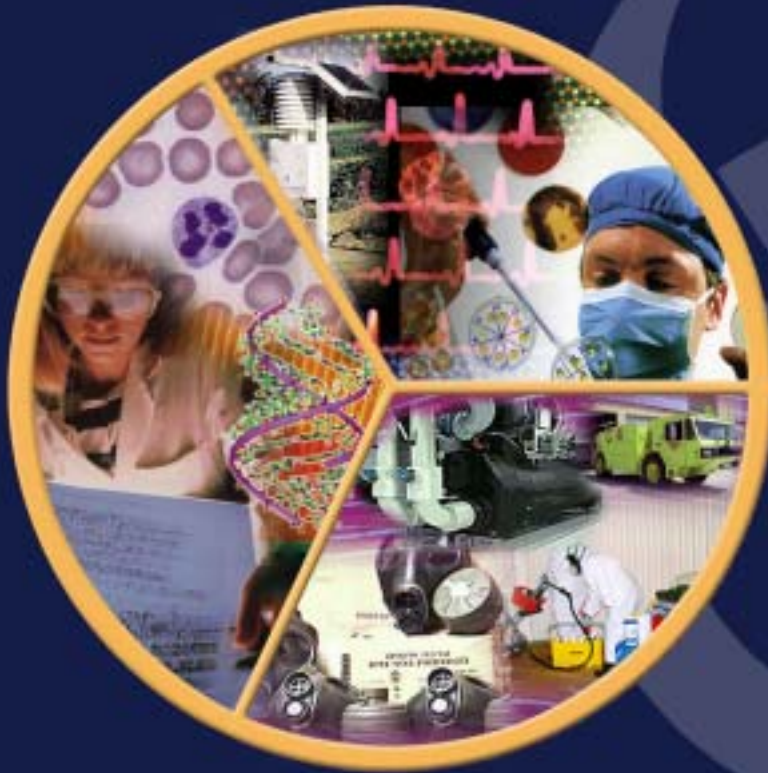


All slides have been cleared for public release

**DARPA**

**BWWD**



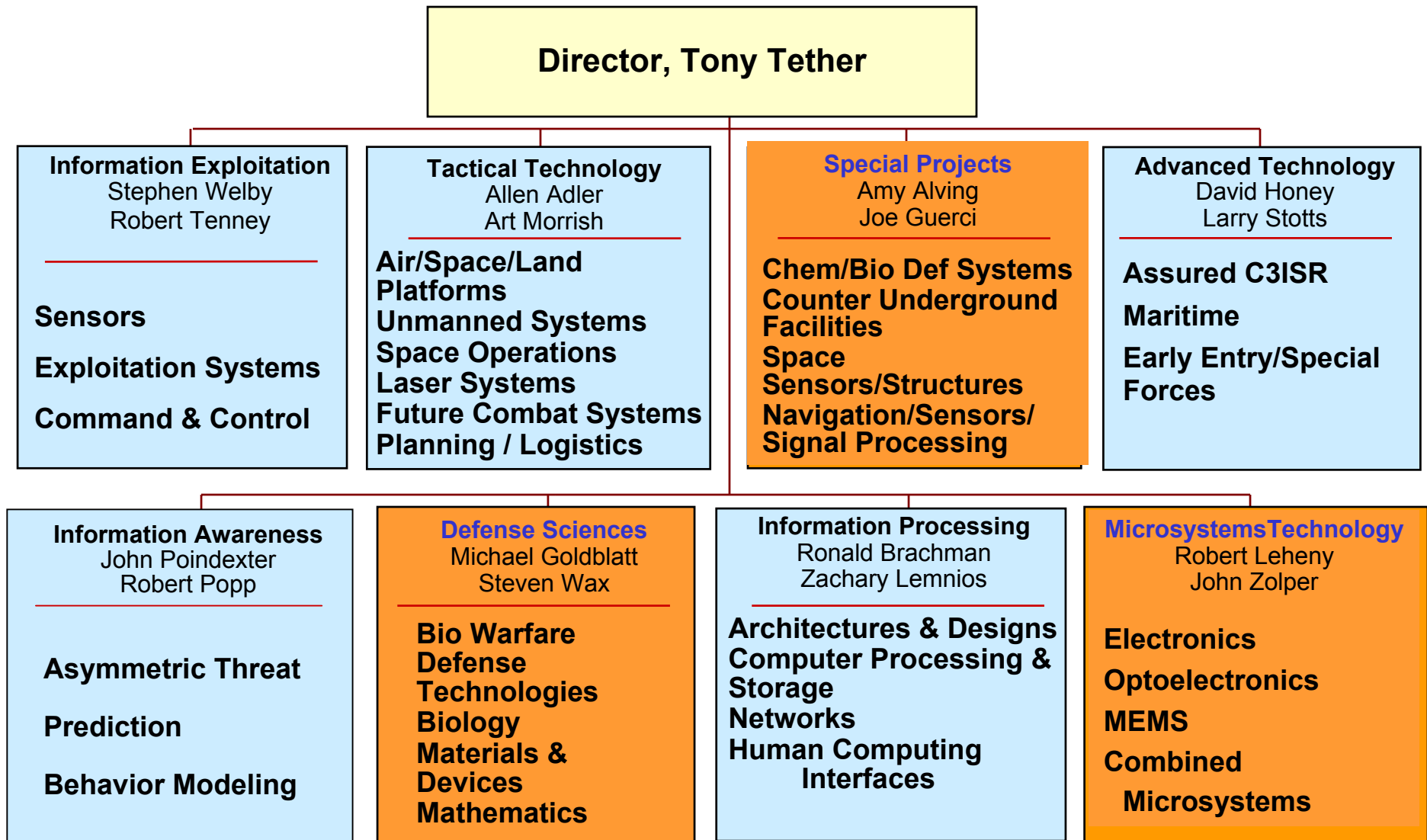
**Biological Warfare Defense**

Dr. Mildred A. Donlon  
Program Manager,  
Defense Advanced Research Projects Agency  
Defense Sciences Office  
3701 North Fairfax Drive  
Arlington, VA 22203-1714  
[mildonlon@darpa.mil](mailto:mildonlon@darpa.mil)

