Project Proposals: Menachem Stern

Project Title: Neuromorphic Soft Matter for Adaptive Biointerfaces: Deciphering the Brain's Language Through Physically Embodied Neural Networks

1. Project Rationale and Objectives

- **Societal Problem:** Neurological disorders, including epilepsy, Parkinson's disease, and Alzheimer's disease, impose a significant burden on individuals and healthcare systems worldwide. Current treatment options often provide symptom management but fall short of addressing the underlying complexities of neural communication and dysfunction. This project seeks to bridge the gap between human neural networks and artificial systems, enabling a better understanding of the brain and novel therapeutic approaches.

- **Scientific Problem:** Understanding how information is processed and encoded in the brain remains a fundamental challenge in neuroscience. Current computational models, while powerful, lack the physical embodiment and complexity inherent to biological neural networks. This limits their ability to capture the nuances of synaptic plasticity, dynamic feedback loops, and emergent behaviors found in the brain.

- **Technological Problem:** The development of biocompatible, adaptive interfaces for interacting with neural tissues presents a significant challenge. Traditional rigid electrodes limit the long-term stability and functionality of neural interfaces due to mechanical mismatch and immune responses. Intelligent soft matter offers a unique opportunity to design materials that seamlessly integrate with delicate neural tissues, facilitating long-term monitoring and modulation of brain activity.

- **EU Call Alignment:** This project directly aligns with the Horizon Europe Health Cluster call for proposals on "Understanding the Brain" and "Advanced Technologies for Health". It specifically addresses the need for innovative approaches to decipher the complexity of brain function and develop novel therapeutic strategies for neurological disorders.

- **Project Vision:** To develop neuromorphic soft materials that act as physically embodied neural networks, enabling a deeper understanding of brain function and opening new frontiers in the treatment of neurological disorders.

- **Measurable Impacts:**
    - **KPI 1:** Design and fabricate neuromorphic soft materials that exhibit functional properties of neural networks, including synaptic plasticity, signal propagation, and learning. Success will be measured by demonstrating these functionalities in controlled laboratory settings using established electrophysiological and imaging techniques.
    - **KPI 2:** Develop biocompatible and adaptive neural interfaces based on neuromorphic soft materials. Success will be assessed by achieving long-term stability and functional integration with neural tissues in vivo, demonstrated through chronic implantation studies in animal models.
    - **KPI 3:** Translate the insights gained from neuromorphic soft matter to develop novel therapeutic strategies for specific neurological disorders. Success will be measured by demonstrating therapeutic efficacy in ameliorating disease symptoms or restoring lost functionalities in pre-clinical animal models.

- **Contribution to EU Policy Priorities:** This project supports the EU's commitment to advancing healthcare and promoting innovation within the European Research Area. It aligns with the European Green Deal by prioritizing biocompatible materials and minimizing environmental impact. The project also contributes to the digital transformation by pushing the boundaries of bio-electronic technologies.

2. State of the Art and Novelty

Current State of the Art:

- **Neuroscience:** Understanding of neuronal signaling and network dynamics is rapidly growing, but a complete picture of how information is processed and encoded in the brain remains elusive. Computational models are limited by their lack of physical embodiment.
- **Soft Matter:** Advanced functional materials are being developed, but the ability to create truly intelligent soft matter capable of mimicking neural function is in its early stages.
- **Neural Interfaces:** Existing neural interfaces based on rigid electrodes have limitations in long-term stability, biocompatibility, and adaptive capabilities.

Project Novelty:

- **Physically Embodied Neural Networks:** This project introduces a novel approach by creating physically embodied neural networks based on intelligent soft matter. This moves beyond traditional computational models, allowing for the investigation of neurocomputational principles within a material framework.
- **Bio-inspired Material Design:** The project will leverage biological concepts of neural plasticity and signal transduction to design soft materials that exhibit analogous

functionalities.
- **Adaptive Biointerfaces:** The developed materials will be engineered to seamlessly integrate with neural tissues, enabling adaptive, long-term monitoring, and modulation of brain activity.

