Department of Defense
Fiscal Year (FY) 2014 President's Budget Submission

April 2013

Defense Advanced Research Projects Agency

Justification Book Volume 1 of 1

Research, Development, Test & Evaluation, Defense-Wide

Exhibit R-2A, RDT&E Project Justification: PB 2014 Defense Advanced Research Projects Agency		DATE: April 2013
APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 1: *Basic Research*	R-1 ITEM NOMENCLATURE PE 0601101E: *DEFENSE RESEARCH SCIENCES*	PROJECT BLS-01: *BIO/INFO/MICRO SCIENCES*

B. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Demonstrated the utility of new compressive measurement theory via improvements in imaging and radar applications. ***FY 2013 Plans:*** - Identify fundamental bounds on performance and cost associated with linear and nonlinear signal priors. - Demonstrate novel reconstruction algorithms that incorporate both signal and task priors to enable improved reconstruction quality and/or reduced measurement resources. - Demonstrate visible imaging using 10x fewer measurements than reconstructed pixels. - Demonstrate RADAR imaging using 10x less bandwidth than a conventional non-compressive system. - Exploit the benefit of adaptation in order to achieve additional reductions in performance and/or measurement resources. - Exploit the benefit of information-optimal measurements within a signals intelligence application. ***FY 2014 Plans:*** - Demonstrate hyperspectral imaging using 100x fewer measurements than reconstructed voxels. - Explore application of compressive sensing concepts to alternate sensing modalities such as X-ray imaging. - Investigate the potential gains available from compressive sensing within a video application. - Leverage advances in neuroscience and neurological measurements to develop predictive, quantitative models of memory, learning, and neuro-physiologic recovery.			
Title: Physics in Biology ***Description:*** Understanding the fundamental physical phenomena that underlie biological processes and functions will provide new insight and unique opportunities for understanding biological properties and exploiting such phenomena. Physics in biology will explore the role and impact of quantum effects in biological processes and systems. This includes exploiting manifestly quantum mechanical effects that exist in biological systems at room temperature to develop a revolutionary new class of robust, compact, high sensitivity and high selectivity sensors. Finally, the quantum phenomena uncovered will be exploited to control the attraction of insects to humans with the potential to completely eliminate insect bites and thus the transmission of parasitic, bacterial or viral pathogens. ***FY 2012 Accomplishments:*** - Developed theory and performed simulations for the transduction of the magnetoreception signal on the visual field. - Developed concepts and initial designs for sensors inspired by biological quantum effects. - Developed a general theory for photosynthetic transport, governed by a single parameter, that shows that it is an example of a quantum 'Goldilocks effect', i.e., the degree of quantum complexity and coherence is 'just right' for attaining maximum efficiency. - Formulated a new concept of "excitonic circuits" (that concentrate and direct excitons as in photosynthesis) and designed generic circuit elements.	9.450	7.678	7.500

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B. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Verified that molecular vibrations, and thus quantum effects, are essential to describing olfaction. ***FY 2013 Plans:*** - Develop prototype synthetic sensors that utilize biologically inspired quantum effects and model their performance. - Demonstrate the ability to control quantum effects in biological systems by reorienting magnetoreception through the radical pair mechanism using radio frequency fields. - Demonstrate the biological and evolutionary advantage of quantum effects in photosynthetic systems. ***FY 2014 Plans:*** - Demonstrate prototype quantum biological sensors against their equivalent state-of-the-art sensor and quantify the increase in sensitivity, selectivity and other performance metrics. - Explore quantum physics-based mechanisms of mosquito bio-sensing related to mosquito attraction to humans for novel, vector-born disease protection against diseases such as malaria or dengue fever.			
Accomplishments/Planned Programs Subtotals	30.463	39.678	29.771

C. Other Program Funding Summary ($ in Millions)

N/A

Remarks

D. Acquisition Strategy

N/A

E. Performance Metrics

Specific programmatic performance metrics are listed above in the program accomplishments and plans section.