<http://www.darpa.mil/dso>

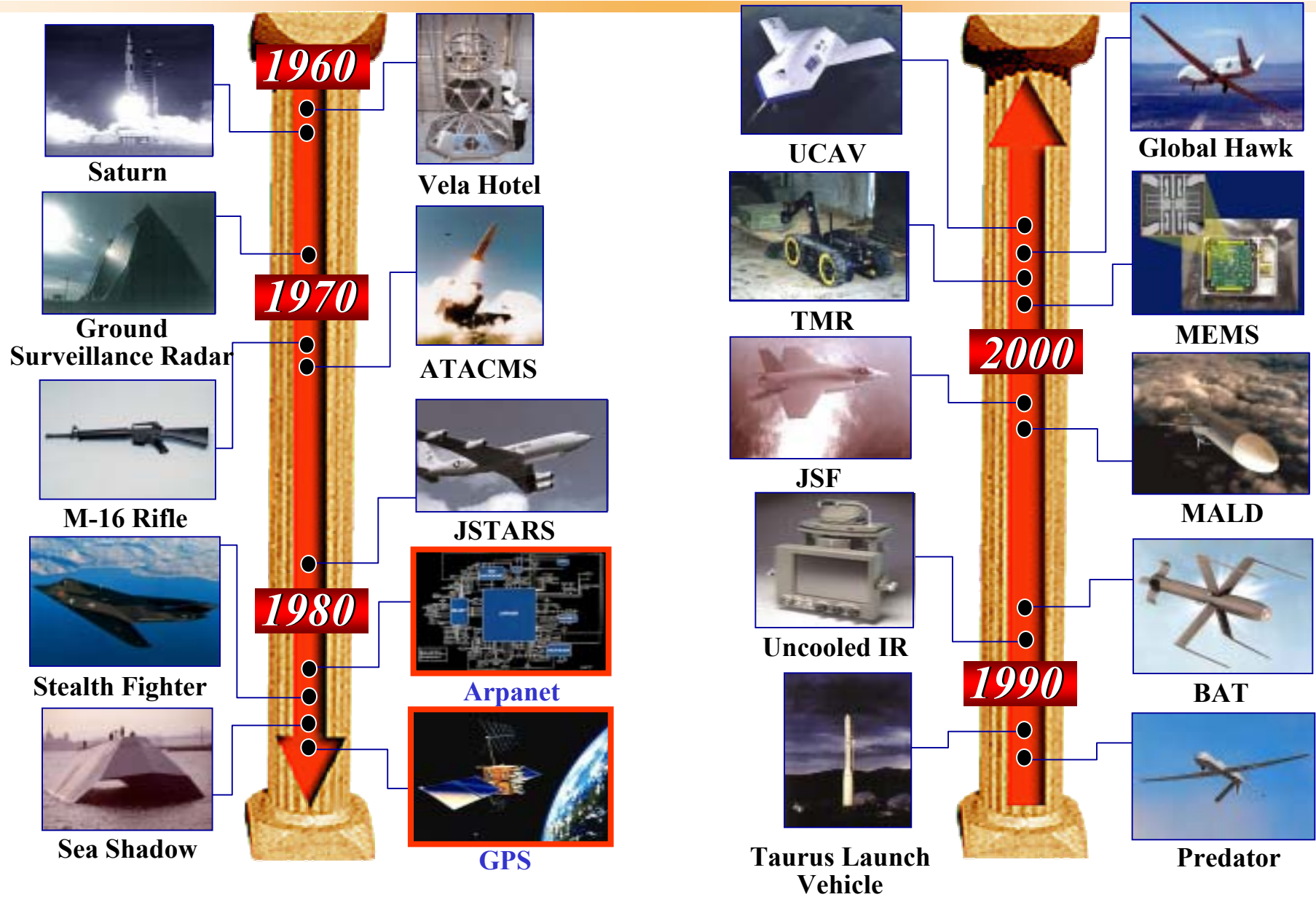


# DARPA Organization



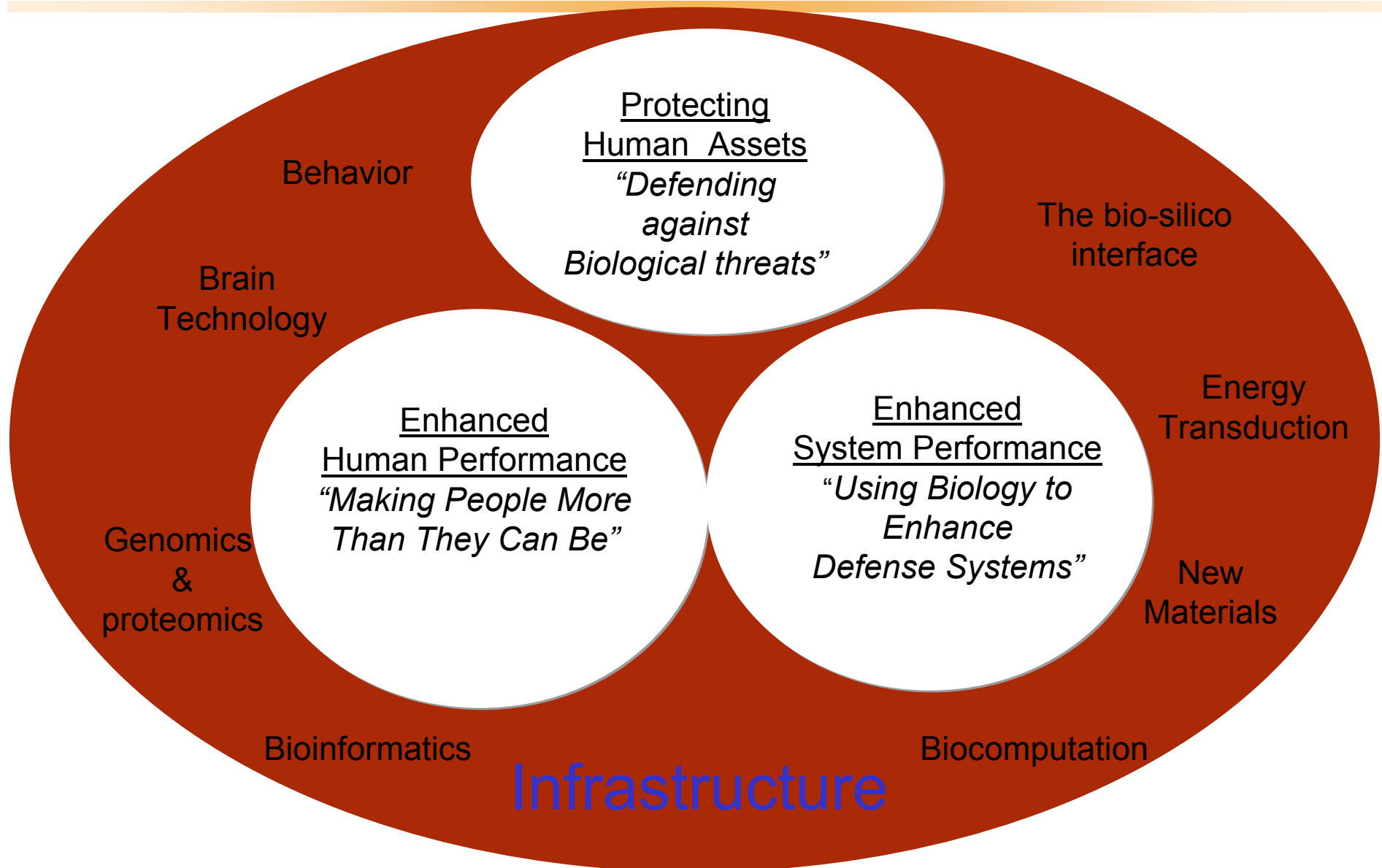


# DARPA Accomplishments





# Harvesting Biology for Revolutionary Technologies at DARPA

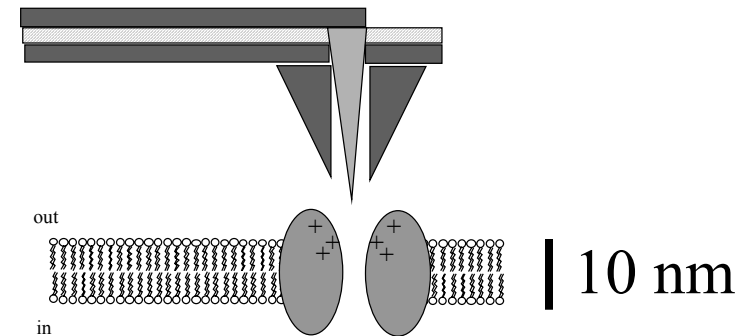




# Biology is a major driver for new math and physics

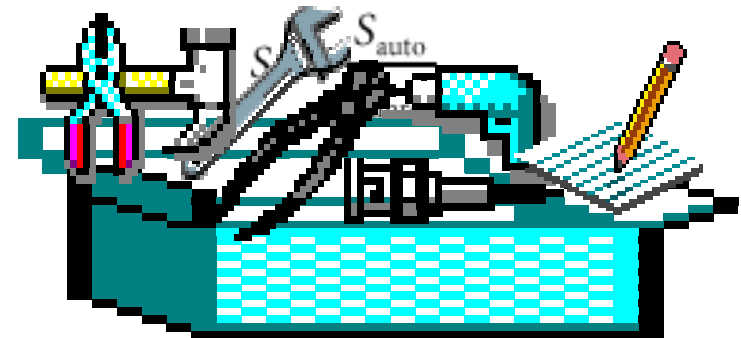


- Interrogate and manipulate biological systems with modern physical devices
- Analyze, model, simulate & design with a new arsenal of math and computational tools



$$S_{\text{unreg}} = f'_{\text{unreg}}(R^*) = -k_{\text{deg}}$$

$$S_{\text{auto}} = f'_{\text{auto}}(R^*) = -\frac{nk_p P k_1 a k_r}{(1 + k_p P + k_r R^*)^2} - k_{\text{deg}}$$







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## Highlights

- ▶ Presentations from the 23rd DARPA Systems and Technology Symposium, held July 29-August 2, 2002 are [now available](#).



