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Image: Firefly

Helmholtz Biomedical Engineering

Turning world class Science into Health Solutions

White Paper
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"The past century has been the Age of Physics, followed by the Information Age, where we saw vast engineering contributions to the mapping and control of our external world, from the creation of computer disks to GPS and the prospect of self-driving cars. This century will be about engineering our internal world: mapping, controlling, and engineering genes, tissues, organ systems, and ultimately the human brain. As engineers, we take pride in our role as the creators of disruptive technologies - technologies that will change the future of not only biology, but of medicine as well." [1]

[1] Michael I. Miller (director of the Johns Hopkins, Department of Bioengineering) at the BMES Annual Meeting in 2017

Summary

In the next decades, society will face escalating challenges caused by an increasing prevalence of cancer, cardiovascular, neurological, metabolic, and other chronic diseases, coupled with an aging global population[2]. Overcoming these challenges requires a paradigm shift in healthcare, with a greater emphasis on early disease prediction, prevention, new diagnostics and more precise and personalized medicine. To catalyze this transformation, there is a pressing need to create a new generation of scientists with a solution-driven, problem-solving mindset - complementing discovery-focused researchers - that will accelerate the translation of biological knowledge into cost-effective and safe solutions for the patient. Similarly to how electrical and mechanical engineers catalyze discoveries in physics into applications, it is vitally important to invest in biomedical engineering as a discipline and integrate bioengineers into interdisciplinary teams that invent new tools by integrating expertise in natural sciences, computation, biology and medicine.

The United States, United Kingdom, China, Switzerland are examples of countries that have recognized and actively promoted a 'bioengineering revolution' with programs and increased funding for biotech ventures. In stark contrast, the European Union, particularly Germany, lags behind in applying and transfering its rich engineering culture into the life sciences, thus delaying societal and economic benefit.

This white paper advocates for a biomedical engineering-driven cultural and educational shift. It calls for the seamless integration of academic knowledge creation with a solution and translation orientated culture to deliver high societal impact. The authors propose a vision for how 'Helmholtz Biomedical Engineering' can be an engine to drive the creation of pioneering biotechnological concepts and breakthrough solutions. The paper highlights structural challenges that need to be addressed, flagship solution-orientated concepts that could be driven from within interdisciplinary organizations such as Helmholtz and the support measures required. Supported by appropriate funding and incentive structures, along with a renewed acceptance of high-risk venture investments, the authors anticipate substantial progress in creating the healthcare companies and economy of the future leading to key benefits for patients and healthcare systems. This transformative initiative aims to leverage expertise and infrastructure within the Helmholtz Association to position Germany and Europe as leaders in bio-innovative technology, solutions, and enterprise building, drawing parallels with their distinguished legacy as global leaders in engineering and tool making.

[2] https://ourworldindata.org/burden-of-disease

Definition of Helmholtz Biomedical Engineering

We define Biomedical Engineering as the installment of a solution-driven and problem-solving culture in the life sciences[3] (Fig.1), i.e. the development of concepts, methods and tools that transform discovery into biomedical solutions. This definition moves away from the concept of multi-disciplinary research (Fig.1a) and instead identifies two scientific cultures, one focusing on discovery and one focusing on translation (Fig.1b), in analogy to classical engineering that converts discoveries made in the physical sciences to efficient societal solutions. Biomedical engineering plays the same role in the life sciences, i.e. it accelerates the conversion of discoveries into solutions, serving and facilitating the actual purpose of 'science translation'.

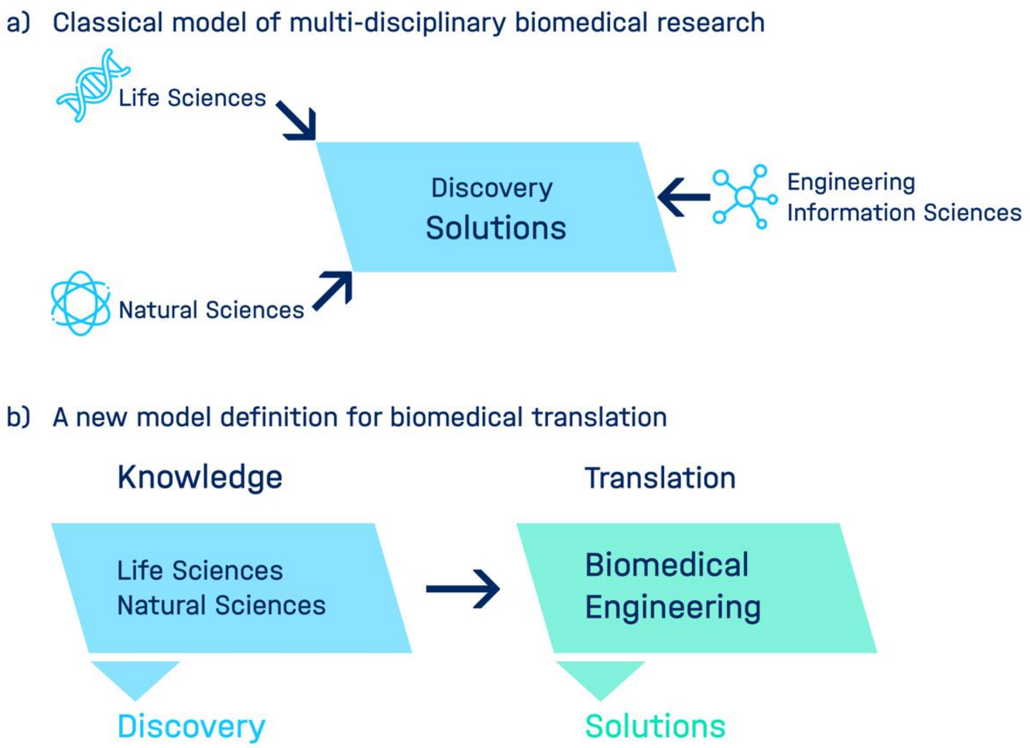


Fig. 1 | Biomedical Engineering as the driving force of translation.
a) Multidisciplinary research denotes the synergy of different skills, typically resulting in accelerating discovery, i.e. reaching new knowledge. However, accelerated discovery does not automatically convert to solutions for the patient.
b) Transformation of knowledge to solutions requires a different model than multidisciplinary research, in which attention is given to a problem-definition and combinatorial problem-solving engineering culture, as a secondary pillar next to discovery. Biomedical Engineering and classical engineering can develop the methods and tools required to accelerate the conversion of knowledge to efficient solutions. (modified from Nature Reviews Bioengineering 1:154 2023)

[3] https://www.nature.com/articles/s44222-022-00015-3

Similar to the division of classical engineering into multiple subdisciplines (i.e. mechanical, electrical, civil engineering etc.), biomedical engineering similarly encompasses different areas, including biomedical imaging, molecular omic technologies, protein- cell- and tissue-engineering, organoid and organs-on-a-chip technologies, biomaterials, implants, as well as medical devices and radiation therapy technology, biomedical signal processing or clinical engineering. While this paper primarily concentrates on bioengineering for healthcare, the authors acknowledge that bioengineering principles are equally crucial in other domains, for example in accelerating biological discovery, sustainable agriculture & energy production, protecting global biodiversity and health as well as addressing climate change. This expanded scope underscores the interdisciplinary and transformative potential of Helmholtz Biomedical Engineering, leveraging cutting-edge technology and research to foster sustainable solutions to improve global health.

Motivation for a Helmholtz Biomedical Engineering Agenda

The mission of the Helmholtz Association is to contribute to solving the grand challenges facing society, science and the economy. As the largest research organization in Germany, Helmholtz is well placed to adopt and leverage the potential of bioengineering to expedite the transformation of biology-inspired technologies into the marketable products required to create a healthier society. By drawing on multi-disciplinary expertise and infrastructure across all Helmholtz Research Centers in six research fields: Health, Information, Matter, Energy, Earth and Environment, and Aeronautics, Space & Transport, the Helmholtz Association provides a unique environment to address several structural challenges and drive the 'Biomedical engineering revolution' in Germany and to rapidly become a leader on the global stage.

Accelerating the translation of discoveries into solutions

The last decade has seen technological innovations that continue to revolutionize biology and medicine[4]. These new technologies are rapidly generating new knowledge and massive amounts of diverse molecular, imaging and health-related data. Nevertheless, the rapid accumulation of knowledge does not automatically translate into benefits for patients. Developing innovative solutions through efficient translation requires a strong solution-driven and problem-solving culture to complement the culture of discovery in biomedical sciences. Fostering such a culture

[4] https://www.nature.com/articles/s41591-022-02104-7
https://www.nature.com/articles/d42473-022-00215-w
https://www.nature.com/articles/s41591-022-02160-z

goes beyond collaborations between scientists, clinicians and business innovators and nessitates the development of transdisciplinary solution-driven professionals, i.e. bioengineers trained in both engineering and biology, with the skill-set required to invent new tools for impactful prevention strategies, early detection technologies or developing more precise and effective therapeutics. With its broad research portfolio and network covering the innovation chain, the Helmholtz Association is a fertile ground for connecting key expertise and leveraging bioengineering to drive the conversion of knowledge into healthcare innovations and amplify new economy-generating engineering into the life sciences.

Overcoming the investment gap

The US is the global leader in biotech funding, attracting 35% of global biotech investments in 2023 (about $56.7 billion), followed by China (12.7%; $20.6 billion) and Europe with only 7% totaling $11.4 billion. Of note, the Chinese biotech sector secured larger funding rounds, with the 20.6 billion distributed between only 69 firms, while US- and European- investments benefited 583 and 229 companies, respectively[5]. Although German venture investments reached a record high in 2021 ($16.5 billion total, of which according to an EY report roughly 25% accounts for Health and Life-sciences), this only amounts to ~5% and 15% of investments seen in the US and Europe during the same period[6]. To further illustrate the scale of the transatlantic investment gap, in 2021 Europe, with a population of ~746.4 million, attracted a similar amount of venture capital as California with a population of ~39.5 million). An analysis into German investments paints a more alarming picture: with the German startup ecosystem being much younger than that in the US, investors focus on early phases meaning they often lose out on growth capital. This void is often filled with global capital and has economic consequences, since startups that raise foreign capital often end up moving their operations abroad[7]. Such funding opportunities in internationally desired locations that link to leading research institutions, innovation hubs and other research infrastructures[8] at least partly explains why the US, with its East- and West-coast clusters, continue to produce leading global biomedical and bioengineering innovation and biotech start-ups such as CRISPR therapeutics, Editas Medicine or Ginkgo Bioworks. Accelerated innovation and effective translational structures across all participating centers through Helmholtz Biomedical Engineering has the potential to begin to reshape the entire biotech start-up ecosystem and reduce the investment gap by engaging with angel, institutional and VC investors, at the national, if not the European level.