Exhibit R-2, RDT&E Budget Item Justification: PB 2014 Defense Advanced Research Projects Agency	DATE: April 2013
APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 1: *Basic Research*	R-1 ITEM NOMENCLATURE PE 0601117E: *BASIC OPERATIONAL MEDICAL SCIENCE*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Develop models that predict the evolution of neural firing patterns following brain injury, and following the introduction of artificial neural connections aimed at facilitating recovery. ***FY 2014 Plans:*** - Demonstrate the ability of non-human primates to perform a dexterous sensorimotor task through the use of a neural interface, without the use of neural spike recordings. - Develop new methods of analysis and interpretation for measuring brain tissue alterations without the need for image reconstruction. - Develop novel technologies, such as optical/non-optical tools and cellular dyes, to detect the functional dynamics of a cell or a group of cells in the tissues and organs of a living organism in a non-invasive manner. - Develop methods of data analysis and interpretation that will allow the mathematical characterization of normal and abnormal cellular processes in situ.			
Title: Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) ***Description:*** The Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program will develop the underlying technologies to rapidly respond to a disease or threat and improve individual readiness and total force health protection by providing capabilities, which are currently available only in centralized laboratories in the U.S., to non-tertiary care and individual settings. ADEPT will develop and exploit synthetic biology for the in vivo creation of nucleic acid circuits that continuously and autonomously sense and respond to changes in physiologic state and for novel methods to target delivery, enhance immunogenicity, or control activity of vaccines, potentially eliminating the time to manufacture a vaccine ex vivo. ADEPT advancements to control cellular machinery include research to optimize orthogonality and modularity of genetic control elements; identify methods to increase sensitivity and specificity; and demonstrate methods to control cellular machinery in response to changes in physiological status. ADEPT will develop methodologies for measuring health-specific biomarkers from a collected biospecimen to enable diagnostics at the point-of-need or resource limited clinical facilities (point-of-care), in-garrison or deployed. Additionally, ADEPT will develop techniques that will enable the rapid establishment of transient immunity through stimulation of the production of components of the immune system to impart effective but temporary protection. This transient immunity would bridge the time gap between the delivery of a vaccine and the development of a long term protective immune response. Applied research efforts are budgeted in PE 0602115E, Project BT-01. ***FY 2012 Accomplishments:*** - Initiated development of modular and orthogonal nucleic acid-based elements for application within a sense-and-respond circuit operating within the context of a mammalian cell. - Investigated controlled expression in mammalian cells of synthetic circuit that responds to physiological biomarkers associated with health status. - Developed novel concepts and molecular approaches to enable deployable diagnostics.	19.511	24.500	40.500

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Developed novel reagents and materials for stabilizing self-collected biospecimens at room temperature for simple shipment and storage. - Developed methods for sample preparation that require no operator manipulation and are consistent with point-of-need and point-of-care settings. - Developed new methods for signal amplification amenable to deployable diagnostics. - Investigated the ability of administered synthetic oligonucleotides to direct cells to produce elements of the immune response.			
FY 2013 Plans: - Demonstrate development of modular and orthogonal nucleic acid-based elements for application within a sense-and-respond circuit that operates within the context of a mammalian cell. - Demonstrate controlled expression in mammalian cells of synthetic circuit that responds to physiological biomarkers associated with health status. - Quantify sensitivity and specificity of developed molecular approaches designed for deployable diagnostics using physiological concentrations of clinically relevant analytes in complex biospecimens. - Quantify performance of biostabilization reagents/materials to evaluate analytical recovery of clinically relevant molecules as compared to traditional stabilization methods that require cold-chain storage. - Quantify performance of methods for room temperature analyses and reagent stabilization to demonstrate analytical results with similar-to-enhanced performance as compared to current laboratory methods for clinical diagnostics. - Quantify detection limits achieved with signal amplification methods to demonstrate performance superior to current state of the art methods for quantification of low abundance biomarkers in an actionable timeframe. - Demonstrate performance of new sample preparation methods suitable for simple and multiplexed analysis of biospecimens that are either self-collected under low-resource settings or collected by trained professionals at the physician-office settings. - Design integration of developed diagnostic methodologies. - Quantify the level of antibody and immunoadhesin production directed by the administration of synthetic oligonucleotides in comparison to standard vaccine delivery. - Investigate the impact of the antibody sequence on the therapeutic strength of immune response in vivo.			
FY 2014 Plans: - Demonstrate in mammalian cells the function of a synthetic circuit that can integrate multiple signals associated with health status and respond with a targeted change in cell function. - Demonstrate the ability to generate synthetic nucleic acid and protein circuit components that respond to an exogenously supplied small molecule drug trigger. - Demonstrate in mammalian cells the function of an orthogonal, multi-functional nucleic acid-based circuit with sense-and-respond functionality that responds to biomarkers of cell state. - Refine developed molecular approaches and develop targeted molecular assays designed for deployable diagnostics.			