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## Defense Sciences Office (DSO)



Information about solicitations sponsored by the Defense Sciences Office, including Proposer Information Pamphlets, is also available from the [DSO Solicitations Web Page](#).

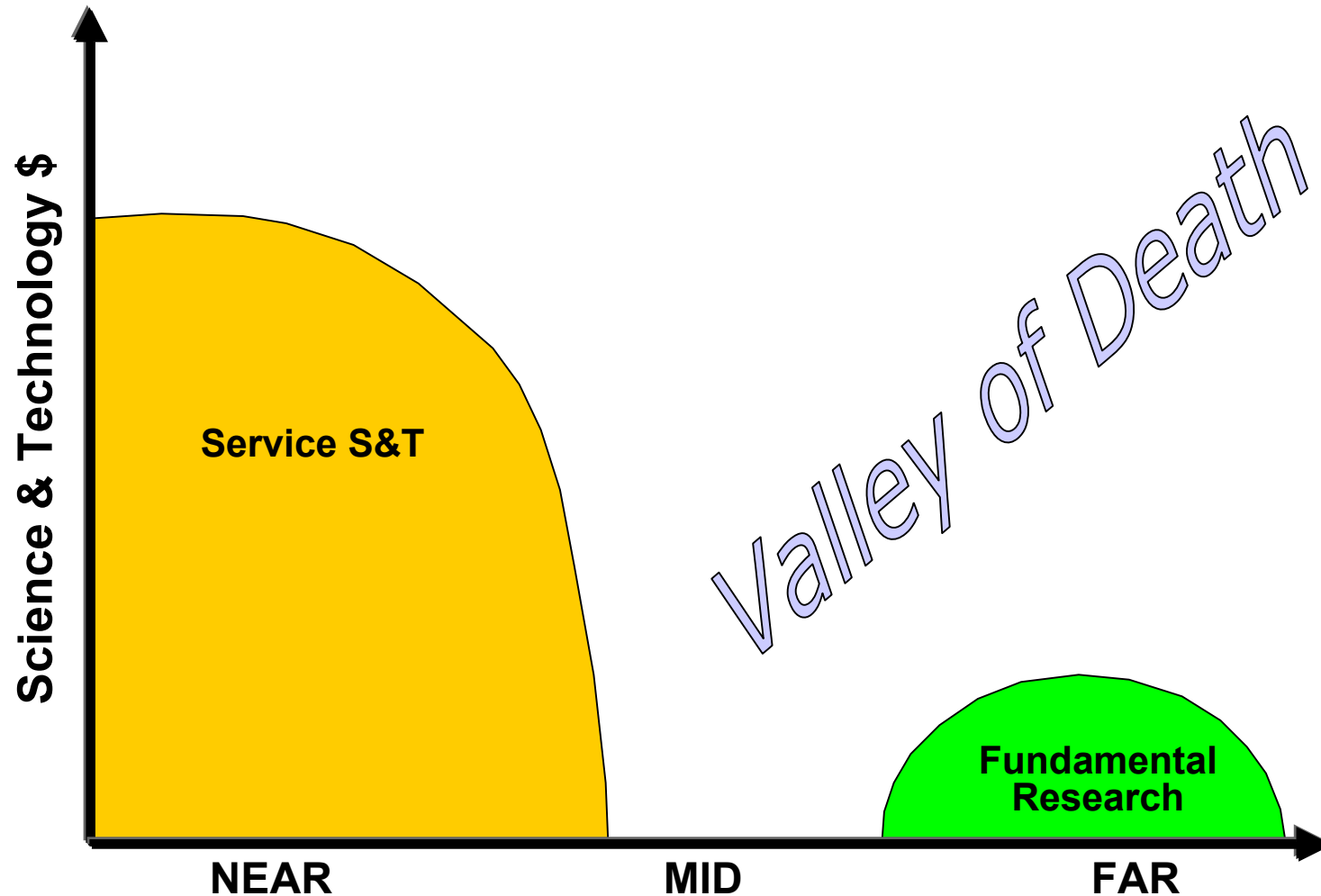
- Title: **A -- Defense Sciences Research and Technology**
  - Announcement #: **BAA01-42**
  - [FedBizOpps Reference](#): **September 4, 2001**
  - [Modification](#): **July 15, 2002**
  - [Modification](#): **August 12, 2002**
  - Closing Date: **December 15, 2002**
- 

- Title: **A -- Defense Sciences Research and Technology**
  - Special Focus Area: **Brain Machine Interfaces**
  - Announcement #: **BAA01-42, Addendum 1**
  - [FedBizOpps Reference](#): **September 17, 2001**
  - Closing Date: **See Primary Solicitation**
- 

- Title: **A -- Defense Sciences Research and Technology**
- Special Focus Area: **Biological Input/Output Systems (BIOS)**
- Announcement #: **BAA01-42, Addendum 2**
- [FedBizOpps Reference](#): **October 17, 2001**
- Closing Date: **See Primary Solicitation**