[5] https://www.drugdiscoverytrends.com/biotech-funding-landscape-2023/
[6] https://www.deutschland-startet.de/venture-capital-rekord-2021/
https://www.ey.com/en_us/growth/venture-capital-activity-in-the-second-half-of-2021
[7] https://pitchbook.com/news/articles/foreign-investors-tapping-into-germanys-late-stage-vc-boom
[8] https://www.nature.com/articles/d41586-022-02885-4

Building a bright future for innovation and job creation

US initiatives can serve as blueprints for effective instruments and measures to fuel a succesful Bioengineering agenda. Similarly, in December 2023, the UK Government revealed a national vision for engineering biology as a measure to create economic value, security, resilience, and preparedness. A complementary Helmholtz Biomedical Engineering program has the potential to stimulate innovation and boost local and national job creation in Germany, with the employment of trained bioengineers projected to grow six percent from 2020 to 2030[9], adding much sought-after entrepreneurs and innovators to an emerging bioengineering ecosystem that promises to shape the future of biology and medicine.

Helmholtz Biomedical Engineering workshop

A recent Helmholtz Biomedical Engineering workshop attended by 36 top-level scientists and administrators representing nine out of 18 Helmholtz Centers, revealed advanced research activities within the Helmholtz Centers and opportunities to shape a comprehensive 'Biomedical engineering agenda' for rapid and sustained health solutions. A task force was assembled to develop a strategy for how Helmholtz Biomedical Engineering could leverage expertise and research outputs within the Helmholtz Association to accelerate the translation of discoveries into globally impactful solutions. This white paper provides several recommendations to initiate a national 'Biomedical engineering revolution' that matches the productivity, precision, and global reputation of 'German engineering.' In essence, Helmholtz Biomedical Engineering seeks to create the tools and preventive, diagnostic, or therapeutic solutions and corresponding businesses to propel Germany into a globally leading position in ‘engineering biology and medicine for future health’.

[9] https://www.bls.gov/ooh/architecture-and-engineering/biomedical-engineers.htm

Societal Impact, Applications and Solutions

The mission of Helmholtz Biomedical Engineering is to pioneer solutions that improve health. It focuses on creating innovative technologies for novel observations, analytics and validation and which provide new opportunities to develop advanced diagnostic, theranostic and treatment approaches. By pushing the boundaries of interdisciplinary innovation, Helmholtz Biomedical Engineering aims to operate along the entire translational pipeline, spanning early and late technology readiness levels, from building new knowledge of biological systems, creating and validating prototypes to clinical studies of earlier detection, precise prevention and improved therapy strategies.

To fulfill this mission, the Task Force has identified six forward-looking, solution-orientated flagship concepts, based on research expertise available within the Helmholtz Centers. The appendix showcases a compilation of visible and published use cases for each flagship within the Helmholtz Association. The outlined flagships, together with the proposed measures described in detail in the next chapter, will not only promote the remarkable expertise within the Helmholtz Association, but also facilitate rapid progress and position Germany at the forefront of bioengineering.

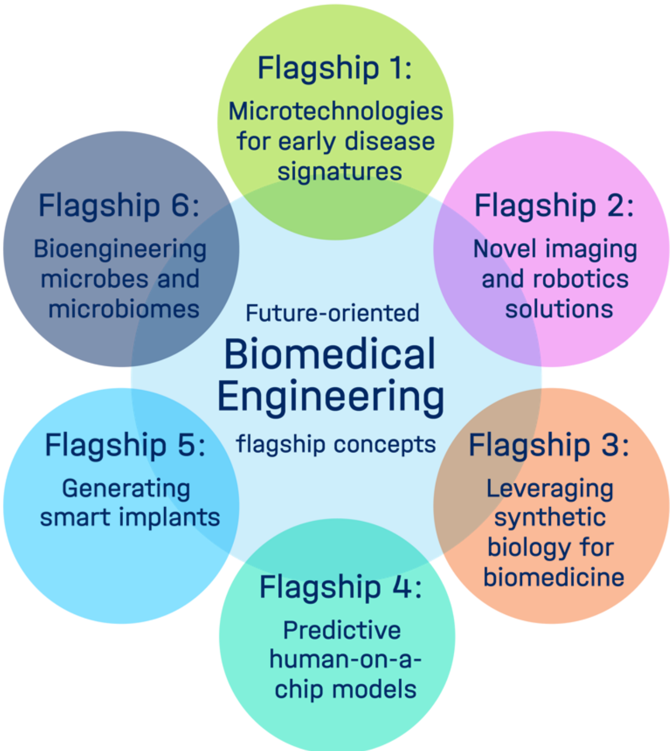
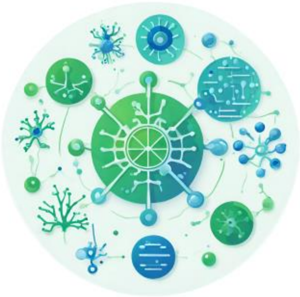


Fig. 2 | Future-oriented Biomedical Engineering flagship concepts within the Helmholtz Association.
The Task Force has identified six solution-oriented Flagship concepts that leverage the research capabilities available across the Helmholtz Centers. These outlined flagships, supported by several use cases (see appendix), aim not only to highlight the remarkable expertise within the Helmholtz Association, but also to significantly accelerate progress and position Germany at the forefront of bioengineering.

Flagship concept 1 – Micro- and nanotechnologies for early disease signatures



Develop micro and nanotechnologies for the discovery and detection of early disease signatures

Relevance

Increasing incidences of chronic diseases associated with an aging society requires new strategies for early detection that enable precise treatment of the underlying cause.

Challenge

A key challenge is developing sensitive and precise diagnostics that detect diseases or relapse much earlier than is currently possible, potentially before clinical symptoms occur, and guiding therapeutic intervention before disease progression. Innovative biomedical technologies, materials, nanotechnologies, AI, molecular, spatial and single-cell multi-omics together with the human disease models are making it possible to study diseases at unprecedented resolution. The next leap is to scale these technologies using bioengineering approaches such as micro- and nanofabricated systems and microfluidic platforms, microarrays and sensors - to create scalable and cost-effective diagnostic platforms for population, patient subpopulations or cohorts of patient-derived human disease models (Flagship 4). Discovery of the information-rich and multi-modal signatures, biomarkers and rare pathological cell sub-populations in a diverse biological contexts will lay the foundation for new diagnostic strategies for early disease detection. Translating these discoveries into new diagnostic devices will again require bioengineering approaches to create flexible multiplexed platforms, employing microfluidics, paper or wearables in concert with engineered biomolecules (Flagship 3) to rapidly and cost-effectively detect biomarkers in a clinical setting. The success of these endeavors hinges on interdisciplinary collaboration, bridging the gap between molecular biology, AI and data science, and engineering to translate these high-resolution diagnostic technologies from the lab bench to clinical application.

Role of Helmholtz

Helmholtz researchers are well positioned to work together to identify disease signatures and biomarkers and engineer new diagnostic technologies for their detection. They are at the forefront of developing and scaling single-cell and spatial technologies, imaging and AI-based analyses. Several hold patents in CRISPR-based diagnostics and a spin-off, Leopard Biosciences has been founded based on the LEOPARD technology developed at Helmholtz for multiplexed molecular diagnostics at the point-of-care. Across the research fields, there is also strong expertise in portable optical and electronic biosensors and lab-on-a-chip technologies with the potential to be used towards digital health.

Impact and deliverable

Scalable microtechnologies will facilitate new tools and solutions to address key societal health challenges such as the early detection of cardiovascular disease, cancer, dementia, diabetes, and infectious diseases as well as complex multi-organ diseases. These will enable the identification of potential strategies for primary disease prevention and the monitoring of disease progression or treatment response. Ultimately, this approach will enable a switch from reacting to diseases to proactively detecting them before they progress, thereby increasing an individual's health span and leading to a healthier society.

Flagship concept 2 – Novel imaging and robotics solutions

Develop novel medical imaging and robotics solutions for advanced diagnostic, theranostic and treatment methods

Relevance

Technology advancements such as imaging hardware, novel biosensors and contrast agents in conjunction with surgical robots open entirely new opportunities to track disease location and progression much earlier and more precisely as well as to determine the most effective interventions. AI-based integration of imaging, multi-omics and robotic technologies enables diagnostic, in-treatment and theranostic monitoring of a variety of diseases in real-time and in a minimally-invasive manner, allowing disease-related abnormalities to be addressed at an earlier stage to improve quality of life and achieve healthier aging.

Challenge

A key future challenge is the development of clinically informative imaging, sensing, and reaction paradigms that enable the reliable detection of disease onset at the earliest possible time point as well as adaptation during the course of treatment. The revolution in molecular imaging and visualization technologies including biosensors and engineered contrast agents tailored to read specific structure or function from biological systems can reveal a tremendous amount of relevant biological information. Portable or wearable 'live-tracking' capabilities add to the promise of home-based health monitoring through continuous or frequent measurements of disease-related parameters. At the same time, unraveling interdependent mechanisms that contribute to disease and the discovery of unique biomarkers indicative of cure and recovery are pivotal for the design of future devices (Flagship 5). Such molecular, cellular, tissue, metabolic or other parameters (see Flagships 1 and 3) are most effective if delivered to physicians in real time. Thus, multimodal in situ imaging across scales will not only transform the precision characterization of disease location, extent, and histopathological subtype, but also expedite the delivery of best interventions and therapies. Moreover, the application of artificial intelligence and machine learning algorithms incorporated with robotic platforms and novel therapy technology can significantly enhance diagnostic accuracy as well as treatment planning and execution, offering more personalized, adaptive and targeted care. Multiple data streams, including imaging and sensing, can be collated and correlated into a coherent and comprehensive model of individual patients, the digital twin. The emerging holistic picture, ranging from local features to global disease properties, will shift clinical decision making from still anecdotal 'trial and error' to evidence-based, molecularly founded, precise and individualized treatments. Ultimately, molecular engineering of natural building blocks (Flagship 3) will advance the development of disease specific reporters and sensors for research, diagnostic imaging, image-guided surgery, adaptive radiotherapy, or the efficacy of gene- and cell-based therapeutic approaches.

Role of Helmholtz

Helmholtz researchers are already developing imaging and robotics solutions for real-time diagnostics as well as surgical and radiation therapy. These new technologies enable innovation and provide novel capabilities along the entire translational pipeline, from new imaging devices and multiscale robots, to novel information acquisition, reconstruction and visualization algorithms, to targeted biological and synthetic reporters to assess treatment-relevant tissue properties. Researchers within Helmholtz develop cloud-based and decentralized imaging systems, enhancing accessibility and efficiency. By building on expertise in genetic, protein, cellular, and physical engineering, as well as data science, they are pioneering the development of novel biosensors, establishing multiplexed imaging approaches and advancing telemedicine capabilities through remote diagnostics and interventions as well as AI-based data analysis and integration. They are also developing online-adaptive surgical and radiation therapy technologies combining imaging, immediate treatment adaptation and continuous treatment monitoring in AI-supported closed feedback loops, paving the way for more personalized, targeted and accessible healthcare solutions.