Unique Selling Points (USPs):

- **Novel Material Platform:** The project introduces a new paradigm of neuromorphic soft matter for investigating brain function.
- **Direct Translational Potential:** The development of highly biocompatible and adaptive neural interfaces has the potential to revolutionize the treatment of neurological disorders.
- **Interdisciplinary Approach:** The project combines cutting-edge research in materials science, neuroscience, and engineering to create a new and exciting field of inquiry.

Cutting-Edge Research:

- The project represents a unique approach to understanding the brain and developing novel therapeutic interventions.
- It aligns with global research efforts to create bio-inspired, intelligent materials, strengthening the EU's position at the forefront of scientific innovation.

Chosen Collaborators and Research Domain Field Shift:

For this project, the ideal collaborators are **Wolfgang Parak**, with his expertise in synthesis and functionalization of quantum dots, and **Rene van Roij**, with his expertise in theoretical modelling of soft matter. Combining the knowledge from both domains will bring a novel solution to problem of mimicking neuron in smart materials. Parak's work on functionalized nanoparticles and their biocompatibility provides the foundation for creating the "neurons" of our system, while van Roij's expertise in soft matter theory and computational modeling provides the tools for understanding their collective behavior and dynamics.

Research Domain Field Shift - Neurons in biological systems are complex entities that exhibit various functionalities related to signal transmission, processing, and modulation. We propose a new concept using functionalized quantum dots (QDs) as artificial neurons within a soft matter matrix to achieve cognitive-like properties, mimicking the basic functionalities of neurons within a material context. By encapsulating tailored QDs with specific light-emitting and light-sensing properties, these artificial neurons will be able to communicate with each other via controlled light signals within the material itself, similar to the electrochemical signaling in biological neuron networks. This will be achieved using the expertise of WP in synthesizing and controlling the QDs' properties and using RvR's expertise in developing a theoretical model to control and orchestrate a signal within the polymer network.

3. Alignment with EU Priorities

Contribution to EU Strategic Objectives:

- **Horizon Europe Missions:** This project directly aligns with the Horizon Europe mission on "Cancer" and "Healthy oceans, seas, coastal and inland waters" by fostering the development of new therapeutic strategies for brain cancers and promoting sustainable materials and technologies.
- **Sustainable Development Goals (SDGs):** The project aligns with SDG 3 ("Good Health and Well-being") and SDG 9 ("Industry, Innovation and Infrastructure") by advancing healthcare technologies and promoting scientific research and innovation within the EU.

EU-Specific Challenges and Opportunities:

- **Challenge:** The EU faces an aging population and a growing prevalence of neurological disorders. This project addresses this challenge by developing novel therapeutic strategies.
- **Opportunity:** The EU is a global leader in materials science and bio-electronic technologies. This project leverages existing expertise to strengthen the EU's competitive advantage in these areas.

Integration of Cross-Cutting Issues:

- **Inclusivity:** The project will promote inclusivity by involving researchers from diverse backgrounds and ensuring that the developed technologies are accessible to all.
- **Sustainability:** Biocompatible materials and energy-efficient designs will be prioritized to minimize the environmental impact of the research.

Added Value for European Citizens:

- **Improved Healthcare:** The project's goal is to develop novel, less invasive treatments for neurological disorders, improving the quality of life for European citizens.
- **Economic Growth:** The development of cutting-edge technologies can create new industries and jobs within the EU.

4. Methodological Excellence

Innovative Methodologies:

- **Material Synthesis and Characterization:** The project will employ state-of-the-art techniques in materials science to synthesize and characterize intelligent soft materials,

including the use of stimuli-responsive polymers, nanoparticles, and biocompatible components. Advanced microscopic techniques like AFM and STM will be used by WP's group to ensure reproducibility of the synthesis and to control the properties of materials.

- **Computational Modeling:** Advanced computational modeling techniques, including molecular dynamics simulations and finite element methods (FEM) developed by RvR's group, will be used to guide material design, optimize properties, and predict material behavior in complex biological environments. Machine learning will be used to create predictive models for self-organizing behavior in these new materials and enable the adaptation of structural networks within materials.
- **Neuroscience Techniques:** The project will utilize electrophysiology, calcium imaging, and optogenetics to study the interaction of neuromorphic soft materials with neural tissues. This will be done in a controlled environment to understand the biocompatibility and the interaction of materials in controlled environment and will be used in vivo for further research development.
- **Bio-Integration and Device Fabrication:** Microfabrication techniques will be employed to create biocompatible interfaces and integrate the intelligent materials with microfluidic devices for testing their performance in vitro and in vivo.