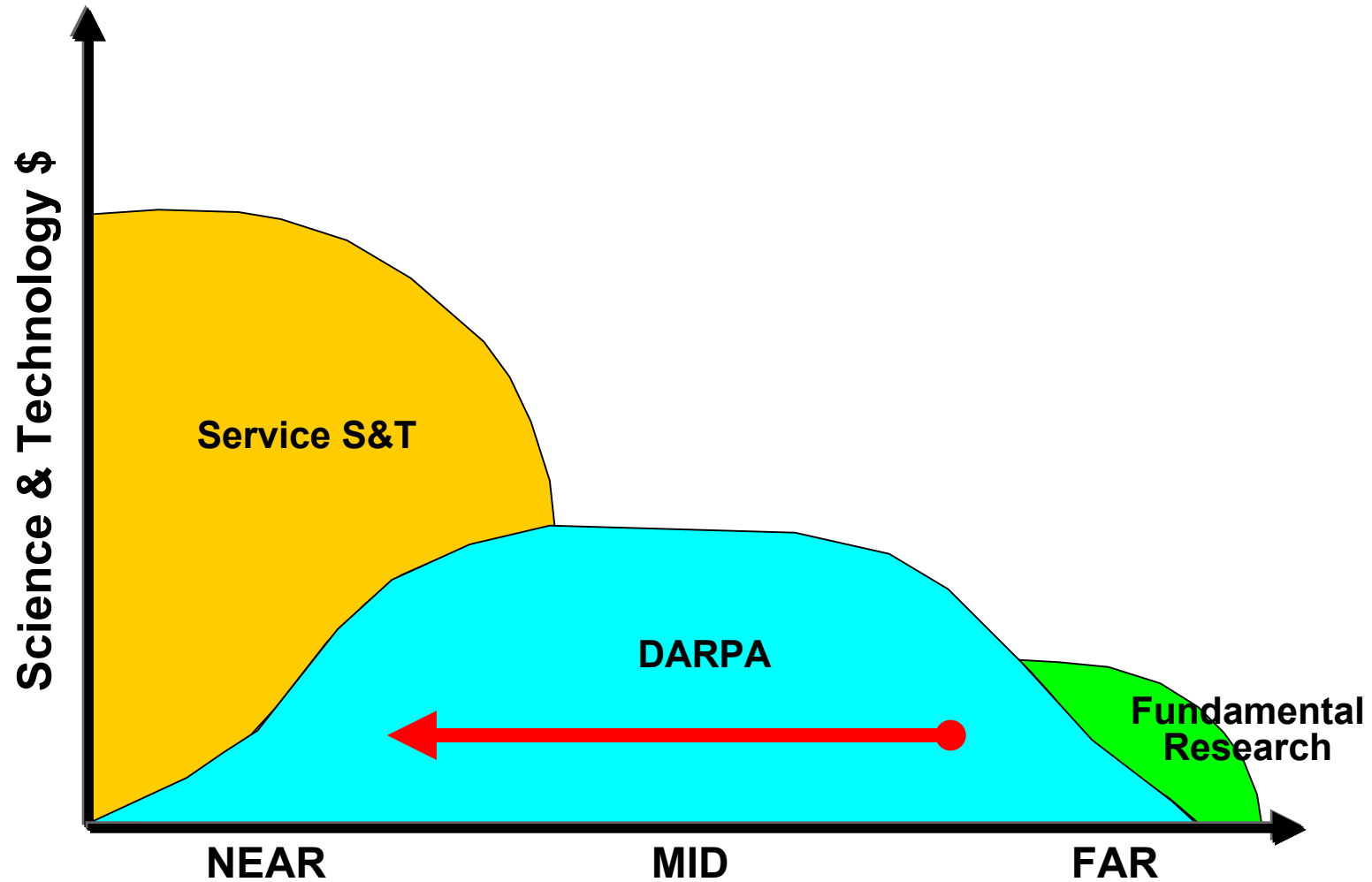
# DARPA Role in Science and Technology





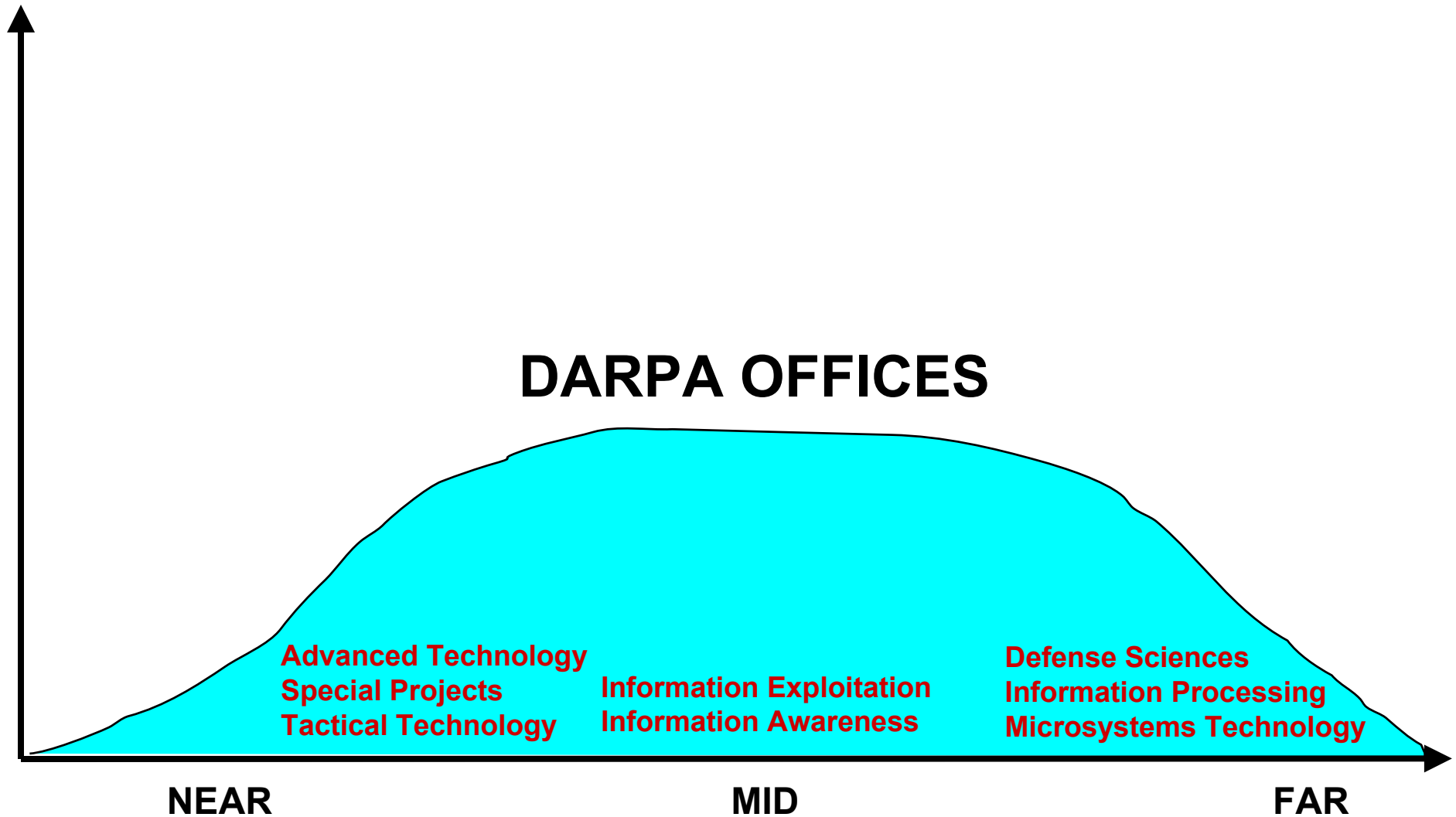


# DARPA Role in Science and Technology





# Internal Technology Flow





# BioWarfare Threat



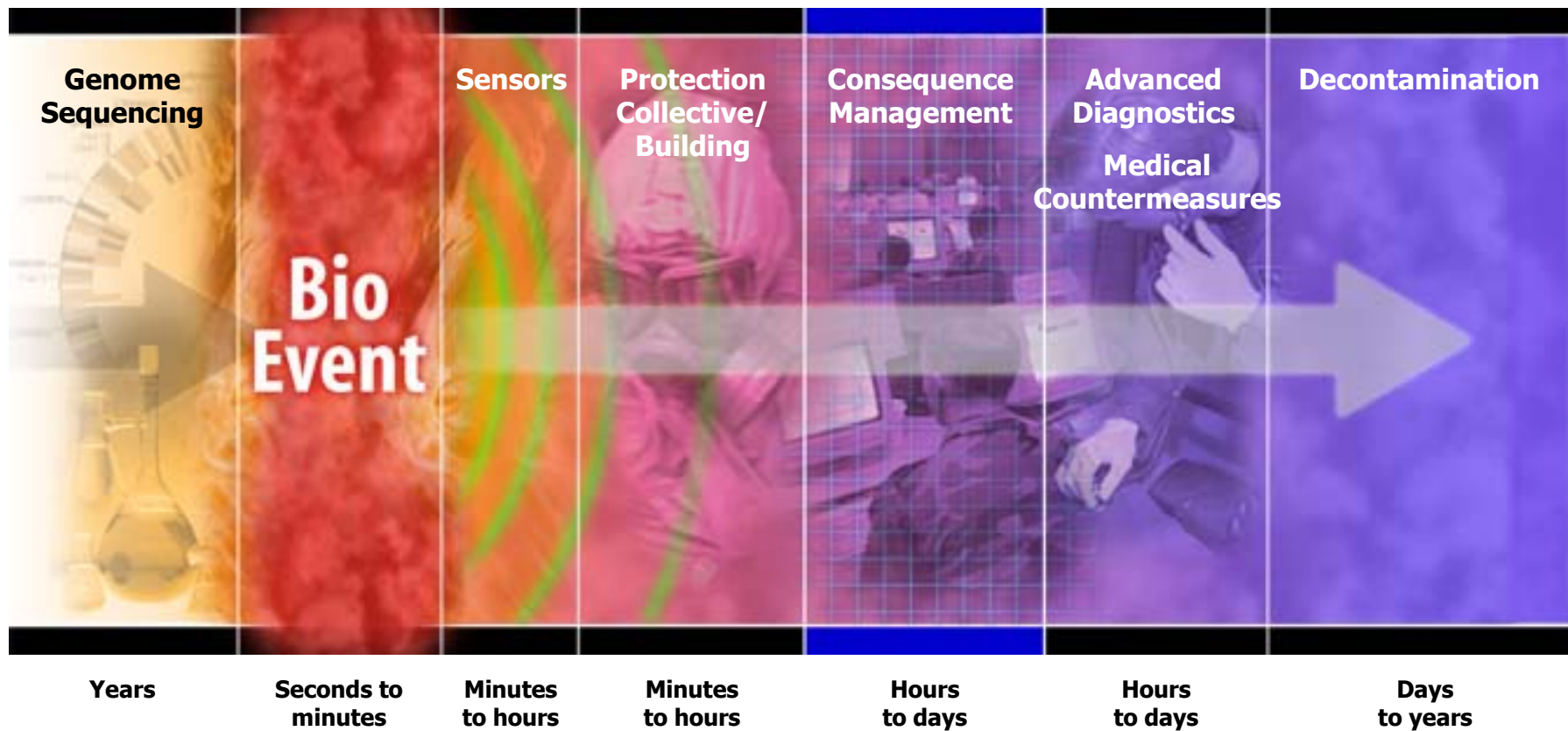
## *Update: The Trend Lines*

- The growing threat of BW is generated by three disturbing trends:
  - The number of players possessing biological weapons or seeking to acquire a biological warfare capability is increasing.
  - Biological agents with increasing lethality are being developed.
  - Detection of BW programs and the acquisition of BW-related capabilities is difficult.
- It happened here

*National Intelligence Council Report: The Biological Warfare Threat, Jan 2001.*



# Protecting Human Assets





# Simbiosys Program

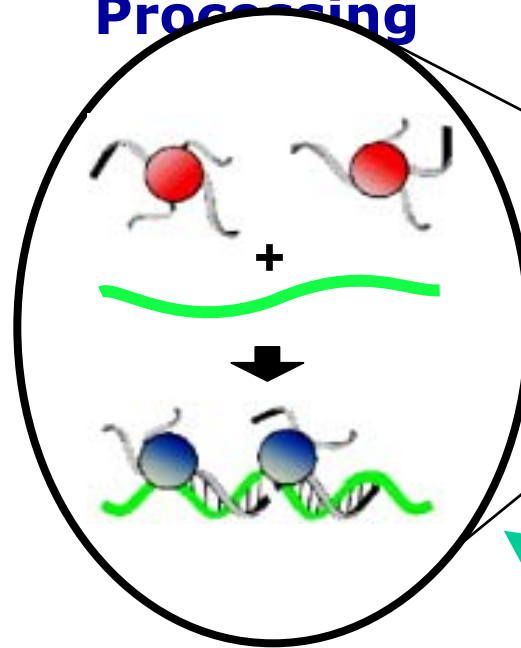
Anantha Krishnan, DSO



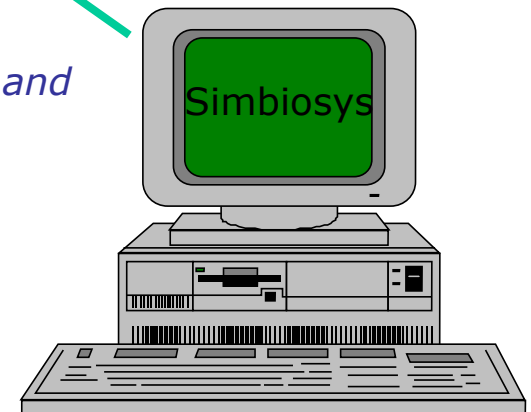
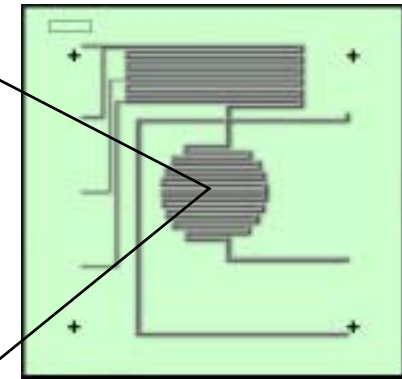
