UNDERSTANDING THE RULES OF LIFE: PREDICTING PHENOTYPE (URoL)

URoL Funding
(Dollars in Millions)

	FY 2018 Actual	FY 2019 (TBD)	FY 2020 Request
Stewardship Activities (BIO)	**-**	**-**	**$30.00**
Foundational Activities	**$118.18**	**-**	**$85.00**
BIO	35.00	-	30.00
CISE	6.00	-	5.00
ENG	10.03	-	3.00
GEO	4.00	-	4.00
MPS	53.65	-	39.00
SBE	4.50	-	4.00
IA	5.00	-	-
Total	**$118.18**	**-**	**$115.00**

Overview

Imagine a world where we can forecast how life will respond to a changing planet and where we can prevent the emergence of infectious diseases and other dangerous species; a world where a bio-economy uses bioengineered organisms to ensure human and environmental well-being and provides a safe and stable food supply; and a world where genetic and neurodegenerative disease is a thing of the past. Recent advances in understanding and engineering organisms at the fundamental level of the genome place us on the cusp of turning this vision into reality, of re-engineering cells, organisms, and natural systems, and of creating innovative biochemicals and biomaterials that sustain a vibrant bio-economy and strengthen society. Understanding the rules that govern how key features of life, such as robustness, resilience, and adaptability, emerge from the interaction of genome, phenotype, and environment, through convergence approaches of all NSF science and engineering will provide a framework for the design of new biological systems from the molecular to ecosystem scale that will enhance human well-being.

The NSF Big Idea, URoL, aims to create a new paradigm at the convergence of science, engineering, and technology that will elucidate theoretical frameworks (rules) to enable prediction of the diversity of evolutionary solutions that biological systems use to support life processes seen across the planet. URoL also aims to train the next generation of researchers capable of using those rules/theories not only to predict the behavior of biological systems, but to design biological systems that benefit humankind.

NSF released a number of dear colleague letters (DCLs) to announce URoL opportunities for catalytic activities in FY 2018. Building on those catalytic activities, in FY 2019, NSF anticipates funding projects submitted in response to two Foundation-wide URoL solicitations: *Understanding the Rules of Life: Synthetic Cell: An Ideas Lab Activity*[1] and *Understanding the Rules of Life: Epigenetics*.[2] NSF anticipates URoL will run through FY 2023.

Goals

1. To support a convergence of science, engineering, and technology in discovery of rules governing the emergence of robust, resilient, and adaptable phenotypes at three levels of biological organization: (1)

[1] www.nsf.gov/funding/pgm_summ.jsp?pims_id=505600
[2] www.nsf.gov/funding/pgm_summ.jsp?pims_id=505582

cells and cell systems; (2) multi-cellular organisms and their co-dependent microbial associations; and (3) complex networks of organisms and species involving social, ecological, and population dynamics. These rule sets are referred to as, respectively, minimal rules, interaction rules, and complexity rules. Understanding the rules at these three different scales should enable the prediction of the behavior of biological systems and how those systems interact with, respond to, and modify the environment, and will facilitate the design of new biological systems at each scale that can serve humankind.

2. To support the discovery of scale invariant rules that govern biological systems. These theories should begin to explain the existence of a diversity of solutions that biology creates and uses to solve the essential problems of living systems at all scales: maintenance and transmission of information (genome), capture and conversion of raw materials to make the biochemicals and biomaterials that make up a living system, capture and conversion of energy to support all life processes, and reproduction to perpetuate the species. These universal, scale-invariant rules will serve to help improve human health and safety (e.g., agricultural adaptability, food safety, and environmental sustainability).
3. To support networks of researchers, technology developers, and educators engaged in URoL activities such that a robust community is developed, with an impact that is sustained beyond the five-year investment in the URoL Big Idea. The convergence nature of research addressing emergent properties of life stimulates technological innovation that feeds back to drive the science forward. This includes development of: new and improved techniques in molecular, genomic, and cellular examination and manipulation; improved technologies for the capture, analysis, and interpretation of biological, behavioral, and social phenotypic data in free-living organisms; new sensors and observing capabilities from nano- to macro-spatial and temporal scales; more capable cyberinfrastructure to support robust, data- and computational-enabled URoL discovery and sharing of research results; new approaches for data analysis, such as machine learning; advances in computation and complex modeling to support learning and simulation-driven URoL investigations; and advances in theory coming from all of these sciences and engineering. The predictive goals of URoL also guide investments in training and workforce development to produce scientists that have a firm grounding in the life sciences as well as the mathematical, physical, computational, behavioral and/or social sciences and engineering that enable them to work collaboratively across disciplinary boundaries. Finally, URoL provides a rich context in which to expand science literacy efforts, in both formal and informal learning environments, aimed at diverse communities across the nation. Research networks provide a mechanism for sustained support of distributed groups of investigators all working to achieve URoL goals.

FY 2020 Investments

FY 2020 activities will build upon the investments made in FY 2019. New solicitations will be released to support networks of researchers, technology developers and educators (Goal 3), as well as research to elucidate interaction rules (Goal 1). In addition, new catalytic activities, including workshops and exploratory grants, will be awarded in FY 2020 to seed investments in convergence approaches to the discovery of scale invariant rules that govern biological systems (Goal 2), which will be fully funded in future years.