Impact and deliverable

New imaging methodology, including in situ capabilities, and AI-enabled robotic procedures not only facilitate research and early disease detection and cure, but also integrate predictive analytics for preemptive healthcare strategies. Research is directed to technologies that can detect a much larger number of biomedical parameters addressing a wider spectrum of diseases. These will span the spatial dimensions from the microscopic to the macroscopic and ultimately lead to better health by addressing global health challenges such as cancer, cardiovascular, infectious, neurodegenerative, and metabolic diseases. Additionally, their role in enhancing real-time monitoring for treatment adaptation and post-treatment follow-up is significant, further personalizing patient care. New imaging technologies will also assist in democratizing healthcare by providing tools that can be extended to underserved segments of the global population, especially through telemedicine and remote or distributed diagnostic capabilities, making quality healthcare more accessible and equitable.

Flagship concept 3 –

Leveraging synthetic biology for biomedicine

Leveraging synthetic biology to engineer biomolecules, adaptive cells, genetic programs, and delivery vehicles as next-generation diagnostics and therapeutics

Relevance

Recent synergistic advances in synthetic biology, particularly the convergence of CRISPR-guided genome engineering, AI-driven (de novo) protein design, and cell and organoid engineering, have created unprecedented opportunities to transform biomedicine, moving from conventional small molecules and biopharmaceuticals to a new generation of gene and cell therapies. This paradigm shift will enable the engineering of customized cellular machinery and enhanced functionalities, accelerating biomedical discoveries and paving the way for effective, safe, and adaptive theranostics.

Challenge

To enable future biomolecular, cell and gene therapies, we need to gain the ability to execute customized genetic programs in engineered cells to enable image-guided control of cell function, ensuring reliable, effective, bioethically responsible, and safe application.

Role of Helmholtz

Helmholtz researchers are already making key innovations in synthetic biology and biological engineering, particularly in genome, protein, and mammalian cell engineering and smart delivery vehicles, as evidenced by numerous ERC and EIC grants, publications, patents, start-ups, clinical translation, participation in national and international networks, clusters, and research centers. As synthetic biomedicine is a rapidly evolving field where actionable discoveries are being made in all kingdoms of life, there is a particular need for close collaboration and integration of biological research across Helmholtz to identify and promote safe synthetic biology solutions.

Impact and deliverable

Implementing an AI-assisted design-build-test-learn cycle will ensure continuous quality control and improvement of programmed cells for neurological, metabolic, cardiovascular, and immunological tissue environments. Advanced techniques to synthesize and construct large DNA sequences and whole chromosomes provide means to customize target genomic regions with high precision. Specialized generative AI models combined with directed evolution will enable the engineering of tailored proteins, biomolecules, (Flagship 1) and genetic programs (Flagships 2, 6) that will undergo rigorous validation by structural biology, multiscale molecular imaging (Flagship 2), and multi-omics analyses to ensure their efficacy and safety. Reporter cells derived from human induced pluripotent stem cells (hIPSC) will provide key insights into disease-relevant tissue processes that will inform future biological engineering solutions such as tissue engineering (Flagship 4) and interfaces to implants (Flagship 5) in a virtuous cycle of innovation. Diagnostic and therapeutic cells, such as immune cells with engineered receptors or neuronal progenitor cells meticulously engineered with genetically controlled molecular sensors such as MRI-PET or optoacoustic tracers (Flagship 2) and actuators, will enable remote spatio-temporal interrogation and prevention of disease-causing aberrations, providing real-time insights into disease progression and enabling proactive intervention. Delivery vehicles with synergistic synthetic, chemical, and biological properties will enable precise delivery of therapeutic genetic programs and biologically active molecules to specific target cells to advance both cell and tissue engineering (Flagship 4) and gene therapies, including gene editing. Our integrated synthetic biology framework will deliver new adaptive, diagnostic, and therapeutic solutions, ushering in a new era of individualized biomedicine.

Flagship concept 4 - Predictive human-on-a-chip models

Engineer truly predictive human-on-a-chip and microphysiology models for precision medicine

Relevance

Implementing precision medicine requires human cell-based systems that are able to model and interrogate disease heterogeneity and to predict how an individual patient would respond to treatment.

Challenge

The challenge is to create robust, predictive cell-based human disease models that will reveal causative early mechanistic changes that lead to disease onset – to identify new early detection signatures and disease-modifying therapies – and reliably assess drug sensitivities, response and efficacy for a patient. This requires engineering a human-on-a-chip by combining complex, vascularized and immune-competent organoids into connected multi-organ microfluidically integrated systems. Achieving this involves not only the integration of various biological systems but also addressing the scalability and reproducibility of these models to ensure they can be used widely in research and clinical settings. Such a system requires the convergence of stem cell biology, genome editing and bioengineering solutions such as microfluidics, microfabrication, miniaturization, sophisticated opto-genetic, gene-, protein-, cellular-, tissue-engineered sensors, reporters, and accentuators as well as 3-D bioprinting technologies. The selection and integration of bio-compatible materials that mimic the natural environment of human tissues are vital to creating models that accurately replicate human organ functions. Additionally, ensuring the physiological relevance of these models to human biology and overcoming the challenges of heterogeneity in patient-derived cells are crucial for the successful application of these technologies. Moreover, advanced in vitro models whose production can be up-scaled in number, automated, and made compatible with patient-derived cells would be valuable for high-throughput screenings in applications such as drug discovery, personalized medicine, and the development of novel cell- and protein-based therapies. Furthermore, integrating computational modeling and machine learning algorithms with these in vitro systems could significantly enhance the predictive accuracy and efficiency of drug screening and disease modeling processes. In terms of preventive health technologies, these avatars can accompany the patients during a lifespan to monitor the early onset of diseases.

Role of Helmholtz

The Helmholtz Centers leverage a range of cutting-edge technologies, including microfluidics for multi-organ models, vascularization techniques for organoids, multimodal sensors and reporters, high-throughput and miniaturization technologies designed for screening to engineer a human-on-a-chip. They are at the forefront in developing human models, including organoids, of the brain, pancreas, gut, tumors and neuromuscular systems. In addition, there is a large expertise in the field of tissue reconstruction by 3D bioprinting, such as skin, retina, heart, bone marrow, liver, neurovascular unit and lung tissue gas exposure cells etc. This expertise includes ERC grants, patents, start-ups and collaborations with industry. As an example, bioengineering is advancing vascularized human tissues by integrating 3D-bioprinting and cellular self-assembly, reconstruction of the neurovascular unit, heart and liver tissue or vascularized retina using Helmholtz proprietary technology together with several industry partners. Key publications from within Helmholtz include showing clinical grade human recombinant soluble ACE2 blocks SARS-CoV2 infection of engineered human blood vessel organoids and human kidney organoids, new antiviral strategy for Herpes-simplex virus infection of brain organoids, spatial temporal control of gene expression using optogenetics, immunomodulatory drugs for managing severe asthma, and using engineered human heart , retina and neurovascular tissue for drug discovery as well as first 3D printed structures in organoids for vascularization or electronic stimulation.

Impact and deliverable

Human microphysiology and human-on-a-chip models will provide new tools to address key societal health challenges being addressed by Helmholtz, such as understanding the mechanisms of cardiovascular and infectious diseases, cancer, dementia, diabetes, as well as complex multi-organ diseases. These models will also be instrumental in evaluating the systemic effects of new drugs and therapies, offering a more holistic view of treatment impact. They will provide a basis for developing and testing biomaterials to regenerate or restore the function of diseased or injured tissues, cells and complex organs. More predictive human models will improve the success of drug and advanced therapy medicinal product development and facilitate rapid prototyping in drug discovery. Additionally, these models could be used as patient avatars to test the predicted effectiveness of therapeutic strategies before being administered to an individual, thus minimizing the risk of adverse reactions and maximizing treatment efficacy.

Flagship concept 5 – Generating smart implants

Bioengineering of patient-specific, adaptable, degradable and smart implants

Relevance

Development of degradable, adaptable, intelligent implants are at the forefront of bioengineering innovation and poised to revolutionize a spectrum of fields including biomachine interfaces, electroceuticals, biomimetics, smart biomaterials, prosthetic solutions, and beyond, heralding a new era in multifaceted, personalized medical technology."

Challenge

In the coming years, a pivotal challenge will be the development and design of a diverse range of implants, including those incorporating soft tissues for body part replacements. These implants need to be patient-specific, adaptive, degradable multifunctional and particularly "smart" to monitor, detect and respond to changes in a patient's body or the physiological environment. This necessitates a fundamentally new approach to rapidly, safely, and personally engineer biomaterial systems. The design space for biomaterials is vast, irrespective of the material class used, with an equal complexity in potential biological interaction partners – not only in terms of sheer number but also in (patho)physiological state, modification, location, etc.. Machine learning (ML) and artificial intelligence (AI) technologies will significantly impact the innovation pipeline. The utilization of Digital Twin technology allows for the virtual creation of an extensive array of potential solutions for an implant without the need for intermediate product production. This approach can predict the function, potential complications, and even the durability of the implant, coupled with the potential for drastically accelerated development cycles. The twin approach inherently provides freedom for material selection and optimal process routes, enabling not only performance prediction but also the optimized production of the device. The translation of these biomaterials into new implants will necessitate bioengineering approaches, incorporating innovative biomedical technologies such as patient-derived stem cell propagation and tissue engineering, advanced 4D bioimaging technologies, and additive manufacturing, such as 3D bioprinting. This integrated approach aims to create flexible, multiplexable, and potentially self-driving bioengineering platforms for faster translation.

Role of Helmholtz

Helmholtz researchers are well positioned to engineer new biomaterials systems for the bioengineering of implants. Especially bringing together digital tools such as AI, simulation, and modeling, alongside advanced experimental techniques and clinical data, is pivotal in the patient-specific design of materials and devices. The participating scientists from Helmholtz health contribute essential knowledge and data on fundamental biological processes and patient-specific information, while scientists from the Helmholtz Information (for example within the program "Materials Systems Engineering" and the Research Field Matter), are at the forefront of developing ML/AI-based processes for biomaterials systems and smart implants by integrating AI-based algorithms based on pre-clinical data. This collaboration is instrumental in developing a Digital Twin that encompasses the entire lifecycle of the device. Furthermore, the impact of the participating Helmholtz centers is shown by key innovations in the fields of sensors and biomedical engineering, as evident from the numerous received ERC (soft sensors, soft bioelectronics etc.), high impact publications, the participation of Helmholtz scientists in Excellence Clusters of 3D additive manufacturing and EXIST fundings for spin-offs. Several of them hold patents in "smart" biomaterials and implants and during COVID 19 pandemic a bioengineered material patent was one of the most licensed for personal point of care diagnostics. In addressing complex challenges in medical device development, a "Convergence Research" strategy is employed, emphasizing transdisciplinary, which is a strength of Helmholtz. This approach brings together experts from natural science, medicine, informatics, and facilitates close interactions with clinics and industry partners. The incorporation of new data mining and analysis approaches, including foundation models, is essential to embrace the broad field of research, ensuring a holistic understanding and effective solutions to complex problems.