## Novel Tools (Devices, Models, Databases, Algorithms) for High Performance Biological/Chemical Sensing and Processing

### Challenges

- Experimental/Theoretical Characterization of the elements of a Bio-Molecular System :
  - Molecular Recognition Elements (sensitivity, selectivity and speed)
  - Signal Transduction Elements (Signal Amplification with High SNR)
  - Bio-Fluidic Transport Elements (High Efficiency, Low Power Pumping, Valving and Mixing Methods)
- Demonstration of device models on design of Bio-Microsystems



*Interface Between Biology and Micro/Nano-Technology*



**Novel Processes, Experimental Methods, Computational Models and Design Tools that significantly improve speed, sensitivity, specificity and efficiency of chemical/biological processing and analysis**



# SUVOS - Semiconductor Ultraviolet Optical Sources

John Carrano, Program Manager, MTO

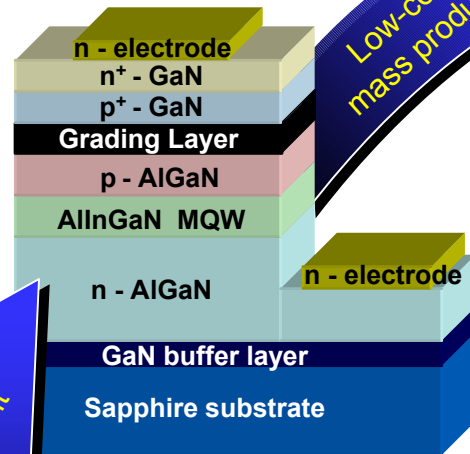


## Develop Solid-State UV Sources down to 280 nm

Compared to conventional technology

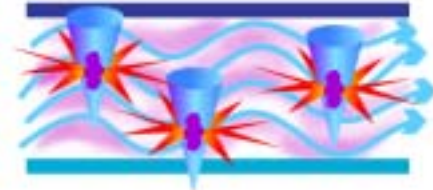
- Power consumption reduced by 50X
- Size & weight reduced by 100X