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C, Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Demonstrate biostabilization reagents/materials with numerous biospecimen types and processing/fluidic approaches to be eventually integrated into disposable and on-person diagnostic devices. - Demonstrate methods for room temperature analyses and reagent stabilization with numerous biospecimen types and fluidic approaches to permit collection and transport of patient samples for diagnostic analysis. - Demonstrate signal amplification methods in conjunction with processing/assay methods. - Demonstrate developed sample preparation methods in conjunction with simple and multiplexed analysis of biospecimens representative of those either self-collected under low-resource settings or collected by trained professionals at the physician-office settings to assist the diagnosis of an individual. - Demonstrate delivery of synthetic oligonucleotide constructs to cells appropriate to produce an antibody response. - Demonstrate antibody and immunoadhesin production targeted to specific disease classes. - Optimize antibody sequence for maximal therapeutic strength of immune response in vivo.			
Title: Dialysis-Like Therapeutics	5.000	5.000	0.000
Description: Sepsis, a bacterial infection of the blood stream, is a significant cause of injury and death among combat-injured soldiers. The goal of this program is to develop a portable device capable of controlling relevant components in the blood volume on clinically relevant time scales. Reaching this goal is expected to require significant advances in sensing in complex biologic fluids, complex fluid manipulation, separation of components from these fluids, and mathematical descriptions capable of providing predictive control over the closed loop process. The envisioned device would save the lives of thousands of military patients each year by effectively treating sepsis and associated complications. Initial basic research will develop the component technologies that will ultimately make up the integrated device. Included in this effort will be the development of non-fouling continuous sensors for complex biological fluids; design of high-flow microfluidic structures that do not require the use of anticoagulation; development of intrinsic separation technologies that do not require pathogen specific molecular labels or binding chemistries; and predictive modeling and control (mathematical formalism) with sufficient fidelity to enable agile adaptive closed-loop therapy. Applied research efforts are budgeted in PE 0602115E, Project BT-01. ***FY 2012 Accomplishments:*** - Achieved detection over 10 days of ricin toxin B chain in whole blood using a surface enhanced Raman spectroscopy (SERS) substrate functionalized with degradation-resistant aptamers. - Flowed whole blood at 3 L/hr for 60 minutes without clotting in specially functionalized medical tubing. - Removed > 80% of pathogens and inflammatory molecules from flowing blood using label-free separation technologies. - Improved the outcome of 7x more virtual patients as compared to static treatment using a 4-state predictive control model. ***FY 2013 Plans:***			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Improve sensing technologies to achieve continuous detection of pathogens and biomolecules in flowing blood, blood components, and wound fluid. - Refine microfluidic architectures and coatings for continuous blood flow without platelet activation or clotting. - Enhance label-free separation technologies to successfully remove pathogens and select bioagents from blood or blood components. - Validate the sepsis predictive modeling using data from small animal testing within the program.			
Accomplishments/Planned Programs Subtotals	44.445	39.676	49.500

D. Other Program Funding Summary ($ in Millions)

N/A

Remarks

E. Acquisition Strategy

N/A

F. Performance Metrics

Specific programmatic performance metrics are listed above in the program accomplishments and plans section.

