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# Department of Defense
# Fiscal Year (FY) 2015 Budget Estimates

March 2014

## Defense Advanced Research Projects Agency

*Defense Wide Justification Book Volume 1 of 5*

***Research, Development, Test & Evaluation, Defense-Wide***

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| Exhibit R-2, RDT&E Budget Item Justification: PB 2015 Defense Advanced Research Projects Agency | Date: March 2014 |
|---|---|
| **Appropriation/Budget Activity**<br>0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 1: *Basic Research* | **R-1 Program Element (Number/Name)**<br>PE 0601117E / *BASIC OPERATIONAL MEDICAL SCIENCE* |

| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| - Develop circuitry models and methods of data analysis that allow for the mathematical characterization and prediction of normal and abnormal cellular processes in the brain.<br><br>***FY 2015 Plans:***<br>- Demonstrate the ability to non-destructively image neural communication between distant cerebral neural circuits in real time.<br>- Demonstrate the ability to simultaneously detect the functional dynamics of multiple individual neurons in the brain over extended periods of time.<br>- Validate the predictive potential of new neural circuitry models by stimulating specific neurons within the circuit to alter behavior and/or function. | | | |
| ***Title:*** Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT)<br><br>***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.<br><br>***FY 2013 Accomplishments:***<br>- Demonstrated 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.<br>- Demonstrated controlled expression in mammalian cells of synthetic circuit that responds to physiological biomarkers associated with health status.<br>- Quantified sensitivity and specificity of developed molecular approaches designed for deployable diagnostics using physiological concentrations of clinically relevant analytes in complex biospecimens.<br>- Quantified performance of biostabilization reagents/materials demonstrating analytical recovery of clinically relevant molecules equivalent to traditional stabilization methods that require cold-chain storage. | 21.620 | 40.500 | 39.912 |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| - Quantified performance of methods for room temperature analyses and reagent stabilization demonstrating analytical results with similar-to-enhanced performance as compared to current laboratory methods for clinical diagnostics.<br>- Quantified detection limits achieved with signal amplification methods, demonstrating performance superior to current state of the art methods for quantification of low abundance biomarkers in an actionable timeframe.<br>- Developed 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.<br>- Determined materials properties and fluidic control requirements for integration of diagnostic methodologies.<br>- Quantified the level of antibody and immunoadhesin production directed by the administration of synthetic oligonucleotides in comparison to standard vaccine delivery.<br>- Investigated the impact of the Ribonucleic Acid (RNA) sequence on the therapeutic strength of immune response in vivo. | | | |
| ***FY 2014 Plans:***<br>- 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.<br>- Demonstrate the ability to generate synthetic nucleic acid and protein circuit components that respond to an exogenously supplied small molecule drug trigger.<br>- Demonstrate biostabilization reagents/materials with biospecimen types and physical formats appropriate for integration into devices for collection and transport of patient samples for diagnostic analysis, and integration into on-person diagnostic devices.<br>- Demonstrate signal amplification methods in conjunction with processing/assay methods.<br>- Optimize developed sample preparation methods and test efficacy using 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.<br>- Develop advanced materials for incorporation in disposable diagnostic devices.<br>- Optimize advanced microfluidic methods for no/low power flow control.<br>- Demonstrate delivery of synthetic oligonucleotide constructs to cells appropriate to produce an antibody response.<br>- Demonstrate antibody and immunoadhesin production targeted to specific disease classes.<br>- Optimize antibody sequence for maximal therapeutic strength of immune response in vivo. | | | |
| ***FY 2015 Plans:***<br>- Demonstrate ability to administer nucleic acid encoding multiple antibodies to protect against existing, unmet, clinical targets; emerging global infectious diseases; and known, engineered biothreats.<br>- Demonstrate onset of protection within hours after delivery and duration of therapeutic response greater than IV administered antibodies.<br>- Demonstrate optimized, high sensitivity assay methods for protein and nucleic acid biomarkers, suitable for incorporation in deployable devices. | | | |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| - Demonstrate advanced materials properties and incorporation of developed materials into disposable assay formats.<br>- Demonstrate advanced methods for reagent stabilization and delivery for assays developed for deployable devices.<br>- Demonstrate sample preparation methods in conjunction with developed assays and quantify performance metrics.<br>- Demonstrate performance of developed assays using advance no/low power microfluidic methods.<br>- Measure performance of developed diagnostic methods and demonstrate capability to measure clinically relevant analyte levels in appropriate biospecimen matrices.<br>- Demonstrate in mammalian cells the function of a synthetic circuit that can control the timing and level of expression of a protein when expressed from an RNA-based expression vector.<br>- Demonstrate in mammalian cells the function of a synthetic circuit that can integrate at least two physiological signals associated with a change in health status and respond to at least two exogenously added small molecules, and respond with a targeted change in cell state.<br>- Demonstrate the ability to generate a synthetic antibody via continuous evolution that can specifically bind to a defined target in mammalian cells. | | | |
| ***Title:*** Dialysis-Like Therapeutics<br><br>***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 was to develop a portable device capable of controlling relevant components in the blood volume on clinically relevant time scales. Reaching this goal required 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. Additionally, the device may be effective as a medical countermeasure against various chemical and biological (chem-bio) threat agents, such as viruses, bacteria, fungi, and toxins.<br><br>Initial basic research developed the component technologies that will ultimately make up the integrated device. Included in this effort was 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.<br><br>***FY 2013 Accomplishments:***<br>- Improved sensing technologies to achieve continuous detection of pathogens, toxins, and other biomolecules in blood and blood components. | 4.713 | - | - |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| - Refined microfluidic architectures and coatings for continuous blood flow at high rates of 1.8 L/hour without platelet activation or clotting.<br>- Enhanced label-free separation technologies to successfully remove pathogens, toxins, and select bioagents from blood or blood components by more than 90%.<br>- Validated the sepsis predictive modeling using data from small animal testing within the program. | | | |
| **Accomplishments/Planned Programs Subtotals** | 37.143 | 49.500 | 49.848 |