Scientific Rigor and Reproducibility:

- **Open Science Principles:** The project will adhere to Open Science principles by sharing data, methodologies, and results through open-access publications and data repositories.
- **Reproducibility Plan:** A detailed reproducibility plan will be developed outlining the protocols for material synthesis, characterization, device fabrication, and experimental procedures. This plan will be shared with all consortium members to ensure consistency and transparency in research methods. Standardized protocols and detailed documentation will be established to ensure reproducibility.
- **Independent Validation:** A portion of the budget will be allocated for independent validation studies by external collaborators. This ensures impartial assessment and rigorous scrutiny of the results.

Interdisciplinarity and Synergies:

- **Consortium Structure:** The project consortium will bring together experts in soft matter physics, neuroscience, engineering, and clinical research.
- **Joint Workshops and Meetings:** Regular meetings and workshops will foster communication and collaboration between researchers across disciplines. Weekly meetings and online communication platform will allow for continuous exchange of data and ideas.
- **Shared Training and Knowledge Transfer:** The project will involve cross-disciplinary training activities, enabling researchers to develop skills and knowledge in areas outside of their primary discipline. The joint training will be carried out in both research groups

using expertise from both sides.

Stakeholder Engagement:

- **Patient Advocacy Groups:** The consortium will engage patient advocacy groups for neurological disorders to ensure development of relevant and impactful solutions.
- **Industry Partners:** Collaboration with medical device companies will be explored to facilitate the translation of research outcomes into real-world products.

5. Expected Impacts and EU Added Value

Economic Benefits:

- **New Market Opportunities:** The development of neuromorphic soft matter has the potential to create a new market for bio-electronic technologies, leading to economic growth and job creation in the EU.
- **Reduced Healthcare Costs:** Effective treatments for neurological disorders can significantly reduce healthcare costs in the long run.

Social Benefits:

- **Improved Quality of Life:** Novel therapies based on neuromorphic soft matter can improve the quality of life for individuals suffering from neurological disorders.
- **Increased Accessibility:** Biocompatible and adaptive devices based on soft matter can improve accessibility for individuals with disabilities.

Environmental Benefits:

- The use of biocompatible and biodegradable materials will minimize the environmental footprint of the developed technologies.
- Increased understanding of the brain through non-invasive techniques can lead to the development of efficient and sustainable solutions for brain-related disorders.

EU Leadership in Science, Technology, and Innovation:

- This project positions the EU at the forefront of research in intelligent soft matter and bio-electronic technologies.
- It strengthens the EU’s role in creating groundbreaking solutions for global healthcare challenges.

Impact on Specific Sectors:

- **Healthcare:** New therapeutic strategies for neurological disorders.
- **Biotechnology:** New opportunities for biomaterial development.
- **Electronics:** Advancements in flexible and biocompatible electronics.

Strengthening EU Collaboration:

- **Consortium Diversity:** The consortium will include partners from multiple EU countries, promoting cross-border collaboration within the European Research Area.
- **Knowledge Transfer:** The project will disseminate knowledge and expertise through publications, conferences, and training programs, strengthening the EU's scientific workforce.

Benefits for European Citizens:

- Improved healthcare outcomes through novel therapies.
- Economic growth and new job opportunities in emerging technology sectors.
- Enhanced quality of life through advanced technologies.

6. Risk Management

Critical Risks:

- **Technical:**
  - Difficulty in achieving desired material properties and functionalities.
  - Challenges in bio-integration and device fabrication.
- **Financial:**
  - Potential budget overruns due to unforeseen technical challenges.
- **Organizational:**
  - Delays or difficulties in communication and coordination within the consortium.

Mitigation Strategies:

- **Technical:**
  - Extensive pilot studies will be conducted to assess the feasibility of proposed materials and methodologies before full-scale development.
  - Regular monitoring and assessment of technical results will allow for timely adjustments to the research plan.
- **Financial:**
  - A detailed risk assessment will be conducted to identify potential sources of budget overruns.
  - A contingency plan will be in place to address unforeseen financial challenges.
- **Organizational:**

    - Clear roles and responsibilities will be established for all consortium members.
    - Regular communication and project management meetings will ensure timely progress and effective coordination.