Exhibit R-2, RDT&E Budget Item Justification: PB 2014 Defense Advanced Research Projects Agency	DATE: April 2013
APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 2: *Applied Research*	**R-1 ITEM NOMENCLATURE** PE 0602115E: *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Develop a platform to reproducibly demonstrate the evolutionary pathway of a virus under multiple selective pressures. - Validate algorithms' abilities to predict viral evolution in the presence of one or multiple pressures. - Predict timing, location(s) and nature of genetic mutation(s) responsible for antiviral failure in an infected viral host (animal) model. - Predict number of viral generations necessary for the acquisition of antiviral resistance in an infected viral host (animal) model. - Predict location of genetic mutation(s) responsible for failure of a monoclonal antibody to neutralize a virus. - Correlate influenza vaccine failure in syngeneic/specific pathogen-free poultry with pathogen evolution in the natural ecologies of Asia. - Use in vitro evolution reactors to predict emergence of novel, variant influenza strains from within-reservoir species, and to predict emergence of dengue virus mutations in a region where dengue has recently appeared. - Demonstrate that the in vitro evolution platform accelerates evolution of drug resistance or immune escape. ***FY 2014 Plans:*** - Demonstrate that the in vitro bioreactor can be used to predict alteration in cell tropism or host range. - Validate viral evolution platforms and predictive platforms with a live fire test. - Transition predictive algorithms and in vitro evolution platforms to the Center for Disease Control (CDC) and other interested government agencies to increase preparedness for seasonal influenza as well as other emerging pathogens. - Transition predictive algorithms and in vitro evolution platforms to the pharmaceutical industry for prediction of emergence of drug-resistant strains of commercially relevant viruses.			
Title: Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) ***Description:*** The overarching goal of the Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program is to increase our ability to rapidly respond to a disease or threat and improve individual readiness and total force health protection by providing centralized laboratory capabilities at non-tertiary care settings. ADEPT will focus on the development of Ribonucleic Acid (RNA)-based vaccines, potentially eliminating the time and labor required for traditional manufacture of a vaccine while at the same time improving efficacy. ADEPT will also focus on advanced development of key elements for simple-to-operate diagnostic devices. A companion basic research effort is budgeted in PE 0601117E, Project MED-01. ***FY 2012 Accomplishments:*** - Increased stability of RNA-based vaccines. - Demonstrated efficacy of RNA-based vaccines in a small animal model. - Demonstrated sample preparation methods designed for integration in disposable diagnostics that can be carried on-person, or in reusable diagnostics that can be used at the point-of-care.	11.169	15.000	29.852