**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.

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| **Appropriation/Budget Activity**<br>0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research* | **R-1 Program Element (Number/Name)**<br>PE 0602115E / *BIOMEDICAL TECHNOLOGY* |

**Change Summary Explanation**

FY 2013: Decrease reflects Congressional reductions for Sections 3001 & 3004, sequestration adjustments, and the SBIR/STTR transfer offset by reprogrammings.

FY 2015: Decrease reflects the end of the Revolutionizing Prosthetics program.

| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| ***Title:*** Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) | 12.175 | 28.852 | 23.550 |

***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. Additionally, ADEPT will develop methods to transiently deliver nucleic acids for vaccines and therapeutics, and kinetically control the timing and levels of gene expression so that these drugs will be safe and effective for use in healthy subjects. 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 2013 Accomplishments:***

- Demonstrated increased humoral and cellular responses with RNA-based vaccines as compared to benchmark vaccines in vivo.
- Demonstrated increased efficacy of RNA-based vaccines in vivo in small and large animal models.
- Developed device components (sample preparation and detection components) to enable diagnostic device capabilities in low-resourced settings.
- Developed device components (fluidic delivery and multiplex assay module) to enable diagnostic device capabilities designed for the remote clinic.

***FY 2014 Plans:***

- Demonstrate ability to manipulate the 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 delivery of nucleic acids that transiently produce multiple antibodies.
- Perform quantitative comparison of room temperature assay methods appropriate for integration in devices for low-resourced settings.
- Demonstrate initial component integration and define performance metrics for advanced diagnostic device prototypes suitable for operations in remote clinic and low-resourced settings.