LEDs and Laser Diodes:  
The Next Step  
in efficient  
UV power  
generation

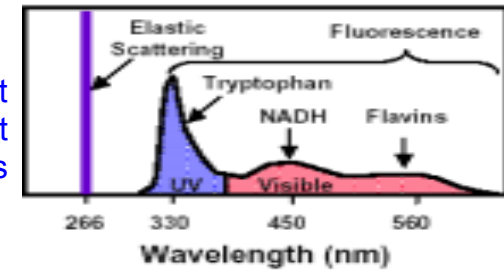


UV LED

Emitter -  
Detector  
sensor  
arrays

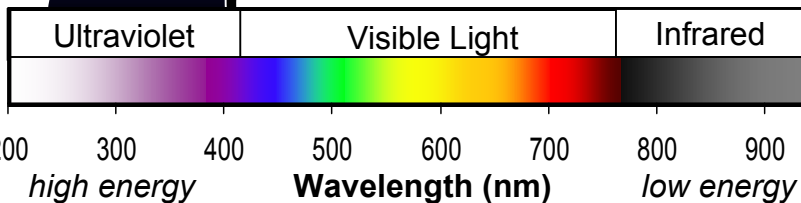


Bio-agent  
fluorescent  
signatures

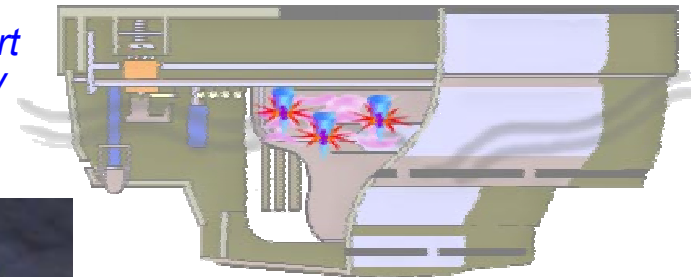


Enabling new classes of  
bio-agent detection systems

SUVOS sources  
100X smaller  
50X more efficient

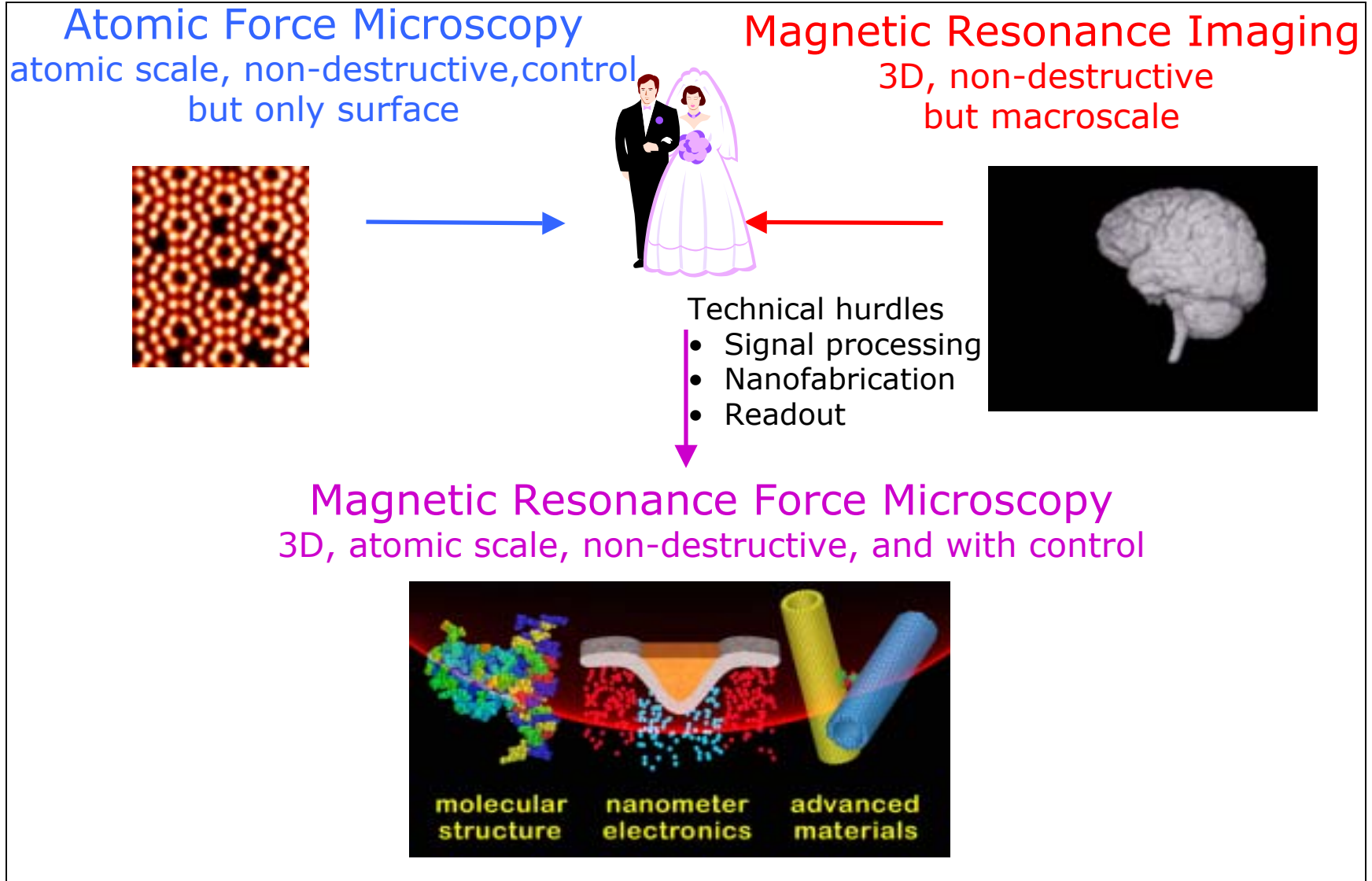


Bio-Alert  
in every  
office



Aerosol samplers –  
small and efficient  
for MAV deployment







# BIOS



**Techbase program to make plug & play (PnP) biocircuits that enable engineering of organisms for use as sentinel devices**





# Activity Based Detection: A Conceptual Framework

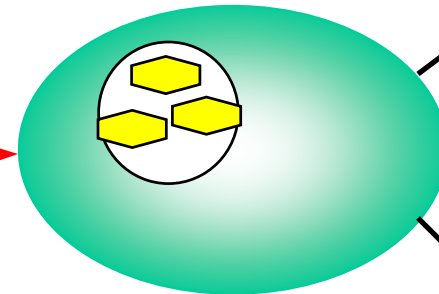
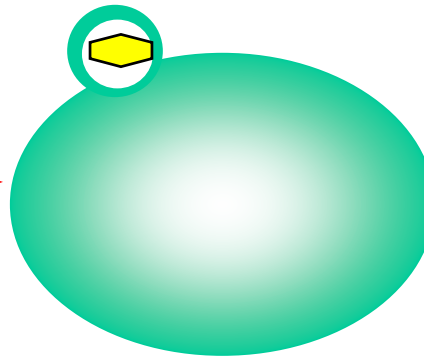
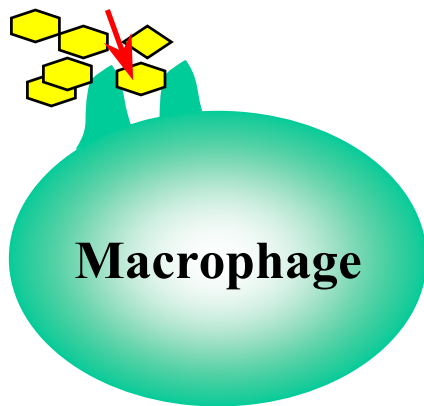
Alan Rudolph, DSO



Bacteria enter the cell in body (lung) or sensor

Bacteria invade alveolar cells

Bacteria internalize and multiply



*In vitro*

Evaluate Activated Pathways for Sensor

*In vivo*

Report Infection for Medical Diagnostic

*Cellular or Tissue activity can be used as diagnostic or to engineer markers for sensors*