EU Compliance:

- **Data Protection (GDPR):** The project will comply with GDPR regulations in the collection, storage, and processing of all data.
- **Ethical Considerations:** The project will be subject to ethical review by the relevant institutional review boards (IRBs).

Contingency Plans:

- If a critical technical hurdle is encountered, alternate approaches will be investigated.
- If a partner experiences delays or difficulties, other consortium members will provide support to minimize disruption to the project.

7. Resources and Justification for EU Funding

Project Budget:

- The total project budget is estimated at €5 million over 4 years.
    - The budget is aligned with the cost guidelines set forth in the Horizon Europe program guidelines.
- Detailed justification for all requested funds will be provided in the budget proposal.

Budget Distribution:

- Personnel Costs (40%): Skilled researchers and technicians required to conduct the research.
- Equipment and Consumables (30%): Materials, consumables, and specialized equipment for material synthesis, characterization, and device fabrication.
- Travel and Subsistence (10%): Facilitating collaboration through meetings, workshops, and conferences.
- Dissemination and Exploitation (10%): Disseminating project results and exploring commercialization opportunities.
- Overheads and Management (10%): Administration, project management, and overhead costs.

Human Resources:

- The consortium brings together experienced researchers with expertise in soft matter

physics, material science, synthetic biology, nanoengineering, neuroscience, and clinical medicine.
- A detailed breakdown of the expertise, roles, and responsibilities of each team member will be provided in the proposal.

Resource Optimization:

- Each partner will contribute their existing resources and facilities to the project.
- A clear division of responsibilities ensures the avoidance of redundancy and promotes efficient resource allocation.

EU-Specific Facilities: The project will leverage existing EU research infrastructures, such as synchrotron facilities and advanced microscopy centers, to conduct specific experiments requiring specialized equipment.

8. Work Plan and Deliverables

Work Packages:

- WP1: Design and Synthesis of Neuromorphic Soft Materials (WP, RvR).
- WP2: Modeling, Simulation, and Optimization of Cognitive Material Properties (RvR).
- WP3: Biocompatible Interfaces and Devices (WP, RvR).
- WP4: In Vitro Evaluation and Biocompatibility (WP).
- WP5: In Vivo Assessment and Testing (WP).
- WP6: Dissemination and Exploitation (WP, RvR).

Milestones:

- Year 1: Demonstration of key material properties in laboratory conditions – publications.
- Year 2: Development of functional biointerfaces and prototypes of smart devices – patent application.
- Year 3: In vitro validation of biocompatibility and performance of the materials – publications.
- Year 4: In vivo testing in animal models and completion of proof-of-concept studies - publications.

Deliverables:

- Prototype neuromorphic soft materials with desired functionalities.
    - Biocompatible neural interfaces for long-term monitoring and stimulation.
- Proof-of-concept data demonstrating therapeutic potential in animal models.
- Publications in peer-reviewed journals.

- Patents and technology transfer agreements.
- Dissemination materials (website, brochures, presentations).

Roles and Contributions:

- Each consortium partner will have clearly defined roles and responsibilities.
- A project management framework will ensure effective communication, coordination, and timely delivery of work package outputs.

Progress Tracking:

- Regular project meetings and reports will be used to monitor progress against milestones.
- Key performance indicators (KPIs) will be established for each work package to evaluate achievement of EU-defined success criteria.

9. Consortium and Collaboration

Consortium Partners:

- WP - [Name of Wolfgang Parak's Institution]: Expertise in nanomaterial synthesis, characterization, bioconjugation techniques, and bio-integration.
- RvR - [Name of Rene van Roij's Institution]: Expertise in theoretical modeling of soft matter systems, statistical mechanics, computational simulations, and machine learning integration.
- Name of Institution 3: Expertise in neuroscience, electrophysiology, and animal model development.
- Name of Institution 4: Expertise in microfabrication, device design, and bio-integrated electronics.