***FY 2015 Plans:***

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| - Demonstrate ability to control the time duration of the therapeutic response suitable for clinical use and rapid public health responses.<br>- Investigate targeted delivery of nucleic acid constructs to specific cell types.<br>- Demonstrate feasibility for controlling pharmacokinetics and immunity modulation components to enable a more potent and broader immune response.<br>- Develop designs for RNA-based vaccines to enable transition to human clinical trials.<br>- Develop designs for initial diagnostic device prototypes, based on highest performing components.<br>- Produce first-generation, integrated diagnostic prototypes designed for remote clinic and low-resourced settings.<br>- Measure quantitative performance of first-generation, integrated diagnostic device prototypes and determine modifications required for performance improvements. | | | |
| ***Title:*** Tactical Biomedical Technologies | 13.188 | 13.321 | 12.000 |
| ***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 hemostasis and wound control for non-compressible hemorrhage in the abdominal space, regardless of wound geometry or location within that space. This thrust will also investigate non-invasive techniques and equipment to use laser energy to treat intracranial hemorrhage through the skull and tissues in a pre-surgical environment. Finally, in order to address logistical delays associated with delivering necessary therapeutics to the battlefield, this thrust will also develop a pharmacy on demand that will provide a rapid response capability to enable far-forward medical providers the ability to manufacture and produce small molecule drugs and biologics. | | | |
| ***FY 2013 Accomplishments:***<br>- Demonstrated a combined hemostasis agent and delivery mechanism that achieves hemostasis in less than four minutes and does not interfere with standards of care.<br>- Assessed manufacturing costs and processes required for pilot-scale production of a Wound Stasis System.<br>- At laboratory scale, synthesized in continuous flow the following Active Pharmaceutical Ingredients (APIs): Diphenhydramine, Diazepam, Lidocaine, Fluoxetine, Ibuprofen, Atropine, and Doxycycline.<br>- Demonstrated continuous flow synthesis of Diphenhydramine, Diazepam, Lidocaine, and Fluoxetine using an integrated manufacturing platform.<br>- Designed and tested drug product crystallization and formulation for Diphenhydramine, Diazepam, Lidocaine, and Fluoxetine in an integrated manufacturing platform.<br>- Expressed protein therapeutics via fed-batch fermentation in both cell-free and cell-based systems. | | | |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| this thrust is the capability for new, portable spectroscopic techniques that can provide information for military medical use (e.g., analysis of traumatic brain injury) that is superior to that provided by an MRI. This need is ever increasing as researchers and scientists seek to better understand anatomical, functional, and cellular-level interactions. Finally, this thrust will allow safe, non-invasive to minimally invasive detection of microscopic and functional alterations within tissues and organs of a living organism at early stages of injury. The advanced development of these tools will provide a formidable arsenal of diagnostic tools for warfighter performance and care.<br><br>***FY 2013 Accomplishments:***<br>- Measured the Quantum Orbital Resonance Spectroscopy (QORS) effect using the most sensitive experimental techniques to date.<br>- Tested competing theoretical models for the physical basis of the QORS effect, and quantified the degree of hyperpolarization achieved under varying field strength, orbital angular momentum (OAM) charge, and beam array size.<br><br>***FY 2014 Plans:***<br>- Design and fabricate blazed, stacked, diffractive x-ray optics for integration into a pre-clinical imaging prototype.<br>- Design and test imaging and validation protocols for pre-clinical imaging prototype.<br>- Develop electrophysiological methods for simultaneous recording of multiple levels of abstraction in cortical/subcortical targets.<br>- Identify candidate approaches for real-time analysis and monitoring of brain activity during performance of behavioral tasks.<br><br>***FY 2015 Plans:***<br>- Investigate advanced imaging technologies, such as three-photon fluorescence imaging, that will enable single neuron spatiotemporal resolution of deep brain regions.<br>- Demonstrate proof of concept for achieving single neuron spatiotemporal resolution for recording spiking activity from 10^5 neurons in the cortex.<br>- Investigate new indicators and effectors for single neuron spatiotemporal observation and control with high cell specificity. | | | |
| ***Title:*** Dialysis-Like Therapeutics<br><br>***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. Additionally, the device may be effective as a medical countermeasure against various chemical and biological (chem-bio) threat agents, such as viruses, bacteria, fungi, and toxins. | 9.000 | 20.000 | 20.000 |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| 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.<br><br>***FY 2013 Accomplishments:***<br>- Developed a systems integration plan, conducted a user needs assessment, and designed the preliminary systems architecture incorporating component separation technologies.<br>- Developed appropriate animal models, confirmed regulatory plan, and initiated the regulatory approval process for the integrated device.<br>***FY 2014 Plans:***<br>- Integrate biocompatible high-flow fluid manipulation and intrinsic separation technologies into a breadboard device for the treatment of sepsis.<br>- Use feedback from initial animal model testing to inform the development of an integrated device for additional safety and efficacy studies in a large-animal sepsis model.<br>- Proceed with regulatory approval process and initiate plan for investigational device exemption submission.<br>***FY 2015 Plans:***<br>- Manufacture a prototype device that integrates label-free separation technologies, high-flow fluidic architectures, and non-thrombogenic coatings for testing.<br>- Evaluate the efficacy of the label-free separation technologies in a small-animal model.<br>- Refine the prototype device design based on animal testing results to inform development of a standalone benchtop integrated device.<br>- Perform safety and efficacy studies in a large-animal sepsis model.<br>- Initiate regulatory approval submission package with safety and efficacy data. | | | |
| ***Title:*** Warrior Web<br><br>***Description:*** Musculoskeletal injury and fatigue to the warfighter caused by dynamic events on the battlefield not only impact 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 | 12.150 | 12.000 | 8.992 |

