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RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2005
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense-wide BA1 Basic Research	R-1 ITEM NOMENCLATURE Defense Research Sciences PE 0601101E, Project BLS-01

- Demonstrate computer analysis methods for commanders to use in the threat assessment of natural and emerging bio-agents. These methods, which predict pathogenicity and virulence of agents from their genomic information, will be far more informed than today's costly wet-experiments.
- Identify new methods for early detection of exposure of soldiers to pathogens and toxins using molecular (gene expression) signatures, which is vital for early intervention and avoidance of death.
- Develop a framework for describing and representing biological knowledge that spans data from molecular (genomic, proteomic) to clinical level, and across organisms, to support deep and rapid knowledge extraction.
- Implement cutting edge learning and reasoning algorithms that act on vast amounts of biological experimental and simulation data, and demonstrate rapid reasoning and knowledge-acquisition.

	FY 2004	FY 2005	FY 2006	FY 2007
Simulation of Bio-Molecular Microsystems (SIMBIOSYS)	9.000	9.000	5.000	3.000

(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 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.

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(U) Program Plans:

- Demonstrate high (signal to noise ratio [SNR] > 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 that, using microcantilevers, a nanoparticle conjugation can successfully enable detection of 10-100 atto-molar DNA concentrations with single base pair selectivity without performing polymerase chain reaction; transition to other DoD agencies and Homeland Defense.
- 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).
- 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.

	FY 2004	FY 2005	FY 2006	FY 2007
Bio Interfaces	5.366	4.000	4.000	4.750

(U) The Bio Interfaces program will support scientific study and experimentation, emphasizing the interfaces between biology and the physical and mathematical/computer sciences. This unique interaction will develop new mathematical and experimental tools for understanding biology in a way that will allow its application to a myriad of DoD problems. Chief among them is the ability to seamlessly integrate and control mechanical devices and sensors within a biological environment – a critical aspect in the successful implementation of a major prosthetics effort.