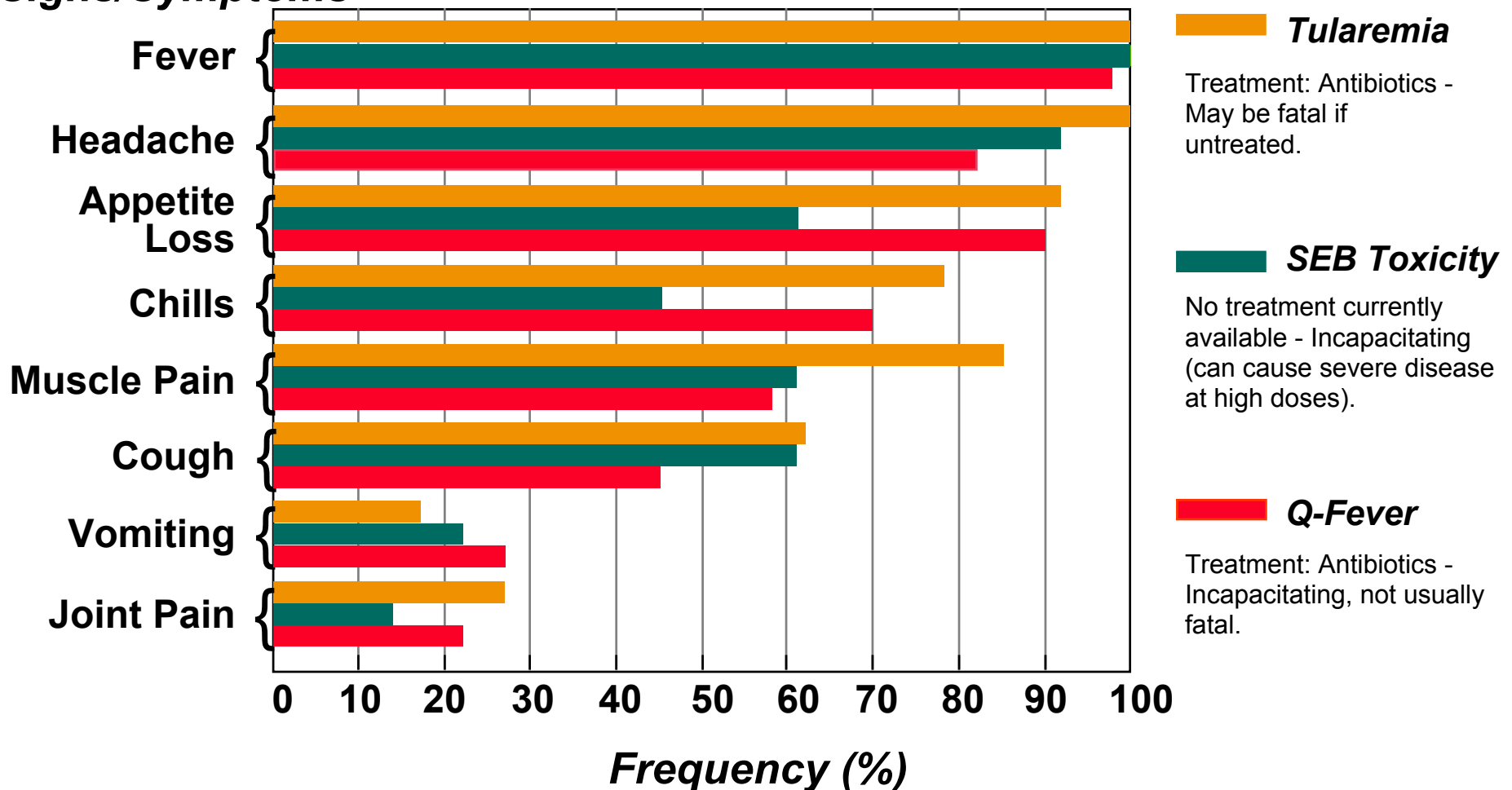


# Advanced Diagnostics... Why We Need It



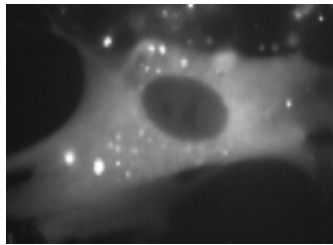
Early symptoms of many BW agents are flu-like and indistinguishable

## Signs/Symptoms

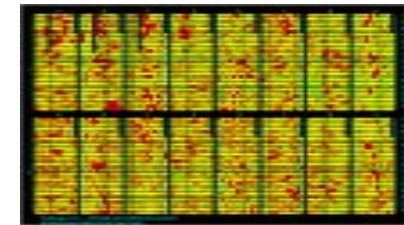




# Signatures of Exposure



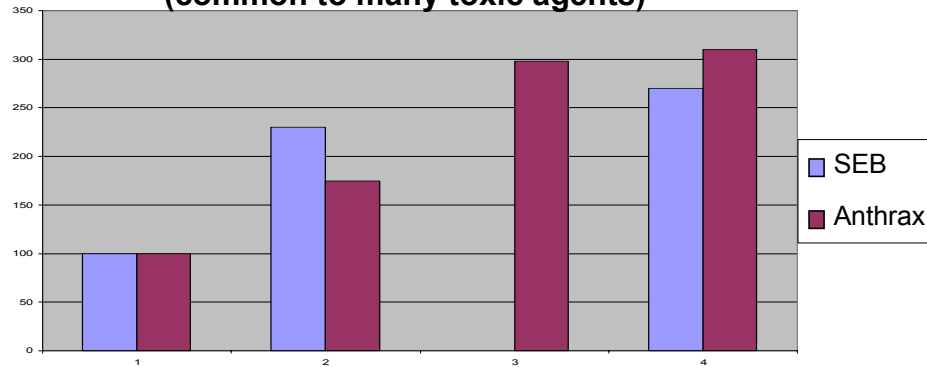
*WRAIR, Georgetown University, Stanford, Umea Sweden, APL*



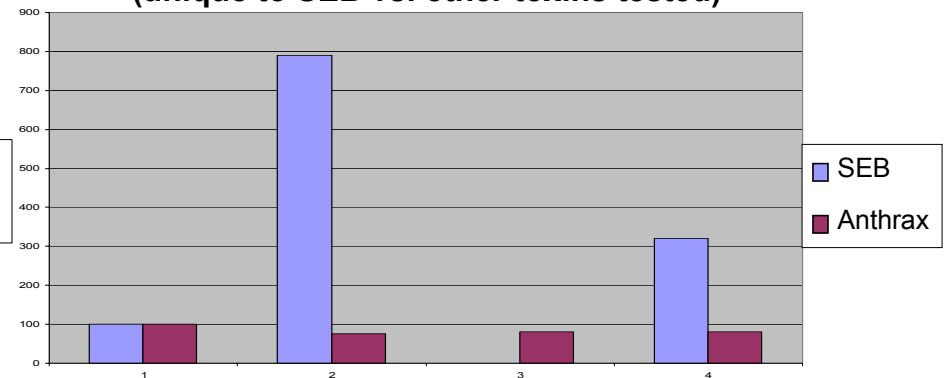
**Program Goal:** Determine cell signatures of early exposure to BW pathogens and develop rapid signature diagnostics

**Concept:** Generate differential expression profiles and cDNA libraries from cells after exposure. Identify differentially expressed transcripts. Create gene reporter elements for diagnostic tests

**Changes in Expression of HIF-1  
(common to many toxic agents)**



**Changes in Expression of a GBP  
(unique to SEB vs. other toxins tested)**





# Unconventional Pathogen Countermeasures

John Carney, DSO



## Broad-Spectrum Approaches

Idea: Develop broad spectrum technologies that effectively counter potential BW threats to the US military and civilians

### Technical Challenges:

- Develop therapeutics effective against all known and unknown (e.g. engineered) BW pathogens
- Develop effective multivalent vaccines with broad efficacy versus industry standard one bug one drug
- Enhance Immune system in order to eliminate the need for vaccines

### Vaccines

Plants for Production of Vaccines and Antibodies

Edible plant vaccines stimulate immune responses  
 Nature Medicine 4: 497-509 (1996)  
 Plant-expressed Abo provide protection in human  
 Nature Medicine 4: 498-506 (1996)

Plants are an economical production system for subunit vaccine proteins to prevent infectious disease, and for antibodies to treat diseases or toxin exposure.

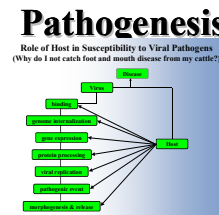
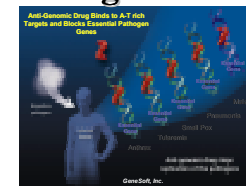
### Antibacterial

Inhibition of Pathogen Growth

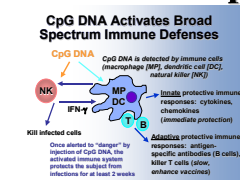
Compound	Antibiotic resistance	Antimicrobial resistance	Antibiotic target
1	Yes	Yes	Yes
2	Yes	Yes	Yes
3	Yes	Yes	Yes
4	Yes	Yes	Yes
5	Yes	Yes	Yes
6	Yes	Yes	Yes
7	Yes	Yes	Yes
8	Yes	Yes	Yes
9	Yes	Yes	Yes
10	Yes	Yes	Yes
11	Yes	Yes	Yes
12	Yes	Yes	Yes
13	Yes	Yes	Yes
14	Yes	Yes	Yes
15	Yes	Yes	Yes
16	Yes	Yes	Yes
17	Yes	Yes	Yes
18	Yes	Yes	Yes
19	Yes	Yes	Yes
20	Yes	Yes	Yes
21	Yes	Yes	Yes
22	Yes	Yes	Yes
23	Yes	Yes	Yes
24	Yes	Yes	Yes
25	Yes	Yes	Yes
26	Yes	Yes	Yes
27	Yes	Yes	Yes
28	Yes	Yes	Yes
29	Yes	Yes	Yes
30	Yes	Yes	Yes
31	Yes	Yes	Yes
32	Yes	Yes	Yes
33	Yes	Yes	Yes
34	Yes	Yes	Yes
35	Yes	Yes	Yes
36	Yes	Yes	Yes
37	Yes	Yes	Yes
38	Yes	Yes	Yes
39	Yes	Yes	Yes
40	Yes	Yes	Yes
41	Yes	Yes	Yes
42	Yes	Yes	Yes
43	Yes	Yes	Yes
44	Yes	Yes	Yes
45	Yes	Yes	Yes
46	Yes	Yes	Yes
47	Yes	Yes	Yes
48	Yes	Yes	Yes
49	Yes	Yes	Yes
50	Yes	Yes	Yes