Consortium Diversity:

- The consortium will be composed of leading research groups from multiple EU countries, ensuring geographical diversity.
- The team comprises experts from different scientific disciplines, fostering a high level of interdisciplinary collaboration.

Collaboration Mechanisms:

- Weekly virtual meetings, biannual physical meetings, and shared online platforms will be implemented for effective communication and coordination between consortium members.
- A dedicated project manager will oversee the project's progress and facilitate

communication between partners.

Synergies and International Collaboration:

- Synergies with existing EU-funded projects and international collaborations will be explored to leverage knowledge, expertise, and resources.
- Joint workshops and information exchange will occur with other research initiatives in the field of Intelligent Soft Matter.

Knowledge Transfer and Capacity Building:

- The project will promote knowledge transfer between consortium partners through the exchange of researchers, joint publications, and the organization of training workshops.
- The project will provide training and mentoring opportunities for young researchers, strengthening the EU's scientific workforce.

10. Dissemination, Exploitation, and Communication

Dissemination Strategy:

- **Peer-Reviewed Publications:** Project results will be disseminated through high-impact scientific publications in peer-reviewed journals.
- **Conferences and Workshops:** The consortium will actively participate in international conferences and organize workshops to present their findings to the scientific community.
- **Open Access Repositories:** All publications and data will be made available in open-access repositories to ensure wide dissemination and knowledge sharing.

Exploitation Strategy:

- **Intellectual Property Protection:** Relevant innovations will be protected through patents or other forms of intellectual property rights.
- **Technology Transfer:** Collaboration with industry partners will be pursued to explore commercialization opportunities for the developed technologies.
- **Spin-off Potential:** The project consortium will assess the feasibility of creating spin-off companies based on the project's intellectual property.

Communication Plan:

- **Project Website:** A dedicated website will be created to provide information about the project, its goals, and its results.
- **Social Media:** Social media channels will be used to engage with the public and disseminate project updates.

- **Press Releases and Media Coverage:** Press releases will be issued to announce significant achievements.
- **Public Engagement Activities:** Workshops and public lectures will be organized to raise awareness about the project and its relevance to society.

Alignment with EU Requirements:

- The dissemination and communication plan will comply with the requirements of the Horizon Europe program and will promote Open Science principles.
- The project will actively participate in the Horizon Results Platform and other EU-driven dissemination initiatives.

11. Ethics

Ethical Principles and Guidelines:

- The project will adhere to the highest ethical standards in all research activities, following the principles outlined in the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers.
- All experimental procedures involving animals will be conducted in accordance with EU Directive 2010/63/EU on the protection of animals used for scientific purposes.
- Ethical considerations related to the potential impact of intelligent soft matter technologies will be carefully considered and addressed throughout the project.

Data Privacy and GDPR Compliance:

- The project will comply with the General Data Protection Regulation (GDPR) in the collection, use, processing, storage, and disposal of personal data.
- A data management plan (DMP) will be developed outlining data storage and security protocols.

Societal and Environmental Risks:

- Potential risks associated with the use of nanomaterials will be carefully assessed and minimized.
- The project will prioritize the use of environmentally friendly materials and processes to minimize its environmental footprint.

Inclusivity, Fairness, and Transparency:

- The consortium will promote inclusivity and diversity in all project activities.
- A clear communication plan will ensure transparency in the project's progress and results.

Responsible Resource Use:

- The project will strive to minimize its environmental impact by adopting sustainable practices, minimizing waste, and using renewable energy sources where possible.

12 Sustainability and Scalability

Post-Funding Sustainability:

- **Exploitation Plan:** The consortium will develop a robust exploitation plan outlining strategies for commercializing the project's outcomes through licensing agreements and the creation of spin-off companies.
- **Seeking Additional Funding:** Efforts will be made to secure follow-up funding from national and European sources to continue research and development activities after the Horizon Europe grant period.

Scalability:

- The project's outcomes will be designed to be scalable, enabling their wider adoption and implementation in real-world settings.
- The consortium will investigate partnerships with industry to facilitate the manufacturing and distribution of the developed technologies.

Environmental Sustainability:

- The project will prioritize biocompatible and biodegradable materials to ensure the environmental sustainability of its outputs.
- Energy-efficient designs will minimize energy consumption.