Impact and deliverable

New data- and AI-driven biomaterials system engineering will provide "smart" implants including different types of diagnostic sensors and bioelectronics as well as implantable personalized soft tissues and body parts to address the key societal health challenges being addressed by Helmholtz. Exploring innovative approaches to accelerate the intricate approval process by the regulatory authorities and cut down on costs is imperative. This involves rethinking the preclinical and clinical phases of implant development, introducing novel study designs for digital studies. These digital studies, performed using real patient data with meaningful outcomes on a computer, can ultimately be linked to pivotal clinical trials. This approach not only minimizes the need for a large number of patients but also paves the way for in silico medicine in the realm of medical devices. Customization of implants is a key focus, leveraging digitalization to tailor implants for diverse anatomic environments, metabolic variations, genetic requirements, and other specific patient needs. This approach aims to achieve a higher level of precision and effectiveness in addressing individual patient characteristics. Normative bodies and approval authorities should be partners to integrate these developments into the approval process. Long-term studies will be conducted to assure feed-back in order to further improve efficacy and safety in the next development cycles. Here, Helmholtz will have a tight interaction of the Research Field Health and Research Field Information. They will enable a switch from reacting to diseases to proactively seeking them before they progress to increase an individual's health span, leading to a healthier society.

Flagship concept 6 –
Bioengineering microbes and microbiomes

Bioengineering microbes and microbiomes as a new source of therapeutic and diagnostic functions

Relevance

Microbes are ubiquitous lifeforms present throughout the human body and in diverse environments, where unlocking their physiological, genetic and metabolic properties, components and functions have the potential to open new avenues for addressing a range of needs in human medicine.

Challenge

The physiological, genetic and metabolic diversity of bacteria as well as their existence in microbial communities creates an opportunity but also poses a central challenge – how to systematically explore and harness these bacteria regardless of identity, origin or application. The unique requirements of a given microbe make it difficult to culture under standard laboratory conditions, while culturable bacteria can pose formidable barriers to DNA transformation and genetic manipulation that can vary even between related strains. Furthermore, these bacteria rarely exist in isolation and instead in mixed communities of microbes that are constantly changing and form large networks of interactions. These communities directly impact human health, as underscored by the many influences between the gut microbiome, yet rationally perturbing these communities remains a major challenge. Finally, achieving the many promising applications of engineered microbes and microbiomes requires gaining not only a fundamental understanding of each microbe from genotype to phenotype as well as its integration into its surrounding community but also making large-scale genetic changes that must interface with existing regulatory programs and faithfully function in the intended body sites and environments. Unique applications of engineered microbes and microbial communities include bacteria engineered to overproduce novel antibiotics, serve as sentinel cells that record their environment or selectively invade and eradicate cancer cells, represent the tip of the iceberg of what could be achieved. A fundamental reason is a lack of engineering strategies and principles to fully overcome these challenges and realize the full potential of microbes and microbiomes.

Role of Helmholtz

Within this broad area of bioengineering, Helmholtz researchers are uniquely positioned to interrogate and harness different aspects of the microbial world. The related expertise and active research programs span efforts to establish systematic approaches for analyzing bacteria inside well-controllable microfluidic habitats, genetically modifying non-model bacteria and engineering bacterial chasses as therapeutic probiotics, tailoring microbial cell factories for the production of small-molecule therapeutics, and environmental sensors. Helmholtz researchers are further positioned to incorporate AI-based approaches, whether to direct image acquisition and cell segmentation and tracking within microfluidic systems or to predict biosynthetic gene clusters and their biosynthetic products as well as develop high-throughput approaches to generate the experimental data used for AI training. The existing experience in relevant medical and environmental systems, such as bacteria that naturally colonize the human gut, provide direct applications of these engineering approaches that could benefit human health.

Impact and deliverable

These capabilities will be leveraged to make a number of important advances in microbial biotechnology. One direct impact will be broadening the available bacterial models and chasses to study human health and disease as well as environmental processes. Few models exist, and engineering is needed to lay a foundation of tools and capabilities that are often taken for granted with existing model organisms. This impact stems from applying microfluidic devices for cultivating and monitoring difficult-to-culture bacteria and microbial consortia as well as applying systematic approaches to achieve DNA transformation and CRISPR-based editing in diverse non-model bacteria that can proceed from a new bacterium to one with genome-wide and high-throughput capabilities paralleling that of model bacteria like E. coli. A potential focus will be on commensal bacteria that are already adapted to colonize the human body but then engineered to provide different health benefits, such as countering dysbiosis of the existing microbiome or blocking invasion by pathogens. Another impact is accelerating the drug discovery pipeline through the use of AI. After developing and applying high-throughput approaches for high-quality data generation, AI will be used to predict promising but otherwise unexplored biosynthetic pathways present in different environmental bacteria. Once identified, synthetic biology can be implemented to either render those bacteria genetically tractable or port the associated pathways into a relevant bacterial chassis. The pathway and chassis strain can then be genetically optimized to maximize titers toward scale-up and commercial production.

Measures and structures to establish Helmholtz Biomedical Engineering as global leader

Helmholtz Biomedical Engineering is committed to being a global leader in advancing health through accelerating the translation of biomedical discoveries into solutions. To achieve this ambitious goal, it is taking a proactive approach by suggesting several key measures and structures.

A unifying 'Helmholtz Biomedical Engineering' brand

To promote synergy and facilitate impact, the authors propose the establishment of a unifying "Helmholtz Biomedical Engineering" brand. This can be achieved through the launch of an appropriately designed and comprehensive online portal, flanked by a relevant and continuously maintained social media presence. The portal serves as a coherent, easily accessible communication platform and central landing hub to ensure broad visibility of all Helmholtz Biomedical Engineering related and relevant activities. It plays a central role in the timely dissemination of the latest research results and serves as an information hub for all interested stakeholders (including scientists, funders, investors, policy makers and, last but not least, the general public). As an important focal point, the online portal provides information on the most important bioengineering activities and their societal and economic impact as well as connects diverse bioengineering expertise across Helmholtz Centers, while at the same time serving as a valuable tool to advertise larger and coordinated recruitment initiatives, general vacancies and other career development, employment and training opportunities across Helmholtz Biomedical Engineering. Finally, the portal provides relevant information for potential new academic, industrial or other partners to initiate collaborations and accelerate investments or attract donations. In addition to the latest publications and news, seminars and conferences as well as protocols, reagents and technical advice can be shared across Helmholtz Biomedical Engineering and beyond. Ultimately, such a portal could evolve into an umbrella for a "virtual institute" that showcases the ambition, technology, people, services and achievements of Helmholtz Biomedical Engineering.

Complementary education, training and support structures

Funding of innovative technological concepts

New funding opportunities for bioengineering projects are essential to advance the field. Similar to the European Research Council's[10] Pathfinder and Transition programmes, funding streams for Helmholtz Biomedical Engineering projects are needed, that do not simply follow conventional approaches, but instead prioritize novel and disruptive concepts that push the boundaries of technological innovation or refine and validate novel technologies in both laboratory and real-world applications. The key to success lies in fostering high levels of academic collaboration, both with partners from different disciplines within Helmholtz and externally. By bringing together expertise from different fields, bioengineering projects can harness the collective expertise and intelligence of researchers and enable a synergistic approach to problem solving. In addition, establishing robust collaborations with industry stakeholders is critical, not only to facilitate the translation of research results into real-world applications, but also to ensure that projects remain aligned with market needs. In essence, the essential funding of bioengineering projects should be accompanied by a commitment to foster collaboration and industry partnerships, with flexible, easily accessible funding instruments to create a vbrant ecosystem that fosters innovative ideas and overcomes traditional silos to ensure that new tools and solutions are delivered to benefit patients and society.

Education & training

The authors emphasize the importance of nurturing, attracting and retaining a global and diverse talent pool to meet the evolving needs of both academia and industry, spanning scientific, technical and entrepreneurial expertise. The long-term success of Helmholtz Biomedical Engineering requires investment at all career levels – from master's[11] to doctoral and postdoctoral training, short and longer-term national and international exchange programs, and a new type of independent research group – to enrich the bioengineering ecosystem with the necessary skills for innovation, development, prototyping, scaling and commercialization. In addition to supporting appropriate education and training, Helmholtz Biomedical Engineering has the potential to lobby for the establishment of bioengineering (PhD-granting) faculties, departments and/or schools at partner universities. Helmholtz's industrial partners would most likely support (Helmholtz-trained) bioengineers – as skilled workers and innovators – to change the professional landscape for easier transitions between academic and corporate environments.

[10] EIC Funding opportunities - European Commission (europa.eu)
[11] KIT - Study programs - Bioengineering Master of Science

Early career-investigator groups & future entrepreneurs

New academic talent and technology hubs are attracting early-career, technology-driven entrepreneurs from the world's leading organizations. Such hubs not only act as magnets for these early-career investigators, but also demonstrate remarkable levels of productivity in both academic output and the development of practical translational concepts, cutting-edge technologies, and innovative devices. For early-career investigators, these hubs offer a unique opportunity to transform their initial seed funding into substantial third-party funding and valuable collaborations with industry players. This transformation is facilitated by the supportive and vibrant innovation environment that characterizes these hubs, providing an ideal setting for creative ideation and collaboration. The Helmholtz Pioneer Campus[12] is an example of such a hub and can provide valuable insights for designing similar initiatives within the larger Helmholtz Biomedical Engineering framework, conducting strategic recruitment, and fostering a culture of innovation and collaboration in the ever-evolving landscape of technology and entrepreneurship. Furthermore, recognizing the critical role that financial support plays in fostering these early stages of a research and entrepreneurial career, it needs to be noted that, in addition to the creation of talent and technology hubs, there is a compelling need to ensure the availability of initial seed funding. Providing these resources not only enables these early-career investigators to rapidly inititiate new research directions, but also sets the stage for attracting additional third-party funding. In essence, the symbiotic relationship between the establishment of technology hubs and the provision of initial seed funding is critical to cultivating a thriving ecosystem of innovation and entrepreneurship.

Post-doctoral programs

The initiation of a Helmholtz-wide postdoctoral program specifically tailored to bioengineering is highly attractive. Such a program provides outstanding training opportunities for promising fellows through interdisciplinary and cross-sectoral placements at Helmholtz centers, hospitals, and companies within the Helmholtz global network. By encouraging collaboration across disciplines, the program aims to cultivate a comprehensive approach to bioengineering. Fellows gain invaluable experience in diverse working environments, fostering the development of versatile skills essential for success in the field. Co-supervision by experts from partner institutions will further ensure the quality of mentorship and promote knowledge exchange. This proposed initiative has the potential to shape the next generation of bioengineers who play a pivotal role in advancing therapeutics and healthcare solutions. The collaborative and innovative framework of the program positions it as a catalyst for meaningful advances in global

[12] https://www.helmholtz-munich.de/en/helmholtz-pioneer-campus/hpc-research

bioengineering. In addition, such a program will facilitate the development of grant writing skills and empower postdocs to begin their journey as junior investigators. The envisioned outcome is not only the advancement of individual careers but also the formation of vibrant young multi-disciplinary investigator networks. Strategic investments in such programs ensure that the next generation of bioengineers is well prepared to tackle complex challenges and develop innovative solutions with a lasting impact.

