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RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2002
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense-wide BA1 Basic Research	R-1 ITEM NOMENCLATURE Defense Research Sciences PE 0601101E, Project BLS-01

nano-structures and engineered nano-technology for use in layout of molecular electronic devices, reliable crystallography, and for design of novel materials. Second, the program will develop validated computational models of internal cellular processes, capturing complex gene and protein interactions, and simulation tools, for in-silico analysis, capable of predicting cellular spatio-temporal dynamics. The application realm includes characterization, prediction, and control of highly conserved mechanisms of interest to DoD, such as those related to pathogenic processes; mechanisms such as circadian rhythms that underlie war fighter performance and well-being in stressed conditions; and design of bio-sensors. The modeling and simulation capability will be extensible from cell level to higher levels such as organ, organism, and to collective groups of organisms. In addition, the program will begin leveraging the modeling, simulation, and bio-informatics capability to explore new methods of biologically-inspired computing principles, architecture, and design of robust and reliable information processing and networking systems.

(U) The Simulation of Bio-Molecular Microsystems (SIMBIOSYS) program will focus on methods to dramatically improve the interaction and integration of biological elements with synthetic materials in the context of microsystems. SIMBIOSYS will explore fundamental properties and compatibility of biological elements at surfaces through experimental and theoretical analyses. Key phenomena to be studied include molecular recognition processes, signal transduction phenomena, and micro- and nano-scale transport of biological molecules. Engineering of biological systems may be used to manipulate these fundamental characteristics and optimize the integration of biological elements with synthetic materials for information collection. It is expected that significant advancements in devices that utilize or mimic biological elements will be realized including sensors, computational devices and dynamic biological materials for force protection and medical devices. Specifically the SIMBIOSYS program will develop methods and tools to simulate and design Bio-Molecular Microsystems with a high degree of multi-disciplinary integration.

(U) The Bio Futures program will support scientific study and experimentation, emphasizing biological software, computation based on biological materials, physical interfaces between electronics and biology, and interactive biology. It will apply information technology to accelerate the analysis and synthesis of biological processes. The seamless integration of information technology and biological processes will provide the ability to exert computational control over biological and chemical processes. The Bio Futures program will also support the development of genomics-based platforms for enhancing the capabilities of biological systems to manufacture, sense, or compute. Genomics–based platforms will enable rational medical drug discovery and broadspectrum antibiotics discovery for pathogens confronting the warfighter.

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- Initiate investigation of a biologist friendly cellular process simulation tool, including database definitions and user interface tools.
- Examine computational abilities of networks of cells and organized groups such as schools or swarms.
- Examine control methods of communication and regulation of activities in cells and organized groups of cells or organisms, such as colonies or mats.
- Develop preliminary miniaturized hardware designs for microchemical oligonucleotide manufacture, manipulation and amplification proof of principle brassboards. Initiate studies on error correction and optimal information encoding of microchemical oligonucleotides.

- Simulation of Bio-Molecular Microsystems (SIMBIOSYS). ($14.000 Million)
  - Engineer biological circuits and architectures that optimize compatibility and information transfer between biological and non-biological materials to improve the interaction and integration of biological elements with synthetic materials in the context of microsystems.
  - Develop methods to characterize interfaces that allow one- and two-way communications, smart control, longevity and stability.
  - Create instrumentation and tools that will improve experimental validation of models that explore biological systems at interfaces.
  - Develop and validate phenomenological models for a range of signal transduction processes.
  - Develop data and models on electrokinetic transport and surface tension driven flows in microsystems.
  - Investigate novel hybrid macro-molecular devices that form specific and controlled transducing functions at the molecular scale.

- Bio Futures. ($8.619 Million)
  - Demonstrate single molecular imaging in living cells. Demonstrate imaging of single molecular species in a living bacterial cell.
  - Demonstrate the application of novel nano-devices to measure, manipulate and control cells, tissues, and biomolecules.
  - Exploit nanoscale fluidic phenomena to achieve control of molecular level activity interrogation and control.
  - Develop nanofluidic interfaces for selective transport of multi-scale bimolecules.

- Biological Adaptation, Assembly and Manufacture. ($5.381 Million)
  - Identify and optimize strategies for manipulating cell and tissue survival in response to exogenous stimuli including stressful conditions.
  - Examine pluripotential and totipotential cells for principles of assembly, manufacture and long term survival.

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- Release first integrated version of open source Bio-SPICE (Simulation Program for Intra-Cell Evaluation) for use in biological experimentation.
- Initiate development of Bio-SPICE architecture that enables easy access to public genomic and protein interaction databases, and distributed computing for cell simulation.
- Investigate methods for reduced order cell models and scalability in cell process simulation.
- Demonstrate ability of individual technologies to overcome current problems caused by the inability of numeric algorithmic processes to handle the growing complexity of future C^2 problems.
- Develop capability to utilize complex biological systems for multiple sequential linked events. Assess the possibility of designing a 'digital human' model for a broad spectrum of applications.
- Investigate parallels between biological and non-biological signal processing via advanced modeling and experimentation tools.
- Finalize miniaturized hardware designs for microchemical oligonucleotide manufacture, manipulation, and amplification proof of principle brassboards and initiate development.
- Complete studies on error correction and optimal information encoding of microchemical oligonucleotides.

- Simulation of Bio-Molecular Microsystems (SIMBIOSYS). ($15.000 Million)
  - Engineer living circuits at material interfaces that perform pattern recognition and information processing.
  - Design working devices that incorporate living components as sensors, actuators and computational devices.
  - Explore the utility of using virtual representations of biological systems to specify their engineering properties.
  - Develop scaling laws and phenomenological models for bio-molecular and fluidic transport.
  - Implement models for molecular binding, signal transduction and bio-fluidic transport into microfluidic system software.
  - Investigate methods to extract and integrate several bio-molecular devices on synthetic substrates to form larger scale systems.

- Bio Futures. ($9.130 Million)
  - Develop new engineering tools for designing and enhancing biological regulatory circuits.
  - Develop functional nanofluidic sensors based on cells or cellular components for high sensitivity sensing.
  - Demonstrate nano-scale fluidic systems for the decoupling, quantification and transduction of multi-scale biomolecular signatures.
  - Demonstrate enhancement of natural metabolic capabilities via design-based approaches to genetic engineering.
  - Demonstrate novel nano devices for measuring and regulatin g cell physiology.