SYSTEMS BIOLOGY IN TWO DIMENSIONS: UNDERSTANDING AND ENGINEERING MEMBRANES AS DYNAMICAL SYSTEMS

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Theme:

The theme of our NIH Nanomedicine Development Center is design of biomimetic nanoconductors and devices utilizing nanoconductors. The model theoretical systems are native and mutant biological channels and other ion transport proteins and synthetic channels, and heterogenous membranes containing channels and transporters. The model experimental systems are engineered protein channels and synthetic channels in isolation, and in self-assembled membranes supported on nanoporous silicon scaffolds. The ultimate goal is to understand how biomimetic nanoscale design can be utilized in devices to achieve the functions that membrane systems accomplish in biological systems: a) Electrical and electrochemical signaling, b) generation of osmotic pressures and flows, c) generation of electrical power, and d).energy transduction.

Broad Goals:

Our Center's broad goals are:

1. To advance theoretical, computational, and experimental methods for understanding and quantitatively characterizing biomembrane and other nanoscale transport processes, through interactive teams doing collaborative macromolecular design and synthesis, computation/theory, and experimental functional characterization.
2. To use our knowledge and technical capabilities to design useful biomimetic devices and technologies that utilize membrane and nanopore transport.
3. To interact synergistically with other workers in the areas of membrane processes, membrane structure, the study of membranes as systems biomolecular design, biomolecular theory and computation, transport processes, and nanoscale device design.
4. To disseminate enhanced methods and tools for: theory and computation related to transport, experimental characterization of membrane function, theoretical and experimental characterization of nanoscale fluid flow, and nanotransport aspects of device design.

Initial Design Target:

A biocompatible biomimetic battery (the "biobattery") to power an implantable artificial retina, extendable to other neural prostheses. Broad design principles are suggested by the electrocyte of the electric eel, which generates large voltages and current densities by stacking large areas of electrically excitable membranes in series. The potential advantages of the biomimetic battery are lack of toxic materials, and ability to be regenerated by the body's metabolism.

Major Emergent Reality Constraints:

The development and maintenance of the electrocyte in the eel are guided by elaborate and adaptive pathways under genetic control, which we can not realistically hope to include in a device.

Our approach will include replacing the developmental machinery with a nanoporous silicon scaffold, on which membranes will self-assemble. The lack of maintenance machinery will be compensated for by making the functional components of the biobattery from more durable, less degradable molecules.

Initial Specific Activities:

1. Making a detailed dynamical model, including electrical and osmotic phenomena and incorporating specific geometry, of the eel electrocyte.
2. Do initial design of biomimetic battery that is potentially capable of fabrication/self assembly.
3. Search for more durable functional analogues of the membranes and transporters of the electrocyte. Approaches being pursued include designing beta-barrel functional analogues for helix-bundle proteins, mining extremophile genomes for appropriate transporters, chemically functionalized silicon pores, and design of durable synthetic polymer membranes that can incorporate transport molecules by self-assembly. These approaches combine information technology, computer modeling, and simulation, with experiment.
4. Fabrication of nanoporous silicon supports for heterogenous membranes in complex geometries.

Organizational Principles of Center:

Our core team is supported by the NIH Roadmap grant, but we welcome collaborations with all workers with relevant technologies and skills, and aligned interests.