Graduate Schools

Bioengineering graduate schools, whether in a virtual format or cross-center collaborations, such as the Helmholtz Information and Data Science Research Academy and its Schools (HIDA)[13] would provide outstanding introductions into the spectrum of challenges in different innovation translation applications. Graduate students should be encouraged to envision the practical applications and market potential of their research, fostering a mindset that aligns with the ultimate goal of technology-to-market success. These programs should place a strong emphasis on identifying and developing key mentalities and skill sets crucial for entrepreneurial or innovation transfer-to-market success. This includes programming skills, machine learning and artificial intelligence to empower students to create and optimize technologies efficiently, while at the same time understanding and responding to market dynamics and changing or emerging trends. A deep understanding of test-learn cycles enables students to efficiently prototype, test, and iterate products based on user feedback and market demands. To achieve these goals, students will be trained to report discoveries early, receive feedback from an intellectual property attorney, and interact with engaged members of the industry ecosystem. In short, the goal is to foster innovation-enhancing and economically prosperous synergies between experienced professionals and emerging talent, successful entrepreneurs and ambitious founders, business angels, venture investors and venture builders, fostering mentorship and creating new products and solutions that benefit patients and economic growth.

Virtual Bioengineering seminars and lecturer series

Embracing the age of digital advances, the authors propose a Bioengineering Virtual Seminar Series to foster cross-center collaborations involving bioengineers. This virtual forum provides an opportunity for researchers to present their discoveries, engage in insightful conversations, and create a broader community. This series will foster the exchange of ideas and facilitate a dynamic and interconnected network of scientists dedicated to advancing the field of bioengineering.

[13] https://www.helmholtz-hida.de/

Instruments for Mobility and Exchange

The implementation of short and long-term exchange programs (e.g. laboratory rotations), industry internships, as well as the promotion of academic-industry collaborations on a national and international level are essential to cultivate expertise in bioengineering. Laboratory rotations will expose postdocs and students to diverse research environments, fostering interdisciplinary perspectives relevant to the field of bioengineering. Industry internships will provide hands-on experience and connect researchers to practical application of knowledge and problem solving in real-world scenarios. Academic-industry collaborations accelerate the translation of research into high-impact technologies. In addition, international collaborations contribute to the global advancement of bioengineering. Together, these initiatives foster a dynamic community of bioengineering professionals who drive innovation and address complex challenges in healthcare and biotechnology.

Establishing a solutions-building research culture & incentive structure

The bioengineering landscape is undergoing a significant transformation driven by the need to accelerate the clinical translation of research from distinct scientific fields. A fundamental shift towards translating the exponentially growing academic knowledge into practical and commercializable medical solutions not only depends on educating and training an entirely new generation of professional bioengineers but also on establishing new and adequate incentives. First, it takes on average 10-15 years, which is much longer than than the time taken to publish an average academic paper, before an idea eventually enters clinical trials, and more before regulatory approval or clinical implementation. Second, traditional academic performance metrics – often still focused on the number of high-impact journal publications often becomes an obstacle for ambitious scientists to turn valuable ideas into commercial reality. Therefore, leading institutions increasingly recognize the importance of development timelines, roadblocks and milestones along the translational product pipeline. As an example, UCSF's Innovation Ventures and MIT's Deshpande Center integrate complementary metrics like patents, spin-outs, and corroborating reports and (mostly specialized) publications alongside conventional academic metrics[14]. Third, and most importantly, fostering a solution-oriented mindset, akin to the principles of classical engineering disciplines, demands the implementation of a truly attractive 'alternative' career path, one that leads to the recognition of bioengineering as credible and independent discipline, one that values a problem-solving mind and tool-making capabilities, the ability to recognize and define clinical problems and to solve them by critically utilizing tools and

[14] https://innovation.ucsf.edu/ https://deshpande.mit.edu/

processes stemming from across the natural-, life- and computational sciences to create valuable applications. Ultimately, it needs new and adequate incentives to reward innovative ideas, easier access to expertise and capital for IP-protection, increase in risk-accepting venture capital and a conducive environment toward incorporation, for more people to pursue the risky and often unpredictable route to overcoming all entrepreneurial challenges.

In summary, the authors propose several initiatives to advance Helmholtz Biomedical Engineering as a comprehensive endeavor. These initiatives include postdoctoral and graduate education and training programs, virtual bioengineering seminars, financial support for early career investigator groups, funding for mobility and exchanges, support for breakthrough ideas and disruptive technologies, the establishment of an online portal for branding and dissemination, and engagement in public outreach activities aimed at promoting Helmholtz Biomedical Engineering to the broader public.

Addressing Regulatory, Intellectual Property (IP) and Ethical issues

From their collective expertise, the authors have identified the most crucial current bottlenecks to accelerating basic science translation that may originate from IP-, regulatory and potential ethical considerations. To overcome these, the authors suggest establishing a central advisory office within the Helmholtz Association to influence relevant regulation toward faster technology and innovation approvals as well as market and clinical implementation. At the same time, all centers would benefit from centralized and best-in class consultancy regarding ethical issues related to bioengineering solutions, IP-filing, best practices for clinical trials, securing royalties associated with Helmholtz (bioengineering) inventions. Moreover, the authors emphasize the need to raise public awareness regarding the significance of rapid regulatory approvals, robust IP protection, and the ethical dimensions of bioengineering solutions. Communicating these aspects to the public is important for fostering understanding and support of Helmholtz activities in Germany and Europe.

Intellectual Property (IP)

Most Helmholtz Centers have robust structures with competent tech-transfer offices that prioritize the protection of IP. However, effective management of the existing IP portfolio is inherently complex and market dynamics constantly changing. Successful product development and commercialization requires strategic timelines, expertise in investor engagement, and adequately evolving decision mechanisms regarding patent filing, out-licensing vs. spin-off creation or incorporation or patent termination. Helmholtz Biomedical Engineering offers the unique opportunity to establish a consistent pipeline to derive products from engineering biology, deploy regulatory sandbox models to navigate the approval landscape more successfully and turn out products and companies more efficiently. Mastering these complex tasks requires meticulous planning, extensive experience, constant adaptation to market dynamics, cooperation and trust between research institutions and regulatory agencies. As a good starting point, the Helmholtz Head Office is currently coordinating a task force whose aim is to pool the expertise of the individual centers and to jointly develop internal guidelines on the subject of intellectual property rights.

Regulatory issues

A key challenge we face is the reluctance of many pharmaceutical, regulatory, and academic researchers to change their established research methodologies. Persuasive data demonstrating the benefits of bioengineering tools - such as human organs-on-a-chip, advanced diagnostic tools, implants, etc. - is essential for gaining acceptance by industry, regulatory bodies and academia. To tackle this challenge, bioengineers and a Helmholtz central advisory office should work together with regulatory authorities and the pharmaceutical industry to seek transparent and expedited processes for validating and approving new technologies. The aim is to bridge the gap between traditional research practices and the transformative potential of bioengineering, facilitating the seamless integration of innovative tools and methods into existing scientific and medical workflows.

Clinical trials

Germany ranks high in international rankings of basic research outputs. However, the translational gap becomes evident when the ratio of preclinical projects to R&D spending, number and funding of biotech start-ups, number of sponsored clinical trials and EMA-approved products is compared to Switzerland, USA and UK. Bottlenecks in regulatory processes, especially in initiating and conducting clinical trials, often compounded by a lack of critical understanding of existing laws, EU directives and national regulations by practitioners, prohibit efficient translation. Therefore, an early flow of information about current and new regulatory requirements is important. Although decentralized information structures and training programs exist at various Helmholtz sites and universities (e.g. KKS Network – Coordination Centre for Clinical Trials), it is crucial to improve their interconnection, accessibility and usage. In addition, active participation of researchers in hearings is encouraged to communicate a solutions-building perspective and influence new directives early - as to maintain patient's safety while establishing rules and regulations conducive to innovation.

EU-mandated IVDR and MDR implementation

Medical technology development is integral to Europe's quality healthcare – throughout all stages of the patient journey – from prevention and diagnosis to treatment and cure. However, there is growing concern that the implementation of recent European regulatory frameworks for medical technologies, (e.g. the In Vitro Diagnostic Medical Devices Regulation 2017/746/EU (IVDR) and the Medical Devices Regulation 2017/745/EU (MDR), respectively) may not efficiently support disruptive technologies or products with enhanced functionality and performance to reach European patients and health systems in a timely manner due to slow, unpredictable, costly and complex regulatory governance[15]. More specifically, about 20 % of the around 500,000 in vitro diagnostics (IVDs) and medical devices (MDs) delivered by about 35.000 companies to European patients[16] are considered to be discontinued in Europe due to the expectation that costs of the transition to the new EU-regulations outweigh product revenue, particularly among SMEs. Even more significantly, 28% of IVD manufacturers and 48% of MD manufacturers are deprioritizing the EU market for first regulatory clearance of new devices due to the unpredictability (time, cost, changes) of the above-mentioned regulations. Such signals certainly impact already ongoing and future science-translation and start-up/societal transfer/business creation ambitions of Helmholtz Biomedical Engineering. Therefore, the Helmholtz Association should have a strong interest and mandate to politically influence Germany's, as well as European MedTech regulatory frameworks in a way that warrant innovative medical technologies and devices to safely and efficiently reach patients and global health systems.

Ethics in Emerging Bioengineering Technologies

Advances in bioengineering often introduce radically new technologies, such as human organs-on-a-chip, new vaccines, gene therapy, or tissue engineering. Given the importance of ethical considerations in this field, several actions are imperative. First, a structured mechanism is needed to discuss potential ethical issues related to critical technologies. This involves establishing a platform for expert discussion and opinion. Many centers have offices or institutes

[15] https://www.medtecheurope.org/resource-library/the-future-of-europes-medical-technology-regulations/
[16] https://www.medtecheurope.org/resource-library/medtech-europe-survey-report-analysing-the-availability-of-in-vitro-diagnostic-medical-devices-ivds-in-may-2022-when-the-new-eu-ivd-regulation-applies/
https://www.medtecheurope.org/resource-library/medtech-europe-survey-report-analysing-the-availability-of-medical-devices-in-2022-in-connection-to-the-medical-device-regulation-mdr-implementation/

for technology assessment and dual use that should be involved. The interface with the German Ethics Council[17] will also be relevant. The results of these discussions should be effectively and transparently communicated to both regulators and the general public to promote informed decision-making and acceptance of these transformative technologies. Second, the Helmholtz Association should strengthen its efforts to communicate scientific results and outcomes in bioengineering to the general public. Clear and accessible information can contribute to understanding and acceptance.

