

## GRAND CHALLENGES IN ORGANISMAL BIOLOGY

- 1) Understanding the organism's role in organism-environment linkages**—Understanding the consequences of climate change and environmental degradation for ecological health and human welfare depends on understanding the biology of diverse organisms. Communities and ecosystems are composed of organisms laced together by a network of interactions among individuals, and feedbacks between organisms and the physical environment. Current global and ecosystem models are overly simplistic owing to inadequate knowledge about basic organismal inputs and the dynamics of organismal responses to environmental changes. To understand the resilience and robustness of critical species and systems in the face of climate change, as well as protection of organisms vital to ecosystem services (e.g., clean water, chemical decontamination, pollination, carbon sinks), we need data in the following key areas:

  - Physical, physiological and genetic factors that constrain or promote adjustment to changing environments over different time scales (e.g., behavior, acclimation, plasticity, adaptation)
  - Mechanistic bases of organism-environment feedback systems
  - Functional and systems-level attributes of organisms that make them resilient or fragile in the face of environmental change
  
- 2) Exploiting the functional diversity of organisms**—Organisms are historical entities representing the successful outcome of millions of years of environmental testing applied to different genetic backgrounds. Each species contains a set of unique or novel solutions to many of the same challenges humans face now, including limited resources, infectious disease, chemical toxicity, temperature extremes, and drought. Basic organismal research has led to unforeseen human benefits (e.g., pharmaceuticals). Organismal diversity represents an irreplaceable storehouse of chemical and functional strategies with demonstrated value to humans. The rapid erosion of this 'database' through extinction and loss of diversity creates an urgent need to study a diverse range of organisms, and to create an infrastructural system within which new and existing data can be organized, synthesized, mined and applied. Key areas include:

  - Integrating organismal biology with the existing NSF 'Assembling the Tree of Life' (AToL) initiative
  - Fostering collaborations between applied researchers (e.g, biomedical, engineering) and organismal biologists to advance bio-inspired technology
  - Identifying organismal processes that might inspire new energy sources (e.g., bio-oils, microbial processes, waste conversion)
  
- 3) Integrating living and physical systems analysis**—Organisms operate across spatial scales from molecules to ecosystems and temporal scales from nanoseconds to eons. They are dynamic, high dimensional, hierarchical, nonlinear, dynamic networks with feedback, ill-defined boundaries and high levels of stochasticity, and operate within environments displaying similar complexity. We need a strong theoretical foundation and a common language to analyze such complex systems involving not only biology, but also the physical sciences. Recent advances in mathematical, physical and computer sciences make this a propitious time for cross-disciplinary approaches to biological problems. One fruitful direction is the application of 'dynamical systems theory' to organismal systems. Others include fostering interdisciplinary exchanges and education in areas such as materials science, biomimetics, robotics, neural networks and evolutionary algorithms. Key areas include:

  - Developing common analytical tools
  - Developing quantitative and predictive models for organismal systems and interactions
  - Using robotics to model organismal function and behavior, and organisms to inspire the engineering of new robots for human applications
  - Cross-disciplinary inspiration and education, and the development of sustained collaborations

- 4) Understanding how genomes produce organisms**—Current focus is on descriptive patterns of gene sequences, single gene responses and a few model species. However, the mechanisms by which genes and genomes produce whole organisms with a variety of complex phenotypes and how these processes regulate and shape organismal function and performance are poorly understood. Understanding ontogeny as a systems-level process will ultimately be crucial for advancing the field and revealing why certain life stages are particularly vulnerable to environmental perturbations (e.g., pollution, endocrine disrupters, climate change). Key areas include:
- A research focus on additional, non-model species
  - Understanding regulatory networks, integration and feedbacks that produce particular phenotypes
  - Understanding how genetic information is conveyed across hierarchical levels of organization during development and is expressed/suppressed throughout life
  - Understanding mechanisms and feedbacks mediating environmental effects on phenotypic expression and performance

- 5) Understanding how organisms walk the tightrope between stability and change**—A central paradox in biology is that organisms must remain stable in order to maintain the integration of complex developmental and functional systems, but they must also change in order to accommodate changing environments. A long period of phenotypic stasis interrupted by a geologically brief period of reorganization to a new stable phenotype is a frequently observed evolutionary pattern. Such a pattern mirrors theoretical systems-behavior where a stable state is buffered against perturbations by system-level properties until some threshold, followed by rapid transition to a new stable state. These properties appear to characterize many organismal systems at all hierarchical levels and across different time scales. A systems-theoretical approach is critical for our understanding of organisms as modular, hierarchical and networked systems (e.g., regulatory networks, cell-cell interactions and signaling pathways, neural networks, functional units, individual and group behavior, environmental inputs). Key areas include:
- Integrating mathematical, statistical and organism-based approaches to understanding organismal system behavior in ecological and evolutionary time
  - Identifying attributes of organisms that make them resilient or robust to environmental perturbation
  - Understanding the spectrum of organismal responses to internal and external environmental inputs (e.g., DNA methylation, hormonal regulation, acclimation, adaptive plasticity, adaptation) and their contributions to robustness and evolutionary persistence