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Developed high sensitivity colorimetric and electrical detection approaches of advanced instrumentation approaches for autonomous diagnostics that will be deployed as either on-person devices, or used at the point-of-care. ***FY 2013 Plans:*** - Demonstrate increased humoral and cellular responses with RNA-based vaccines as compared to benchmark vaccines in vivo. - Demonstrate increased efficacy of RNA-based vaccines in vivo in small and large animal models. - Demonstrate quantitative performance metrics for device components (sample preparation/reagent delivery/detection components) to enable diagnostic device capabilities in the remote-clinic and low resourced settings. ***FY 2014 Plans:*** - Demonstrate quantitative performance metrics for integrated components developed to demonstrate capability toward a complete diagnostic device prototype. - Demonstrate ability to manipulate type of immune response induced by RNA-based vaccines. - Demonstrate ability to target delivery of RNA-based vaccines to specific cell types. - Develop novel methodologies to deliver nucleic acid constructs encoding one or hundreds of antibodies identified from immunized or convalescent patients. - Demonstrate immediate broad spectrum transient immune prophylaxis in host via delivery of nucleic acids that transiently produce multiple antibodies.			
Title: Tactical Biomedical Technologies	18.223	15.500	13.321
Description: The Tactical Biomedical Technologies thrust will develop new approaches to deliver life-saving medical care on the battlefield. Uncontrolled blood loss is the leading cause of preventable death for soldiers on the battlefield. While immediate control of hemorrhage is the most effective strategy for treating combat casualties and saving lives, currently no method other than surgical intervention can effectively treat intracavitary bleeding. A focus in this thrust is the co-development of a materials-based agent(s) and delivery mechanism capable of damaged tissue-targeted hemostasis and wound control. This system will effectively treat compressible and non-compressible wounds regardless of geometry or location. Additionally, rapid response to emerging biological threats on the battlefield is impacted by logistical delays of delivering the necessary therapeutics. Creating a "pharmacy on demand" will enable far-forward medical providers to manufacture and produce small molecule drugs and biologics in order to ensure that the therapeutics are available when they need them. Another effort will develop assessment tools to identify soldiers in real time who represent depression and suicide risk by identifying speech biomarkers. This project will also develop new algorithms, protocols, and methods to allow registration and comparison of disparate sources of data in biology (across species, experimental systems, hierarchies and populations). ***FY 2012 Accomplishments:*** - Demonstrated hemostasis agent stability consistent with operational requirements.			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Investigate options for broadband nuclear magnetic resonance detection for the simultaneous acquisition of multiple nuclear species. ***FY 2014 Plans:*** - Design a compact prototype device for performing novel MRI-like imaging and spectroscopy using quantum orbital resonance spectroscopy (QORS) in military medical environments. - Obtain neurochemical spectra using QORS technique.			
Title: Dialysis-Like Therapeutics ***Description:*** Sepsis, a bacterial infection of the blood stream, is a significant cause of injury and death among combat-injured soldiers. The goal of this program is to develop a portable device capable of controlling relevant components in the blood volume on clinically relevant time scales. Reaching this goal is expected to require significant advances in sensing in complex biologic fluids, complex fluid manipulation, separation of components from these fluids, and mathematical descriptions capable of providing predictive control over the closed loop process. The envisioned device would save the lives of thousands of military patients each year by effectively treating sepsis and associated complications. Applied research under this program further develops and applies existing component technologies and then integrates these to create a complete blood purification system for use in the treatment of sepsis. Included in this effort will be development, integration and demonstration of non-fouling, continuous sensors for complex biological fluids; implementation of high-flow microfluidic structures that do not require the use of anticoagulation; application of intrinsic separation technologies that do not require pathogen specific molecular labels or binding chemistries; and refinement of predictive modeling and control (mathematical formalism) with sufficient fidelity to enable agile adaptive closed-loop therapy. The basic research part of this program is budgeted in PE 0601117E, Project MED-01. ***FY 2012 Accomplishments:*** - Evaluated existing sensing, microfluidic flow, and intrinsic separation component technologies for use in an integrated blood purification system and initiated research plan to achieve significant improvements in line with the overall program goals. - Initiated integration plan for component technologies developed in the basic research aspect of this program. - Identified a regulatory pathway leading to an approved integrated device. ***FY 2013 Plans:*** - Refine integration strategy, develop a bread-board system, and demonstrate bread-board system. - Develop appropriate animal models, confirm regulatory plan, and begin regulatory approval process for the integrated device. ***FY 2014 Plans:***	5.000	10.000	20.000

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Integrate continuous sensing, biocompatible high-flow fluid manipulation, intrinsic separation from complex fluid, and predictive modeling and control in a prototype device for the treatment of sepsis. - Use feedback from initial animal model testing to inform the development of a prototype device for additional safety and efficacy studies in a large animal model. - Continue regulatory approval process and initiate plan for investigational device exemption submission.			
Title: Warrior Web ***Description:*** Musculoskeletal injury and fatigue to the warfighter caused by dynamic events on the battlefield not only impacts immediate mission readiness, but also can have a deleterious effect on the warfighter throughout his/her life. The Warrior Web program will mitigate that impact by developing an adaptive, quasi-active, joint support sub-system that can be integrated into current soldier systems. Because this sub-system will be compliant and be transparent to the user, it will reduce the injuries sustained by warfighters while allowing them to maintain performance. Success in this program will require the integration of component technologies in areas such as regenerative kinetic energy harvesting to offset power/energy demands; human performance, system, and component modeling; novel materials and dynamic stiffness; actuation; controls and human interface; and power distribution/energy storage. The final suit is planned to weigh no more than 9kg and require no more than 100W of external power. Allowing the warfighter to perform their missions with reduced risk for injuries will have immediate effects on mission readiness, soldier survivability, mission performance and the long-term health of our veterans. This effort was previously funded in the Maintaining Combat Performance Thrust in PE 0602715E, Project MBT-02. ***FY 2013 Plans:*** - Complete injury assessment and component technology integration into open source biomechanical model. - Complete initial verification and validation of component technologies in military environments. - Conduct Preliminary Design Review to demonstrate that individual component technologies (e.g., energy, actuation) can be integrated to meet Warrior Web performance requirements. ***FY 2014 Plans:*** - Leverage open source biomechanical model to iterate design. - Complete component technology based on results of Preliminary Design Review. - Initiate design of full Warrior Web including integration into current solider system. - Conduct Critical Design Review of full Warrior Web solider system combination.	0.000	10.750	12.000
Title: Revolutionizing Prosthetics* ***Description:*** *Previously funded in PE 0602715E, Project MBT-02.	0.000	17.000	10.000