In summary, a possible and general solution, could be the consolidation and centralization of IP, ethics, and regulatory resources within a central contact point/structure at the Helmholtz Association that works hand in hand with already existing offices at the Centers. Such an office could facilitate essential and credible links with authorities, industry and offer consultation to all Helmholtz Centers, thereby contributing to sharing best in class practices and procedures, coordination of respective training and dissemination of regular updates on the Bioengineering ONLINE PORTAL. This proactive approach aligns with the shared interests of Helmholtz Association and industry in swiftly bringing new critical biomedical technologies to the public health domain.

Interaction with existing Helmholtz activities

The measures outlined above are central to the consolidation and utilization of the inherent potential in bioengineering in the Helmholtz Centers. However, the Helmholtz Biomedical Engineering Initiative recognizes the importance of existing structures and strives to integrate seamlessly into the overarching framework of the organization as a whole and the distinctive structures of each Helmholtz Center.

With regard to technology and knowledge transfer, the establishment of the Helmholtz Transfer Academies[18], the Helmholtz Enterprise program[19], validation projects[20] and co-creation transfer projects, the Helmholtz School for Innovation and Entrepreneurship (HeSIE)[21] are among the structures that are particularly relevant for Helmholtz Biomedical Engineering and with which interactions will be very fruitful. Furthermore, the existence of dedicated transfer offices within the Helmholtz Centers provides valuable expertise and funding for entrepreneurial activities.

[17] Deutscher Ethikrat
[18] https://www.helmholtz.de/en/transfer/helmholtz-association-transfer-instruments/translate-to-englisch-helmholtz-transfer-academies/
[19] https://www.helmholtz.de/en/transfer/helmholtz-association-transfer-instruments/helmholtz-enterprise/
[20] https://www.helmholtz.de/en/transfer/helmholtz-association-transfer-instruments/helmholtz-validation-fund/?chash=f721e4edb03e61191b0229d3b11b1d53&l=1%27&cHash=c8f055ab8245c3add75e68ef8651eddb
[21] https://www.helmholtz.de/transfer/helmholtz-school-for-innovation-entrepreneurship/

Seamless integration and networking of these offices with Helmholtz Biomedical Engineering activities will increase the potential for successful knowledge transfer and innovation in this research field.

In addition to transfer activities, the Helmholtz Information & Data Science Framework[22], consisting of the five Incubator Platforms and their services, is instrumental for bioengineering. These resources play a pivotal role in enhancing data-driven approaches, which are crucial in the intricate landscape of bioengineering.

Recognizing the interdisciplinary nature of bioengineering, it is noteworthy that the initiative aligns closely with overarching topics within Helmholtz Health and beyond. This includes but is not limited to prevention research, digital health research, and other initiatives such as material sciences. By fostering collaboration across these domains, the Helmholtz Biomedical Engineering initiative ensures a holistic and comprehensive approach to its endeavors.

Looking beyond the confines of the Helmholtz Association, also national partnerships and international collaborations serve as crucial components in advancing bioengineering in Germany. By drawing inspiration from successful role models and blueprints, the initiative can further enhance its impact on a global scale.

[22] https://www.helmholtz.de/en/research/challenges/information-data-science/

Annex

List of use cases per flagship

Note: The following lists show examples, it does not claim to be exhaustive.

Flagship 1

Selected publications

- Single cell proteo-genome of the hemotopoietic system
  https://www.nature.com/articles/s41590-021-01059-0

- Spatial transcriptomics using multiplexed deterministic barcoding in tissue
  https://www.nature.com/articles/s41467-023-37111-w

- Spatial transcriptomics of lung tumors in 3D
  https://www.biorxiv.org/content/10.1101/2023.05.10.539644v1

- Advancing single-cell RNA sequencing
  https://www.nature.com/articles/s41586-019-1369-y
  https://www.sciencedirect.com/science/article/pii/S0092867421013830
  https://www.sciencedirect.com/science/article/pii/S0092867421015622?via%3Dihub
  https://www.nature.com/articles/s41564-020-0774-1

- Reprogramming CRISPR tracrRNAs for RNA detection and recording
  https://www.science.org/doi/10.1126/science.abe7106
  https://www.nature.com/articles/s41587-022-01604-8

- CRISPR-based diagnostics
  https://www.nature.com/articles/s41551-020-0546-5
  https://www.nature.com/articles/s41565-022-01179-0

Major grants & awards

- ERC Starting: Deep Spatial Proteomics: connecting cellular neighbourhoods to functional states
  https://www.mdc-berlin.de/news/press/erc-starting-grant-awarded-fabian-coscia

- ERC Consolidator grant ImmunoChip for digitalized cancer phenotyping
  https://cordis.europa.eu/project/id/101045415/de

- BMBF VIP+ flexMEA biosensor
  https://www.validierungsfoerderung.de/validierungsprojekte/flexmea-biosensor

Start-up activities & technology references

- Spin-off (Leopard Biosciences):
  https://www.helmholtz-hiri.de/en/newsroom/news/detail/news/hiri-team-receives-funding-from-the-helmholtz-association-toward-spinning-off-leopard-biosciences/

- Computer-assisted speech analysis, prognostic language biomarkers, and cognitive function assessments as digital biomarkers
  SARAspeech https://www.nature.com/articles/s41746-023-00787-x
  PROSAstudy https://www.tandfonline.com/doi/full/10.1080/21678421.2023.2239312

- Prospect-AD and DELCODE-II
  https://link.springer.com/article/10.14283/jpad.2023.11

- eHealth solutions for cognitive function assessments
  https://neotiv.com/en
  https://neotiv.com/en/papers
  https://formative.jmir.org/2022/10/e39954/

- Virtual environment (VE) technology
  https://neomento.de/
  https://journals.biologists.com/jeb/article/222/Suppl_1/jeb187252/2801/Thepotential-of-virtual-reality-for-spatial

- Biomarker for movement disorders
  https://movementdisorders.onlinelibrary.wiley.com/doi/10.1002/mds.28478
  https://movementdisorders.onlinelibrary.wiley.com/doi/full/10.1002/mds.28930

- Ataxia assessment at home
  https://www.aparito.com/development-of-sarahome-a-new-video-based-tool-for-the-assessment-of-ataxia-at-home/

- Assisted living technology in care
  https://link.springer.com/article/10.1007/s10676-022-09656-9

Flagship 2

Selected publications

- Novel diagnostic imaging of diabetes complications
https://www.nature.com/articles/s41551-023-01151-w

- AI-empowered multispectral clinical optoacoustic imaging
https://www.nature.com/articles/s42256-023-00724-3

- Genetically encoded electron microscopy-readable barcodes for multiplexing and automation in volume electron microscopy
https://www.nature.com/articles/s41587-023-01713-y

- Non-invasive imaging as a proxy for neuroinflammation in the (human) brain
https://www.sciencedirect.com/science/article/pii/S0092867423007420

- Photoswitching calcium sensor – proof-of-concept towards enabling calcium sensors for super-resolution imaging and optoacoustic whole-animal imaging
https://www.nature.com/articles/s41587-021-01100-5

- First real-time application and analysis of multispectral imaging in laparoscopic surgery in human subjects and in a clinical setting
https://www.science.org/doi/10.1126/sciadv.add6778

- First demonstration of label-free optoacoustic imaging of metabolism
https://www.sciencedirect.com/science/article/pii/S155041311830113X

- Smallest ultrasound detector to date
https://www.nature.com/articles/s41586-020-2685-y

- Multiplexed whole animal imaging with reversibly switchable optoacoustic proteins
https://doi.org/10.1126/sciadv.aaz6293

- Whole-body cellular mapping in mouse using standard IgG antibodies
https://www.nature.com/articles/s41587-023-01846-0

- Whole-mouse clearing and imaging at the cellular level with vDISCO
https://www.nature.com/articles/s41596-022-00788-2

- Machine learning analysis of whole mouse brain vasculature
https://www.nature.com/articles/s41592-020-0792-1

- The coming decade of digital brain research: A vision for neuroscience at the intersection of technology and computing
  https://direct.mit.edu/imag/article/doi/10.1162/imag_a_00137/120391/The-coming-decade-of-digital-brain-research-A

- The virtual aging brain: Causal inference supports interhemispheric dedifferentiation in healthy aging
  https://www.sciencedirect.com/science/article/pii/S1053811923005542?via%3Dihub

- Combining lifestyle risks to disentangle brain structure and functional connectivity differences in older adults
  https://www.nature.com/articles/s41467-019-08500-x

Major grants & awards

- ERC starting grant Propelling microrobots
  https://cordis.europa.eu/project/id/101041975-

- ERC consolidator grant Novel machine-learning method for spectral imaging
  https://cordis.europa.eu/project/id/101002198

- ERC consolidator grant Photo-modulated optoacoustics for whole-animal imaging
  https://cordis.europa.eu/project/id/101002646-

- ERC consolidator grant Exploiting skull-meninges connections to control brain pathologies
  https://cordis.europa.eu/project/id/865323

- ERC consolidator grant EMcapsulin nanospheres as novel electron microscopy gene reporters
  https://cordis.europa.eu/project/id/865710

- ERC advanced grant Portable hybrid multispectral optoacoustic tomography - ultrasound imaging technology
  https://cordis.europa.eu/project/id/694968

- EIC transition challenge to develop a non-invasive optoacoustic in-blood glucose monitoring sensor
  https://cordis.europa.eu/project/id/101058111

- EIC Pathfinder to develop a groundbreaking photoswitching optoacoustic imaging modality
  https://cordis.europa.eu/project/id/101046667

- Finalist for the 2019 German President's Award for Innovation in Science and Technology (Deutscher Zukunftspreis) for the clinical translation of ultra-high magnetic field MRI
https://www.deutscher-zukunftspreis.de/de/team-3-2019

- 2021 Karl Heinz Beckurts Prize for outstanding achievements and pioneering work in the field of biomedical imaging
https://www.beckurts-stiftung.de/prof-dr-vasilis-ntziachristos-preistraeger-des-karl-heinz-beckurts-preises-2021/

- Innovation Award (2021) by the European Forum for Electronic Components and Systems
https://innoderm.munichimaging.eu/2021/11/24/24-november-2021-innoderm-recieves-the-european-commission-ecs-innovation-award/

- EBRAINS 2.0, EU Horizon Europe Programme, Co-PI: Prof. Dr. Dr. Svenja Caspers
EBRAINS 2.0: A Research Infrastructure to Advance Neuroscience and Brain Health | EBRAINS 2.0 | Project | Fact sheet | HORIZON | CORDIS | European Commission (europa.eu)

- EU FET Flagship "Human Brain Project" (HBP), Special Grant Agreement (SGA) 3, Co-PI: Prof. Dr. Dr. Svenja Caspers
Human Brain Project Specific Grant Agreement 3 | HBP SGA3 | Project | Fact sheet | H2020 | CORDIS | European Commission (europa.eu)

