Oregon State University
Corvallis, OR
Kristen Buck, Mya Breitbart
$1,200,000

To determine whether viruses store iron in the surface ocean

In nearly half of the global surface ocean, iron is the primary limiting nutrient for phytoplankton that support the marine food web, fix carbon, and drive the biological pump of atmospheric carbon dioxide to the ocean interior. Due to iron's virtual insolubility in oxygen-rich ocean conditions, nearly all dissolved iron is bound to organic matter. The nature of these organic iron-binding ligands governs iron bioavailability; however, the origin of as much as 90% of the organic dissolved iron pool is unknown. The Oregon State University/ University of South Florida team proposes that marine viruses - highly abundant biological entities within the dissolved size fraction - may hold the key to unlocking an enduring mystery of ocean iron chemistry. Building on evidence demonstrating the presence of iron in viruses that infect non-marine bacteria, as well as conserved iron-binding sequence motifs in marine virus genomes, they hypothesize that marine viruses incorporate iron into their structures and represent a significant form of organic dissolved iron in the oceans. To test this hypothesis, they will use synergistic culture- and field-based approaches, combined with microscopy and high-resolution mass spectrometry, to quantify the elemental composition of marine viruses. Finally, they will perform experimental studies to assess the stability of iron in marine viruses and determine its bioavailability to marine microorganisms through known acquisition strategies. Revealing the presence of iron in marine viruses would provide a fundamentally new perspective on iron chemistry, identifying a novel, overlooked, and ubiquitous organic iron pool with major influences for the biogeochemical cycling of this vital micronutrient.

Princeton University
Princeton, NJ
Peter Melchior, Joshua Winn
$900,000

Exoplanet Discovery with Neural Ordinary Differential Equations

One of the most important goals in astronomy is finding Earth-like planets around other stars. The most promising approach, high-precision radial velocity (RV) spectroscopy, is capable of detecting planets more massive than Earth, or closer to their stars than Earth. Further progress is hampered by the turbulence in the stellar atmospheres, which produces noise that is one order of magnitude larger than the exoplanet signal. A group of researchers at Princeton University developed a neural autoencoder to compress the full spectrum of a star and extract precise RV signals at the level of 0.5 m/s. They now plan to further suppress the noise from stellar variability, Earth's atmosphere, and the instrument itself by learning their time evolution with a novel AI architecture that represents these noise sources as solutions to ordinary differential equations. Provided sufficient observational cadence, the PIs seek to suppress the residual noise and reach the precision of 0.1 m/s necessary to identify true Earth analogs around Sun-like stars. If successful, this project will allow the detection of low-mass exoplanets and form a new pathway for empirical descriptions of dynamical systems.

San Diego State University
San Diego, CA
Elisa Torresani, Wenwu Xu, Eugene Olevsky
$1,200,000

New Materials Processing via Electro-Nano-Pulsing

This project focuses on developing Electro-Nano-Pulse (ENP) technology, an innovation in electric field-assisted material processing. The objective is to investigate interactions between ultra-intense nanopulse electric currents and grain boundaries (GBs) in crystalline materials, enabling precise control over defect structures such as GB complexions and morphologies. Unlike conventional methods that primarily alter bulk material properties, ENP targets localized GB regions at the atomic level, offering unprecedented control over material structure. This technology uniquely modifies material properties by selectively influencing crystalline heterogeneities, including dislocations, grain boundaries, and interfaces. By enabling precise defect-level modifications - such as engineered grain boundary networks, record-high dislocation densities, and novel crystal discontinuities - ENP has the potential to revolutionize materials processing. The project integrates computational and experimental approaches. Atomistic simulations, employing a bicrystal grain boundary model, will distinguish between thermal (Joule heating) and nonthermal (electric field) effects on GBs. An advanced ENP system will be developed to generate ultra-intense nanopulses across various environments, including a Cryo-ENP setup utilizing liquid nitrogen, to validate simulation results. This novel approach has far-reaching implications for materials design, enabling the fabrication of superhard fracture and corrosion-resistant materials, as well as advanced nanocoatings and nanoporous battery materials. This project will lead to the creation of materials with unprecedented strength, durability, and functional capabilities, with transformative applications in aerospace, energy, and manufacturing industries.

University of North Carolina at Chapel Hill

Chapel Hill, NC
Gary Pielak, Brian Kuhlman
$1,000,000

To understand the counterintuitive behavior of natural and designed proteins

Enzymes accelerate the reactions that make life possible. Thus, bending their amazing proficiency to our ends will revolutionize the chemical and pharmaceutical industries. The goal of this project is to advance knowledge of enzymes by revealing relationships between Darwinian evolution and artificial intelligence (AI)-based design. David Baker's share of the 2024 Nobel Prize shows that AI-based design is a reality. But something is fundamentally odd about many AI-designed proteins. For natural globular proteins, stability and function arise from their solid-like interiors. In contrast, designed proteins tend toward two unnatural properties. First, most natural proteins unfold around the temperature of a warm bath, but many designed proteins appear to remain folded at temperatures near that of boiling water. Second, the interiors of many designed proteins display molten-like flexibility. Most surprisingly, these unnatural properties arise from a design process based on natural proteins. To gain the full potential of designed proteins, we must understand how they differ from their natural counterparts. We hypothesize that the folding- and catalytic-thermodynamics of designed and natural enzymes are fundamentally different. This hypothesis will be tested by comparing the dynamics and catalytic prowess of AI-designed enzymes to those of natural globular proteins and using AI to stabilize a natural enzyme and compare its local and global stability, dynamics and catalytic activity to those of the natural enzymes. Protein stability will be quantified using nuclear magnetic resonance spectroscopy (NMR) and catalytic activity assessed using steady-state kinetics.

Vanderbilt University
Nashville, TN
Gianni Castiglione, Allison Walker, and Nicole Creanza
$1,300,000

Reverse engineering the long lifespans of birds

A major limitation of aging research is the sheer number of genes to investigate, many of which have negative side effects when pharmacologically targeted. Other genes can compensate, but they must be simultaneously targeted, resulting in effectively infinite possible combinations—an infeasible number to test. To circumvent this, this project will establish a nature-inspired blueprint for lifespan extension by reverse engineering the long lifespans of birds, which live 3-4x longer than mammals of equivalent mass. Previous studies suggest that long avian lifespans are an evolutionary 'side-effect' of avian flight, which utilizes tremendous amounts of oxygen and requires increased cellular protection against oxidative stress—a hallmark of aging in humans. Birds achieved this by an ancient genetic mutation (deletion of redox regulator KEAP1) hyperactivating a key transcription factor (NRF2) that controls antioxidant gene expression. However, NRF2 hyperactivation is lethal in mammals. How birds compensate for this mutation is unknown. Initial studies indicate that birds achieved this through an extensively rewired NRF2/KEAP1 genetic pathway, with gene duplications and deletions that may synergistically compensate for deleterious effects of NRF2 hyperactivity. The project will use phylogenomics, biochemistry, cell biology, in vivo studies, and machine learning to untangle these network interactions and determine which genetic modifications enabled birds to achieve the best of all worlds—long lifespans and low oxidative stress without negative side effects. Rather than reinvent the wheel, this research will harness evolution to determine which specific gene target combinations, out of nearly infinite possibilities, should be targeted by pharmaceuticals to safely extend human lifespan.