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RESEARCH, DEVELOPMENT, TEST AND EVALUATION, DEFENSE-WIDE

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RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2004
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense-wide BA1 Basic Research	R-1 ITEM NOMENCLATURE Defense Research Sciences PE 0601101E, Project BLS-01

The application realm includes characterization, prediction, and control of biomolecular processes such as those related to pathogens; mechanisms such as circadian rhythms that underlie war fighter performance and well-being in stressed conditions; and design of bio-sensors. This program will also pursue a comprehensive cognitive system that supports rapid analysis and discovery of molecular and cellular level mechanisms underlying pathogenesis relevant to biological threats, and the discovery of potential intervention mechanisms. 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 modeling, simulation, and bio-informatics capabilities to explore new methods of biologically inspired computing principles, architecture, and design of robust and reliable information processing and networking systems.

(U) Program Plans:

- Initiate development of a progressively sophisticated suite of dynamic cellular models and architecture for Bio-SPICE (Simulation Program for Intra-Cell Evaluation), which will enable modeling, prediction, and control of last submission "cell model" processes, with continual validation of each model experimentally. The cell modeling and Bio-SPICE will be capable of analysis of hundreds of gene-protein networks and interactions.
- Continue to incorporate spatial models into Bio-SPICE and explore potential reduced-order models capabilities to analyze the non-linear and stochastic dynamics of thousands of interactions for sophisticated analysis of pathogenic agents.
- Investigate scalable and extensible implementation of Bio-SPICE that utilizes a distributed computing architecture supporting a rich set of spatio-temporal models, with the ability to handle vast amounts of experimental data for prediction and analysis.
- Identify candidate biosystem elements for intervention strategies in sporulation, cell cycle control, and other processes in defense against bioagents.
- Investigate the extension of research in knowledge representation and reasoning tools to integrate data and models across multiple scales.

	FY 2003	FY 2004	FY 2005
Simulation of Bio-Molecular Microsystems (SIMBIOSYS)	12.676	9.000	9.000

(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. Specifically the SIMBIOSYS program will

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develop methods and tools to simulate and design Bio-Molecular Microsystems with a high degree of multi-disciplinary integration. This will be accomplished by exploring fundamental properties and compatibility of biological elements at the molecular surface level 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.

(U) Program Plans:

- Demonstrate high (signal to noise [SNR] ratio > 10) transduction of molecular signals into measurable electrical and mechanical signals using nanopores, micro/nano-cantilevers, and nanoparticles; demonstrate SNR ~ 100 using solid-state nanopores for DNA translocation and using nanopores for ultraselective DNA detection; demonstrate models to correlate transduced signal intensity to bio-molecular structure and binding events.
- Demonstrate low power transport (~ 10X reduction in power) of fluids by modulating surface tension in droplet based transport.
- Demonstrate surface-tension modulated transport of droplets on a substrate; demonstrate computational models to optimize transport characteristics.
- Demonstrate orders of magnitude (> 100X) improvement in microfluidic mixing using electrokinetic and Magneto Hydrodynamic (MHD) schemes (based on modeling studies); demonstrate 10 – 100 X improvement in mixing through MHD and electrokinetic instability mechanism.
- Develop scaling laws and phenomenological models for bio-molecular phenomena such as molecular recognition, signal transduction and bio-fluidic transport processes in bio-microfluidic systems; develop and implement scaling laws into microfluidic system modeling software to enable design of lab-on-a-chip systems.
- Design novel hybrid macro-molecular devices that form specific and controlled transducing functions at the molecular scale; demonstrate design of maltose binding proteins and ion channels with desired selectivity and sensitivity using computational tools.
- Design and demonstrate working devices that incorporate biological elements as sensors, actuators and computational devices.