Start-up activities & technology references

- National Neuroimaging Network to advance diagnostic imaging technologies for neurodegenerative diseases
https://www.dzne.de/en/research/projects/national-neuroimaging-network/about-us/
https://www.frontiersin.org/articles/10.3389/fpsyt.2022.1010273/full
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8387546/

Flagship 3

Selected publications

- improved efficacy and broaden spectrum for genetic ‘prime-editing’
  https://www.nature.com/articles/s41592-023-02162-w

- Intron-encoded cistronic transcripts for minimally-invasive monitoring of coding and non-coding RNAs
  https://www.nature.com/articles/s41556-022-00998-6

- Non-invasive and high-throughput interrogation of exon-specific isoform expression
  https://www.nature.com/articles/s41556-021-00678-x

- Spatiotemporal, optogenetic control of gene expression in organoids
  https://www.nature.com/articles/s41592-023-01986-w

- Immunotheranostic target modules
  https://jeccr.biomedcentral.com/articles/10.1186/s13046-023-02912-w

- Immunotheranostics for prostate cancer managment
  https://www.mdpi.com/2072-6694/14/8/1996

- Targeting glioblastoma using logic-gated RevCAR-T’s
  https://www.frontiersin.org/articles/10.3389/fimmu.2023.1166169/full

- TREM2-activating antibody for therapeutic interventions in Alzheimer’s
  https://www.nature.com/articles/s41593-022-01240-0

- Engineered autoantibodies for T-cell therapy in encephalitis
  https://www.sciencedirect.com/science/article/pii/S0092867423010838?via%3Dihub

- In vitro model of blood brain barrier penetration.
  https://pubmed.ncbi.nlm.nih.gov/35599022/

- AAV vectors for disease modelling
  https://www.sciencedirect.com/science/article/pii/S1878747923001071?via%3Dihub

Major grants & awards

- ERC proof-of-concept grant 'InteRNAlizer'
  https://cordis.europa.eu/project/id/101138939

- EIC Pathfinder challenge CardioRepair
  https://cordis.europa.eu/project/id/101115574

- Horizon Europe MSCA-DN "TOLERATE" for autoimmune diseases
  https://cordis.europa.eu/project/id/101072729

- Carl Zeiss Center SynGen (novel solutions from synthetic DNA and AI
  https://www.carl-zeiss-stiftung.de/en/topics-projects/project-overview/detail/czs-center-syngen

- Horizon Europe MSCA-DN "OncoProTools"Theranostic UniCAR T-cell platform for therapy and imaging of cancer
  https://cordis.europa.eu/project/id/101073231

- Helmholtz International Lab: Monash-Helmholtz Laboratory for Radio-Immuno-Theranostics (MHELTHERA)

- BMBF funded Cluster4Future SaxoCell
  https://www.saxocell.de/en/home/

- BMBF funded TurbiCAR project: Zelluläre Immuntherapien
  https://www.gesundheitsforschung-bmbf.de/de/zellulare-immuntherapien-prazisionsmedizin-gegen-krebs-14166.php

- UniCAR immunotherapy in the Oncological Center of Excellence "NCT/UCC"
  https://www.nct-dresden.de/en/about-nctucc-dresden/research-structure/immunotherapy.html

- Banting Medal for Scientific Achievement 'Overcoming Obesity — The Discovery of Multi Receptor Drugs' Prof. Dr. Dr. Matthias Tschöp 2003
  https://www.adameetingnews.org/live-updates/session-coverage/banting-medal-recipient-discusses-emerging-promise-of-pharmacologic-treatment-for-obesity-and-diabetes/

Start-up activities & technology references

- Spin-off – T-knife
  https://www.mdc-berlin.de/news/press/berlin-start-t-knife-raises-110-million

- CARTemis
  https://www.mdc-berlin.de/news/press/starting-highly-promising-immunotherapies

- Bioproduction of therapeutic proteins
  https://www.ascenion.de/technologieangebote/hdlbp-overexpression-promotes-significantly-increased-expression-and-secretion-of-proteins

- Patents related to UniCAR, RevCAR technology and phase 1 trials in AML patients
  WO2019238722A1, US10766943B2

- Helmholtz Innovation Lab (Brain antibody-omics and B-cell Lab) a customized semi-automated platform for the generation of therapeutic human monoclonal autoreactive antibodies derived from patients' cerebrospinal fluid and blood samples.
  https://www.science.org/doi/10.1126/science.abm5835
  https://www.dzne.de/en/research/projects/baobab/

- GA-VAX: Advancing a vaccine targeting genetic amyotrophic lateral sclerosis
  https://www.embopress.org/doi/full/10.15252/emmm.201607054
  https://www.dzne.de/en/research/projects/ga-vax/welcome/

- ImmunX, an innovative platform using an ex-vivo human PBMC assay combined with automation, imaging and computational methods to systemically profile the human innate immune system.
  https://www.dzne.de/forschung/projekte/immunx/

Flagship 4

Selected publications

- Generation of human neuromuscular organoids (also patented)
  https://www.cell.com/cell-stem-cell/fulltext/S1934-5909(19)30525-9?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1934590919305259%3Fshowall%3Dtrue

- Advances in organoid and organ-on-chip models in the context of microbiome interactions
  https://doi.org/10.1016/j.chom.2021.04.002

- Engineered human heart tissue for intervention studies and drug discovery
  https://www.science.org/doi/10.1126/scitranslmed.abe8952

- Human blood vessel and kidney organoids as platforms to dissect (SARS-CoV-2) infections.
  https://www.sciencedirect.com/science/article/pii/S0092867420303998

- Differentiation of human iPSCs into pancreatic duct organoids on microchips
  https://www.nature.com/articles/s41551-021-00757-2

- Label-free imaging of 3D iPSC differentiation dynamics on chip
  https://www.cell.com/cell-reports-methods/fulltext/S2667-2375(23)00152-2

- Single-cell characterization of human iPSC-derived neovascularization in 3D microenvironments
  https://www.sciencedirect.com/science/article/pii/S2213671123003077?via%3Dihub

- 3D geometry & connectivity dictates neuronal activity
  https://www.sciencedirect.com/science/article/pii/S0142961219300237?via%3Dihub

- Microfluidic, artificial blood vessel scaffold for vascularized 3D tissue
  https://onlinelibrary.wiley.com/doi/full/10.1002/admt.201700246

- Microengineered airway lung chip modeling key features of viral-induced exacerbation of asthma
  https://doi.org/10.1165/rcmb.2020-0010ma

- Robotic fluidic coupling and interrogation of multiple vascularized organ chips
  https://www.nature.com/articles/s41551-019-0497-x

- Tuning Superfast Curing Thiol-Norbornene-Functionalized Gelatin Hydrogels for 3D Bioprinting
  https://onlinelibrary.wiley.com/doi/full/10.1002/adhm.202100206

- Novel Gelatin Hydrogel for Bioprinting
  https://www.mdpi.com/1422-0067/23/14/7939

- Shell engineering for culturing liver spheroids
  https://pubmed.ncbi.nlm.nih.gov/36942860/

- Nanosensors in clinical development of CAR-T cell immunotherapy
  https://www.sciencedirect.com/science/article/pii/S0956566322001646?via%3Dihub

- Droplet Microarray chips for miniaturized cell experiments, tumoroid/3D structures formation and screening
  https://www.nature.com/articles/s41598-023-32144-z
  https://onlinelibrary.wiley.com/doi/10.1002/adhm.202300591
  https://onlinelibrary.wiley.com/doi/10.1002/dro2.39
  https://onlinelibrary.wiley.com/doi/10.1002/adhm.202102493
  https://www.sciencedirect.com/science/article/pii/S2472630321000170?via%3Dihub
  https://www.sciencedirect.com/science/article/pii/S259000642100020X?via%3Dihub
  https://onlinelibrary.wiley.com/doi/10.1002/adma.202006434
  https://onlinelibrary.wiley.com/doi/10.1002/adtp.201900100
  https://onlinelibrary.wiley.com/doi/10.1002/smll.201901299
  https://onlinelibrary.wiley.com/doi/10.1002/adma.201502115

- Swarm Learning for decentralized and confidential clinical machine learning
  https://www.nature.com/articles/s41586-021-03583-3

- Human retinal organoids
  https://www.frontiersin.org/articles/10.3389/fncel.2023.1106287/full

- Optogenetics Actutators
  https://www.nature.com/articles/s41593-022-01113-6

- Fluid/biospecimen biomarkers
  https://www.sciencedirect.com/science/article/pii/S0165032721006169?via%3Dihub
  https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.062235

- Blood-based multi-omics-based high-dimensional biomarker development for patients with neurodegenerative diseases with a current emphasis on Alzheimer’s Disease:
  https://genomemedicine.biomedcentral.com/articles/10.1186/s13073-022-01112-z

Major grants & awards

- ERC Starting Deciphering biomechanics in COPD using 3D human airway disease models
  https://cordis.europa.eu/project/id/950219

- ERC Proof of Concept An Automated Platform for the Large-scale Production of Miniaturized Neuromuscular Organoids
  https://www.developmentaid.org/organizations/awards/view/469699/an-automated-platform-for-the-large-scale-production-of-miniaturized-neuromuscular-organoids-miniorg

- MERCK Sustainability Hub Grant: Generation of vascularized human liver tissue by integrating 3D-bioprinting and cellular self-assembly
  https://www.idd.tu-darmstadt.de/forschung_9/projekte_1/aktuelle_projekte_1/merck_sustainability_hub_lebergewebe.en.jsp

- Chan Zuckerberg Initiative: PCH2cure: Revealing Disease Mechanisms to Cure PCH2. Organoid models for hyperplasia.
  https://chanzuckerberg.com/patient-partnered-collaborations-for-rare-neurodegenerative-disease-rfa-grantees/

Start-up activities & technology references

- Helmholtz Validation microLumen Chip
  https://www.helmholtz-munich.de/en/newsroom/news-all/artikel/adaptable-micro-organ-for-inaccessible-human-tissue

- Helmholtz Validation Early prediction for neurodegenerative diseases on human-on-chip and AI technologies
  https://www.dzne.de/en/research/projects/i3d-markers/

- Neuland Innovation Award (funded by Bosch): VeganValve - 3D bio-printing of personalized bio-heart valves and cartilage implants from vegan gelatin materials (3 patent applications filed)
  https://kit-neuland.de/en/projects/awarding-of-the-neuland-innovation-awards-2023/

- 3D VitaPrint Printing of mucularized gut on a chip.
  https://mlr.baden-wuerttemberg.de/de/unser-service/presse-und-oeffentlichkeitsarbeit/pressemitteilungen/pressemitteilung/pid/landesregierung-foerdert-vier-projekte-zur-erforschung-von-ersatz-und-ergaenzungsmethoden-zum-tierver?highlight=tierschutz

- 3D BioNET KMU-NETC Initiative: 3D bioprinting SME network

- Patent applications covering the Droplet Microarray chip technology (KIT):
  - Method of producing 3D cell structures in hanging droplets and hanging droplet device comprising 3D cell structures (A15034). K. Demir, P. Levkin, A. Popova. EP 16000873.6, 18.04.2016 pending
  - Popova, Levkin Deutsche Patentanmeldung 10 2020 119 332.7 vom 22.07.2020. „Optical detection method".
  - Popova, Levkin, Chakraborty "Parallel direct isolation and manipulation of nucleic acid from cultured cells in nanoliter droplets". EP4186981 Published 31.05.2023.

