doi.ieeecomputersociety.org/10.1109/TKDE.2025.3580671>
51. Zoubin Ghahramani. 2015. Probabilistic machine learning and artificial intelligence. *Nature* 521, 7553 (May 2015), 452–459. <https://doi.org/10.1038/nature14541>
52. Philipp Körner, Michael Leuschel, João Barbosa, Vítor Santos Costa, Verónica Dahl, Manuel V Hermenegildo, Jose F Morales, Jan Wielemaker, Daniel Diaz, Salvador Abreu, and Giovanni Ciatto. 2022. Fifty Years of Prolog and Beyond. *Theory Pr. Log. Program.* 22, 6 (2022), 776–858. <https://doi.org/10.1017/s1471068422000102>
53. Osvaldo Cairó Battistutti and Dominik Bork. 2017. Tacit to explicit knowledge conversion. *Cogn. Process.* 18, 4 (2017), 461–477. <https://doi.org/10.1007/s10339-017-0825-6>
54. Nardi Lam. 2022. Explanations in AI as Claims of Tacit Knowledge. *Mind Mach* 32, 1 (2022), 135–158. <https://doi.org/10.1007/s11023-021-09588-1>
55. Arne Traulsen and Nikoleta E. Glynatsi. 2023. The future of theoretical evolutionary game theory. *Philos. Trans. R. Soc. B* 378, 1876 (2023), 20210508. <https://doi.org/10.1098/rstb.2021.0508>
56. Nicolas Bougie, Takashi Onishi, and Yoshimasa Tsuruoka. 2023. Interpretable Imitation Learning with Symbolic Rewards. *ACM Trans. Intell. Syst. Technol.* 15, 1 (2023), 1–34. <https://doi.org/10.1145/3627822>
57. Kingson Man, Antonio Damasio, and Hartmut Neven. 2022. Need is All You Need: Homeostatic Neural Networks Adapt to Concept Shift. *Arxiv* (2022). <https://arxiv.org/abs/2205.08645>
58. Fan Ouyang, Weiqi Xu, and Mutlu Cukurova. 2023. An artificial intelligence-driven learning analytics method to examine the collaborative problem-solving process from the complex adaptive systems perspective. *Int. J. Comput.-Support. Collab. Learn.* 18, 1 (2023), 39–66. <https://doi.org/10.1007/s11412-023-09387-z>
59. Filip Ślęzyk, Przemysław Jabłocki, Aneta Lisowska, Maciej Malawski, and Szymon Płotka. 2022. CXR-FL: Deep Learning-Based Chest X-ray Image Analysis Using Federated Learning. In *Computational Science – ICCS 2022: 22nd International Conference, London, UK, June 21–23, 2022, Proceedings, Part II*. Springer-Verlag, Berlin, Heidelberg, 433–440. https://doi.org/10.1007/978-3-031-08754-7_50
60. J. Fiszer, D. Ciupek, M. Malawski, T. Pięciak., Federated image-to-image MRI translation from heterogeneous multiple-sites data, 2024 ISMRM & ISMRT Annual Meeting & Exhibition. <https://archive.ismrm.org/2024/2221.html>
61. Jonathan Bader et al. 2023. Novel Approaches Toward Scalable Composable Workflows in Hyper-Heterogeneous Computing Environments. In *Proceedings of the SC '23 Workshops of the International Conference on High Performance Computing, Network, Storage, and Analysis (SC-W '23)*. Association for Computing Machinery, New York, NY, USA, 2097–2108. <https://doi.org/10.1145/3624062.3626283>

62. P. Kica, S. Lichołaj, M. Orzechowski and M. Malawski, "Optimizing Star Aligner for High Throughput Computing in the Cloud," 2024 IEEE International Conference on Cluster Computing Workshops (CLUSTER Workshops), Kobe, Japan, 2024, pp. 162-163 <https://doi.org/10.1109/CLUSTERWorkshops61563.2024.00039>
63. P. Kica et al., "Serverless Approach to Sensitivity Analysis of Computational Models," 2023 IEEE/ACM 23rd International Symposium on Cluster, Cloud and Internet Computing (CCGrid), Bangalore, India, 2023, pp. 627-639, <https://doi.org/10.1109/CCGrid57682.2023.00064>

**Sano
Centre
for Computational
Personalised
Medicine
International
Research
Foundation**

**Research
Agenda
2025-2028**

ISBN 978-83-976637-1-8