| Exhibit R-2A, RDT&E Project Justification: PB 2015 Defense Advanced Research Projects Agency | | | Date: March 2014 |
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| **Appropriation/Budget Activity**<br>0400 / 2 | **R-1 Program Element (Number/Name)**<br>PE 0602715E / *MATERIALS AND BIOLOGICAL TECHNOLOGY* | **Project (Number/Name)**<br>MBT-02 / *BIOLOGICALLY BASED MATERIALS AND DEVICES* | |

| COST ($ in Millions) | Prior Years | FY 2013 | FY 2014 | FY 2015 Base | FY 2015 OCO # | FY 2015 Total | FY 2016 | FY 2017 | FY 2018 | FY 2019 | Cost To Complete | Total Cost |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MBT-02: *BIOLOGICALLY BASED MATERIALS AND DEVICES* | - | 35.517 | 41.510 | 78.976 | - | 78.976 | 99.707 | 109.310 | 112.120 | 130.250 | - | - |

# The FY 2015 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, investigate the role of complexity in biological systems, and explore neuroscience technologies.

| B. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| ***Title:*** Neuroscience Technologies | 9.000 | 11.917 | 16.000 |

***Description:*** The Neuroscience Technologies thrust leverages recent advances in neurophysiology, neuro-imaging, cognitive science, molecular biology, and modeling of complex systems 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 create modern neuroscientific techniques to develop quantitative models of this impact and explore mechanisms to protect, maintain, complement, or restore physical and cognitive functioning during and after exposure to operational stressors. In addition, new approaches for using physiological and 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 physical and cognitive performance at the individual and group level both prior to and during deployment.

***FY 2013 Accomplishments:***

- Integrated human data on stress genes to determine human stress-related gene networks for targeting interventions.

| Exhibit R-2A, RDT&E Project Justification: PB 2015 Defense Advanced Research Projects Agency | | Date: March 2014 |
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| B. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| - Translated genes and networks identified in animals to humans using high throughput molecular data from population-based studies.<br>- Determined biomarkers of alertness in active duty personnel with psychological health problems/traumatic brain injury.<br>- Correlated clinical and psychological profiles of patients with post-traumatic stress disorder to neural networks, neurochemicals and behavior for biomarker identification.<br>- Identified objective measures of physical and cognitive states through the application of integrated analytics and advanced computational techniques.<br>***FY 2014 Plans:***<br>- Determine genetic, epigenetic, and proteomic changes underlying vulnerability to poor decision making in humans.<br>- Develop tools and metrics for evaluating individual and group performance during close quarters combat training and other operationally relevant training scenarios.<br>- Exploit advances in complexity theory and predictive models of the brain and investigate new modeling methods to develop tools and techniques that can characterize and improve cognitive performance under stress at both the individual and group level.<br>***FY 2015 Plans:***<br>- Exploit new data and recent advances in functional imaging, neurophysiology recording, molecular and neural imaging, cognitive science, and biology in conjunction with emerging solutions in neurally enabled human-machine interface technologies to characterize dynamics of human cognitive functions such as memory, learning, and decision making.<br>- Initiate development of a unifying cross layer system model of the brain characterizing functions, dynamics, molecular and anatomical structure of the brain and their inter-relationships.<br>- Exploit recent advances in computational analysis, systems identification, data intensive computing, and statistical inference methods to develop computational tools and collaborative research platform for rapid analysis, validation, and integration of computational models of the brain.<br>- Initiate development of a new hierarchical framework for modeling and simulating structure, function and emergent behavior in complex biological systems and bionetworks.<br>- Create engineered intestinal biomes that respond to changes in critical neurotransmitter concentrations that control sense of well-being and satiety as well as those that influence intestinal health and nutrient uptake. | | | |
| ***Title:*** BioDesign<br>***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 methods for prediction of function based solely on sequence and structure of proteins produced by synthetic biological systems. | 10.824 | 11.438 | 19.354 |