Flagship 5

Selected publications

- Degradable implants, for instance bone fixators, no longer required upon fracture healing
  https://www.sciencedirect.com/science/article/abs/pii/S1742706116301477
  https://www.sciencedirect.com/science/article/pii/S0928493116312851?via%3Dihub

- Supporting conditions of endogenous tissue growth when cavities from for instance tumor resection are initially stabilized by biomaterials.
  https://www.sciencedirect.com/science/article/pii/S2452199X22002134
  https://www.sciencedirect.com/science/article/pii/S0928493121006044
  https://onlinelibrary.wiley.com/doi/abs/10.1002/jbm.b.34375

- Cell-enhanced implants becoming part of the biological network/the micro-environment.
  https://www.sciencedirect.com/science/article/pii/S0142961222006111

- Biomaterial-mediated immunomodulation, e.g. under conditions where transplants predominantly interact with and amplify immune cell signals
  https://www.cell.com/molecular-therapy-family/nucleic-acids/fulltext/S2162-2531(22)00009-9

- Based on the majority of healing effects consolidated by our immune system, material design and material effects need to be taken into account.
  https://www.sciencedirect.com/science/article/abs/pii/S1742706119306907?via%3Dihub
  https://www.sciencedirect.com/science/article/pii/S2452199X23000543

- Biomaterials for tissue regeneration
  https://www.tandfonline.com/doi/full/10.1080/08927014.2017.1303832
  https://www.sciencedirect.com/science/article/pii/S2589152923002053#:~:text=These%20results%20assume%20that%20at,are%20delivered%20via%20hematogenous%20route.

- Optimally balance biomaterials and living system interactions (e.g. materials providing cues for vascularization or to enhance regeneration
  https://iopscience.iop.org/article/10.1088/1758-5090/ac0a32

- Bio-instructive materials
  https://pubs.rsc.org/en/content/articlelanding/2021/cc/d1cc04237h

- Targeted micro-heterogeneity in bioinks for 3D printing
https://iopscience.iop.org/article/10.1088/1758-5090/acee22
Printed Electronic Devices and Systems for Interfacing with Single Cells up to Organoids
https://publikationen.bibliothek.kit.edu/1000165842

- Development of in situ imaging methods to correlate e.g. local features to the global properties to generate a mechanistic picture of the processes
https://doi.org/10.1016/j.bioactmat.2023.05.006

- Azobenzene-based optoelectronic transistors for neurohybrid building blocks
https://www.nature.com/articles/s41467-023-41083-2

- Validation of transparent and flexible neural implants for simultaneous electrophysiology, functional imaging, and optogenetics
https://pubs.rsc.org/en/content/articlelanding/2023/tb/d3tb01191g

- Pyramidal cell types drive functionally distinct cortical activity patterns during decision-making
https://www.nature.com/articles/s41593-022-01245-9

- Aptamer based biosensor platforms for neurotransmitters analysis
https://www.sciencedirect.com/science/article/abs/pii/S0165993623001085

- Highly Customizable 3D Microelectrode Arrays for In Vitro and In Vivo Neuronal Tissue Recordings
https://onlinelibrary.wiley.com/doi/full/10.1002/advs.202305944

Major grants & awards

- ERC starting grant – Biohybrid Synapses for Interactive Neuronal Networks
https://cordis.europa.eu/project/id/949478

- ERC consolidator grant SupraSense on highly specific yet easy-to-manufacture sensors for medical diagnostics and soft implants.
https://www.kit.edu/kit/english/pi_2023_002-erc-consolidator-grants-for-two-researchers-from-kit.php

- ERC advanced grant PRICOM
https://www.kit.edu/kit/english/pi_2022_035_two-erc-advanced-grants-for-scientists-of-kit.php

- BioMAT Foundry: KIT biomaterials platform for ML/AI driven automated development of biomaterials for 3D bioprinting.
https://www.healthtech.kit.edu/110.php

- ERC Starting Grant Brain Act
  https://www.fz-juelich.de/de/ibi/ibi-3/organization/neuroelectronics-interfaces-nei/erc-brain-act

- Helmholtz Young Investigator Group ‘State-dependent modulation of cortical circuits during decision-making’
  Helmholtz Young Investigator Group: State-dependent modulation of cortical circuits during decision-making (fz-juelich.de)

Start-up activities & technology references

- Patent: Liquipolymers: EP3590977B1

- Patent applications (FZJ):

  - Viviana Rincõn Montes, Simon Musall, Erkan Yilmaz, Sofiia Demchenko, and Andreas Offenhäusser. “Mehrsondensysteme für elektrogenes Gewebe, Verfahren zu deren Herstellung und Verwendungen”. Patent application: DE 102024110006.0, filed on April 10, 2024.

  - Jamal Abu Shihada, Marie Jung, Lina Koschinski, Viviana Rincõn Montes, and Andreas Offenhäusser. "Herstellung dreidimensionaler Elektroden mittels schablonengestützter elektrochemischer Abscheidung". Patent application: DE 102023102460.4, filed on February 1, 2023.

  - Viviana Rincõn Montes, Marie Jung, Jamal Abu Shihada, Lina Koschisnki, and Andreas Offenhäusser. "Herstellung dreidimensional strukturierter Elektrodenlagen, insbesondere im Kirigami-Prinzip". Patent application: DE 102023102257.1, filed on January 31, 2023.

Flagship 6

Selected publications

- Microbial optogenetics: Biosensors and light responsive actuators
  https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cbic.201500609

- Lighgt-controlled cell factories
  https://journals.asm.org/doi/10.1128/aem.01457-16

- Mining new CRISPR-Cas12a2 nucleases with unique functions
  https://www.nature.com/articles/s41586-022-05559-3

- Method for RNA recording in single bacterial cells
  https://www.nature.com/articles/s41587-022-01604-8

- CRISPR-driven editing in bacteria
  https://www.nature.com/articles/s41467-023-36283-9

- Cell-free method to boost DNA transformation in non-model bacteria
  https://www.biorxiv.org/content/10.1101/2023.09.16.557782v1

- Preprint (in revision at *Science*) Evolution Inspired Engineering of Megasynthetases
  https://www.biorxiv.org/content/10.1101/2022.12.02.518901v2

- De novo design of artificial BGCs
  https://www.nature.com/articles/nchem.2890
  https://www.nature.com/articles/s41557-019-0276-z

- Bio-combinatorial approaches to designing artificial natural product producing BGCs
  https://doi.org/10.1101/2020.05.06.080655
  https://doi.org/10.1101/2021.10.25.465728
  https://doi.org/10.1021/acssynbio.3c00295

- Single cell microfluidics for bioprocess development
  https://www.sciencedirect.com/science/article/pii/S0958166914000391?via%3Dihub

- DL software for cell segmentation
  https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0277601

Major grants & awards

- ERC proof-of-concept grant (CRISPR-SELECT)
- Helmholtz Young Investigator: Synthetic Biology of Microbial Natural Products
- Helmholtz HIP Project: SATOMI (2020 - 2022)
  https://helmholtz-imaging.de/project/satomi/
- Helmholtz HIP Project: EMSIG (2023 - 2024)
  https://helmholtz-imaging.de/project/emsig/
- Optogenetics: Biosensors & light responsive actuators MibiNet
  https://www.sfb1535.hhu.de/
- Microbial communities and networking MibiNet
  https://www.spp2170.uni-stuttgart.de/

Start-up activities & technology references

- Startup: Myria Biosciences AG, Basel (Switzerland)
  https://www.myria.bio/

Biomedical Engineering Solutions Workshop

Helmholtz Head Office Berlin,
Room K1A/B, Anna-Louisa-Karsch-Straße 2, 10178 Berlin

Agenda

November 3, 2023

9.00 am	**Welcome** Katja S. Grossmann (Helmholtz Head Office)
9.05 am	**Agenda and goals** Chair: Holger Gerhardt (MDC)
9.20 am	**Impulse talk on "BioEngineering Solutions"** Vasilis Ntziachristos (Helmholtz Munich), incl. 5 min. discussion
9.40 am	**Results of the questionnaire** Thomas Schwarz-Romond (Helmholtz Munich)
9.50 am	**Helmholtz as driver of a bioengineering agenda** Discussion in breakout groups according to guiding questions (Rooms; K3A, K3B, K1A/B, 207) Guiding questions: What are current, bioengineering-related, major research activities at your center? What are the grand challenges for which bioengineering can become a game changer? What factors (e.g. partnerships, disciplines, institutional anchoring, infrastructures, policies) are crucial to propel Helmholtz to the forefront of bioengineering and to solve these grand challenges? What structural measures (e.g. patent and start-up focused research, PhD/Post-Doc training etc.) do you consider as most beneficial?
11.00 am	**Coffee break** in lobby

11.30 am	Presentation of results and matching One to two persons per breakout group present the results 10 minutes per group incl. discussions Chair: Holger Gerhardt (MDC)
12.30 am	Funding opportunities Korinna Strobel (Head of Strategy, Helmholtz Head Office) and Jens Jäger (Helmholtz Brussels Office)
12.45 pm	Summary and next steps Chair: Holger Gerhardt (MDC)
1.00 pm	Departure

Participants

Member of the Helmholtz Senate

Rita Schmutzler, University Hospital Cologne

Helmholtz directors

Josef Penninger, HZI
Maike Sander, MDC

Helmholtz researchers

Hayder Amin, DZNE
Larysa Baraban, HZDR
Chase Beisel, HZI (HIRI)
Kenan Bozhüyük, HZI (HIPS)
Oliver Bruns, DKFZ (NCT-Dresden)
Ali Ertürk, Helmholtz Munich
Anja Feldmann, HZDR
Holger Gerhardt, MDC
Mina Gouti, MDC
Richard Harbottle, DKFZ
Ulrich Kalinke, HZI
Michael Kaminski, MDC
Dietrich Kohlheyer, FZJ
Mark Ladd, DKFZ
Markus Landthaler, MDC
Pavel Levkin, KIT
Janna Nawroth, Helmholtz Munich
Vasilis Ntziachristos, Helmholtz Munich
Ute Schepers, KIT
Stefanie Speidel, DKFZ (NCT-Dresden)
Andre Stiel, Helmholtz-Munich
Jörg Vogel, HZI (HIRI)
Gil Westmeyer, Helmholtz Munich
Regine Willumeit-Römer, Hereon
Kristof Zarschler, HZDR