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APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 2: *Applied Research*	R-1 ITEM NOMENCLATURE PE 0602715E: *MATERIALS AND BIOLOGICAL TECHNOLOGY*	PROJECT MBT-02: *BIOLOGICALLY BASED MATERIALS AND DEVICES*	

COST ($ in Millions)	All Prior Years	FY 2012	FY 2013#	FY 2014 Base	FY 2014 OCO ##	FY 2014 Total	FY 2015	FY 2016	FY 2017	FY 2018	Cost To Complete	Total Cost
MBT-02: *BIOLOGICALLY BASED MATERIALS AND DEVICES*	-	47.379	37.623	40.301	-	40.301	50.976	64.357	55.085	55.835	Continuing	Continuing

FY 2013 Program is from the FY 2013 President's Budget, submitted February 2012

The FY 2014 OCO Request will be submitted at a later date

A. Mission Description and Budget Item Justification

This project acknowledges the growing and pervasive influence of the biological sciences on the development of new DoD capabilities. This influence extends throughout the development of new materials, devices, and processes and relies on the integration of biological breakthroughs with those in engineering and the physical sciences. Contained in this project are thrusts in the application of biomimetic materials and devices for Defense, the use of biology's unique fabrication capabilities to produce structures that cannot be made any other way, the application of materials in biological applications, and the development of manufacturing tools that use biological components and processes for materials synthesis. This project also includes major efforts aimed at integrating biological and digital sensing methodologies and maintaining human combat performance despite the extraordinary stressors of combat. Finally, this thrust will develop new cognitive therapeutics, and explore neuroscience technologies.

B. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
Title: Neuroscience Technologies	10.827	10.000	8.000
Description: The Neuroscience Technologies thrust leverages recent advances in neurophysiology, neuro-imaging, cognitive science, and molecular biology to sustain and protect the cognitive functioning of the warfighter faced with challenging operational conditions. Warfighters experience a wide variety of operational stressors, both mental and physical, that degrade critical cognitive functions such as memory, learning, and decision making. These stressors also degrade the warfighter's ability to multitask, leading to decreased ability to respond quickly and effectively. Currently, the long-term impact of these stressors on the brain is unknown, both at the molecular and behavioral level. This thrust area will utilize modern neuroscientific techniques, in conjunction with emerging solutions in neurally enabled human-machine interface technologies, to develop quantitative models of this impact and explore mechanisms to protect, maintain, complement, or restore cognitive functioning during and after exposure to operational stressors. In addition, new approaches for using neural signals to make human-machine systems more time efficient and less workload intense will be identified, developed, and evaluated. This thrust area will have far-reaching implications for both current and future military operations, with the potential to protect and improve cognitive performance at the individual and group level both prior to and during deployment.			
FY 2012 Accomplishments:			