Economic Sustainability:

- The project's outcomes are expected to stimulate economic growth within the EU, creating new jobs and boosting innovation within sectors like healthcare and biotechnology.

Social Sustainability:

- The project's outputs aim to be affordable and accessible, promoting broader access to these technologies and ensuring they benefit a diverse population.

13. Monitoring and Evaluation

Key Performance Indicators (KPIs):

- Demonstration of a fully functioning system of artificial neurons within a soft material. This will be evaluated by the development of computational models that simulate the behavior of the materials, validate the models through experiments and demonstrate integration with biological systems for sensing and responding.
- Demonstrate controlled and programmable communication between adjacent artificial neurons within the soft material context. The functionality will be tested through a combination of spectroscopic and microscopic characterization methods.
- Successful integration and long-term performance of the designed materials when interfacing with biological tissues. This successful outcome will be measured by the performance of the material under biological conditions and its ability to record and interact with the biological system.
- The number of publications in high-impact journals.
- The number of patents filed.
- The number of spin-off companies created.

Evaluation Frameworks:

- A steering committee composed of external experts will provide regular feedback and guidance on the project's progress.
- Peer reviews will be regularly conducted to assess the quality and impact of the research outcomes.

Continuous Improvement:

- Regular project meetings and progress reports will be used to identify areas for improvement and adjust research plans accordingly.
- Stakeholder feedback will be incorporated into project evaluations and used to refine project goals and methodologies.

Success Criteria:

- **Scalability:** The project's success will be determined, in part, by its ability to be scaled up for wider adoption and implementation.
- **Commercialization Potential:** The success will also be measured by the ability to commercialize the developed technologies.
- **Impact on Neurological Disorders:** Ultimately, the project's success will be determined by its impact on the understanding and treatment of neurological disorders.

14. Strategic Outlook

EU Leadership:

- This project positions the EU at the forefront of research in intelligent soft matter and its intersection with neuroscience.
- It fosters expertise in a rapidly growing area of science and technology with significant economic and societal implications.

Emerging Technologies:

- The project will benefit from advancements in AI, machine learning, and materials science, continuously adjusting research plans to incorporate the latest advancements relevant to this field.

Contribution to EU Policy:

- The project's outputs will inform future EU policies regarding research funding, ethical considerations related to intelligent materials, and the development of new healthcare technologies.

Follow-Up Research:

- The project is expected to stimulate further research in this field, leading to new funding proposals, collaborations, and spin-off activities.

Legacy:

- The project's legacy will be a strengthened research and innovation ecosystem in the EU, a more comprehensive understanding of the brain, and novel technologies that improve healthcare outcomes for European citizens.

15. Gender Equality

Gender Equality Plan:

The project will implement a gender equality plan to ensure equal opportunities for all team members during the recruitment phase and throughout the project duration:

- **Recruitment:**
  - Open and transparent recruitment procedures will be used to attract a diverse pool of applicants.
  - Gender balance will be considered a priority during the selection process, adhering to EU policy on equal opportunities for all genders.

- **Career Development:**
  - The project will provide equal opportunities for professional development and training to all team members.
  - Mentorship programs will be established to support female researchers in their career progression.
- **Work-Life Balance:**
  - Flexible working arrangements and support for childcare will be offered to ensure a healthy work-life balance for all team members, regardless of gender.
- **Dissemination and Visibility:**
  - The project will highlight the contributions of female researchers through publications, presentations, and press releases. Gender-balanced representation for authorship and presentation of data and results will be a top priority.
  - Female researchers will be actively encouraged to participate in networking opportunities and high-visibility events to enhance their career development and increase the recognition of female researchers in the field.

This initiative reflects the EU's commitment to achieving gender equality in research and innovation, ensuring that the project benefits from the contributions of all researchers, regardless of their gender.

This detailed project catechism provides a substantial roadmap for how to develop and execute a high-impact research project in the field of intelligent soft matter, utilizing the combined expertise of Wolfgang Parak and Rene van Roij. It is designed to be aligned with the EU Grant requirements and ensures both scientific rigor and societal relevance. Furthermore, the project's interdisciplinary nature and integration with emerging technology trends ensure that it remains relevant and impactful on a global scale.