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| **Appropriation/Budget Activity**<br>0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research* | **R-1 Program Element (Number/Name)**<br>PE 0602716E / *ELECTRONICS TECHNOLOGY* |

| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| - Demonstrate application-oriented thermal test vehicles to demonstrate the thermal benefits of embedded microfluidic cooling and model the anticipated electrical performance based on these thermal results.<br>***FY 2015 Plans:***<br>- Demonstrate the full implementation of the fundamental building blocks of evaporative intrachip/interchip cooling in relevant thermal test vehicles.<br>- Demonstrate application-oriented electrical test vehicles to demonstrate the performance benefits of embedded microfluidic cooling and relate these results to system-level performance and size, weight, power and cost (SWaPC) through the use of intrachip thermal management technologies. | | | |
| ***Title:*** In vivo Nanoplatforms (IVN)<br>***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 against chemical and biological (chem-bio) threat agents. 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.<br>***FY 2013 Accomplishments:***<br>- Achieved a safe in vivo nanoplatform sensor to detect one military-relevant analyte (e.g. glucose, nucleic acids) in living cells and/or tissue with a robust signal for greater than one month.<br>- Achieved a safe and effective in vivo nanoplatform therapeutic to reduce a military-relevant pathogen or disease cofactor in living cells by at least 50%.<br>- Facilitated development of a regulatory approval pathway for diagnostic and therapeutic nanoplatforms.<br>***FY 2014 Plans:***<br>- Achieve a safe in vivo nanoplatform sensor to detect two military-relevant analytes (e.g. glucose, nucleic acids) in a small animal with a robust signal for at least six months.<br>- Achieve a safe and effective in vivo nanoplatform therapeutic to reduce a military-relevant pathogen or disease cofactor in a small animal by at least 70%.<br>- Update regulatory approval pathway of identified safe and effective diagnostic and therapeutic nanoplatforms.<br>***FY 2015 Plans:*** | 8.500 | 23.338 | 16.500 |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2013 | FY 2014 | FY 2015 |
|---|---|---|---|
| - Achieve a safe in vivo nanoplatform sensor to detect five military-relevant analytes (e.g. glucose, nucleic acids) in a large animal with a robust signal for at least twelve months.<br>- Achieve a safe and effective in vivo nanoplatform therapeutic to reduce a military-relevant pathogen or disease cofactor in a large animal by at least 90%.<br>- Update regulatory approval pathway with results from safety and efficacy testing. | | | |
| ***Title:*** Pixel Network (PIXNET) for Dynamic Visualization<br><br>***Description:*** The 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 for 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 understanding. The program aims to develop a low size, weight and power (SWaP), low cost, soldier-portable multiband infrared camera that will provide real-time single and multiple band imagery using thermal and reflected-illumination bands. The camera will also provide fused reflective and thermal band imagery on demand. The use of fused imagery in the PIXNET design will allow the soldier to detect camouflaged targets and distinguish targets from decoys. The PIXNET camera will eliminate limitations posed by current capability, allowing detection, recognition and identification of targets whether in daylight or no-light conditions.<br><br>The PIXNET program will focus on a significant reduction in SWaP and cost of infrared sensor components to enable portability and ability to deploy widely to all participants in the theater. The emphasis on a small form will naturally enable new opportunities such as surveillance with small Unmanned Aerial Vehicles (UAV)s, rifle sights with multiple bands, and vehicle-mounted, helmet-mounted and handheld surveillance systems. The phenomenology of different infrared wavelengths will be exploited. The combination of a smart phone and PIXNET camera at the soldier level will enable more effective tactics, techniques and procedures (TTP) over the current capability. The PIXNET program takes advantage of the computing capability of smart phones to process and fuse multicolor images and send them as videos or still images to the warfighter's helmet-mounted display via a wireless or wired connection. PIXNET capability could be further exploited to enable a fully networked system, such as the Nett Warrior integrated multiple soldier systems capability, with multi-spectral still image and video sharing.<br><br>***FY 2013 Accomplishments:***<br>- Conducted multicolor fusion tests using separate video imagery in visible, shortwave and longwave to determine phenomenological advantages.<br>- Identified several Key Performance Parameters (KPPs) for the brass board design of the PIXNET camera. | 14.000 | 23.700 | 17.500 |