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B. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Began reconstructing a multi-scale network linked to specific stressors and stress response systems using integrated epigenetics, genetics, quantitative model building, bioinformatics, and computational biology approaches. - Continued modeling and verification of causal factors and relationships between variables in the complex systems and networks involved in the response to stress and the ability to resist stress. - Modulated genes and pathways mediating acute and chronic stress-induced dysfunction in circuits for reward, fear, and habit learning for reduction of stress-related dysfunction in animal models. - Developed and implemented interventions for prevention of stress-induced cognitive dysfunction in animal models of acute and chronic stress. - Expanded studies of stress-related dysfunction to include identifying gene, network and specific brain region dysfunction as it relates to suicide. - Demonstrated quantitative biochemical measurement of the impact of stress in real-time through development of advanced biosensors. ***FY 2013 Plans:*** - Integrate human data on stress genes to determine human stress-related gene networks for targeting interventions. - Translate genes and networks identified in animals to humans using high throughput molecular data from population-based studies. - Determine biomarkers of alertness in active duty personnel with psychological health problems/traumatic brain injury. - Relate clinical and psychological profiles of patients with post-traumatic stress disorder to neural networks, neurochemicals and behavior for biomarker identification. - Develop empirically validated intervention strategies to include stress reduction (exercise, meditation), stress inoculation (video training/hyperrealistic training), and/or pharmacological interventions, while maintaining performance. - Identify objective measures of physical and cognitive states through the application of integrated analytics and advanced computational techniques. ***FY 2014 Plans:*** - Determine genetic, epigenetic, and proteomic changes underlying vulnerability to poor decision making in humans. - Exploit advances in the predictive models of the brain to develop tools and techniques that can improve cognitive performance under stress at both the individual and group level.			
Title: BioDesign	6.791	11.023	14.084
Description: BioDesign will employ system engineering methods in combination with biotechnology and synthetic chemical technology to create novel beneficial attributes. BioDesign mitigates the unpredictability of natural evolutionary advancement primarily by advanced genetic engineering and molecular biology technologies to produce the intended biological effect. This thrust area includes designed molecular responses that increase resistance to cellular death signals and improved computational			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Demonstrate proof of concept of fundamental building blocks of intrachip thermal management including microfabrication in relevant electronic substrates and preliminary thermofluid results. - Prepare and refine initial thermal models of intrachip cooling to explain and predict experimental results. - Demonstrate benefits to system-level performance and size, weight, power, and cost (SWaPC) through the use of intrachip thermal management technologies.			
Title: In vivo Nanoplatforms (IVN) ***Description:*** The In vivo Nanoplatforms (IVN) program seeks to develop the nanoscale systems necessary for in vivo sensing and physiologic monitoring and delivery vehicles for targeted biological therapeutics. The nanoscale components to be developed will enable continuous in vivo monitoring of both small (e.g. glucose, lactate, and urea) and large molecules (e.g. biological threat agents). A reprogrammable therapeutic platform will enable tailored therapeutic delivery to specific areas of the body (e.g. cells, tissue, compartments) in response to traditional, emergent, and engineered threats. The key challenges to developing these systems include safety, toxicity, biocompatibility, sensitivity, response, and targeted delivery. The IVN program will have diagnostic and therapeutic goals that enable a versatile, rapidly adaptable system to provide operational support to the warfighter in any location. ***FY 2013 Plans:*** - Achieve a safe in vivc nanoplatform sensor to detect one military-relevant analyte (e.g. glucose) in living cells for one month. - Achieve a safe in vivc nanoplatform therapeutic to reduce a military-relevant pathogen or disease cofactor in living cells by 50%. - Facilitate development of a regulatory approval pathway for diagnostic and therapeutic nanoplatforms. ***FY 2014 Plans:*** - Achieve a safe in vivc nanoplatform sensor to detect two military-relevant analytes (e.g. glucose, pathogen) in a small animal for six months. - Achieve a safe in vivc nanoplatform therapeutic to reduce a military-relevant pathogen or disease cofactor in a small animal by 70%. - Begin to obtain regulatory approval of identified safe and effective diagnostic and therapeutic nanoplatforms.	0.000	5.000	18.500
Title: Pixel Network (PIXNET) for Dynamic Visualization ***Description:*** The Pixel Network for dynamic visualization (PIXNET) program addresses the squad level capability gap for target detection, recognition and identification in all weather and day/night missions. The vision of the program is to offer the warfighter a small and versatile infrared (IR) camera that would be affordable to individual soldiers and provide multiple IR band imagery with fusion capability to take full advantage of different wavelength band phenomenology in a compact single unit. In the future, the availability of the PIXNET camera would enable a peer-to-peer networked system for image sharing within a squad, thereby providing a better common operating picture of the battlefield and significantly enhancing the warfighter's situational	0.000	15.000	22.700