USI resistance breaks not determined to culture macrophages or mice

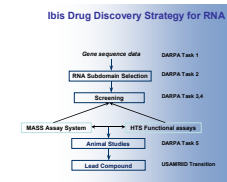
### Antigenomics



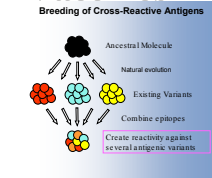
### Immunotherapy



### Antiviral



### Vaccines



### Highlights:

- 5<sup>th</sup> year of funding
- USAMRIID technology transition partner (10 transitions to date, 6 under discussion)
- Possible development of 5 new pharmacological therapeutics

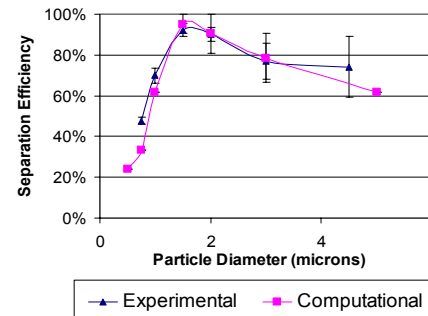
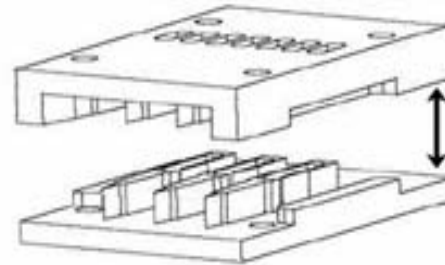




# MicroVIC<sup>®</sup> Bio-aerosol Concentrators



- **Technology:**
  - Virtual Impaction (aerodynamic sorting and concentrating)
  - Developer: MesoSystems
- **Key Features:**
  - Low power
  - Compact and versatile
    - Wet or dry particle collection
    - Wet collection
    - Aerodynamic pre-filtering
    - Particle pre-concentrator for triggers
  - Mass-producible (low cost)
- **Commercialization in progress**



Continuous Air Sampler  
for Lockheed Martin



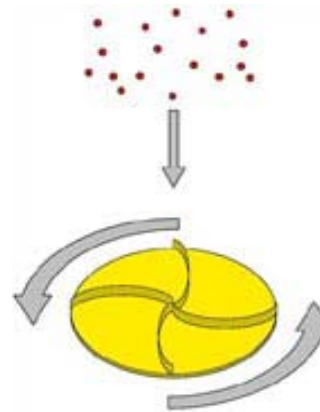
Bioni™ UV trigger by  
Pacific Scientific Instruments



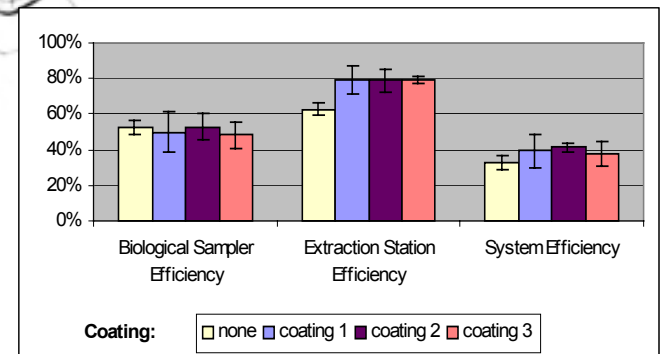
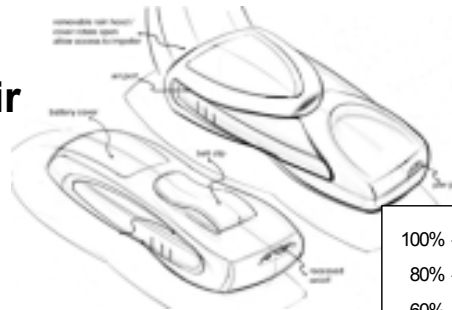
# BioBadge Wearable Bio-dosimetry



- **Technology:**
  - MesoSystems Rotating Impactor combined with SRI International's UPT Immunoassay
  - Field exposure quantification for the individual
- **Key Features:**
  - Low power; field operation
  - Compact and light
  - 15-30 liters/min flow rate
  - 40% overall efficiency from Air → Disk → Liquid sample
- **Commercialization status**
  - Laboratory testing in 2002
  - Field trials in 2003



Air

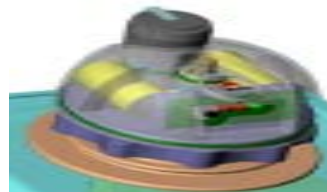




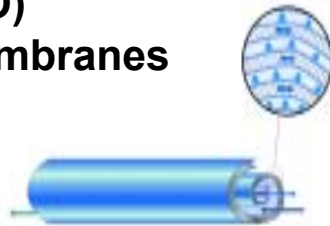
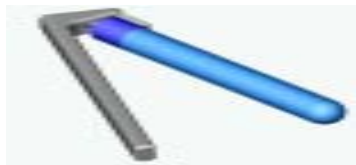
# Personal Water Purification Systems



## MIOX Disinfection Pen/Cap



## Reverse Osmosis (RO) Pump / Advanced Membranes

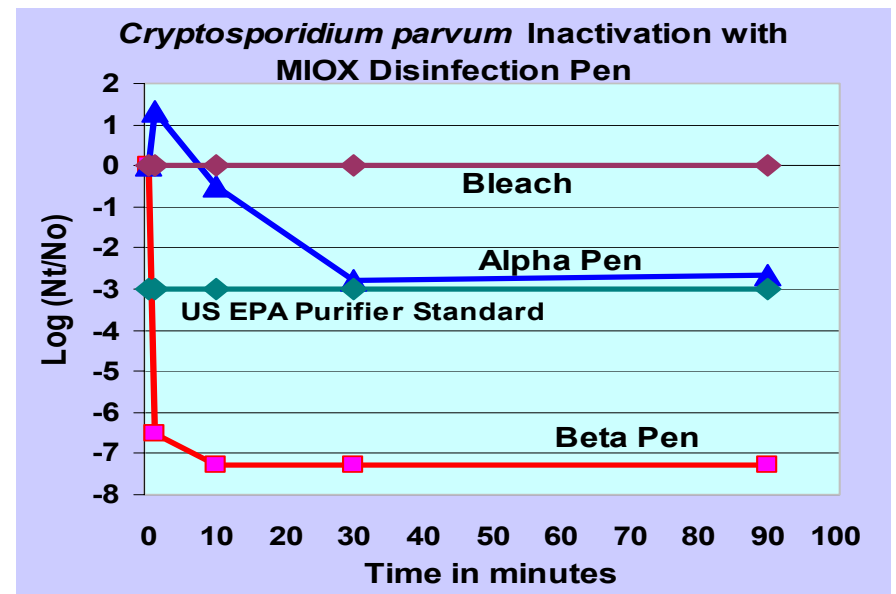


### Tech Approach:

- Effective mixed-oxidant chemistry from table salt
- Smart electrochemical cell and circuit
- Miniaturization of mechanical filters and purifiers
- Pen/pump combo treats any water source
- Low cost to produce
- Working turbidity filtration issues

### New Generation Hydration System

- Lightweight/reduced footprint for “on-the-move” operation (backpack)
- Produces Gatorade-like nutrient drink from contaminated water via FO bag
- **MIOX pen/cap inactivates even extremely resistant microorganisms by 99.99%**



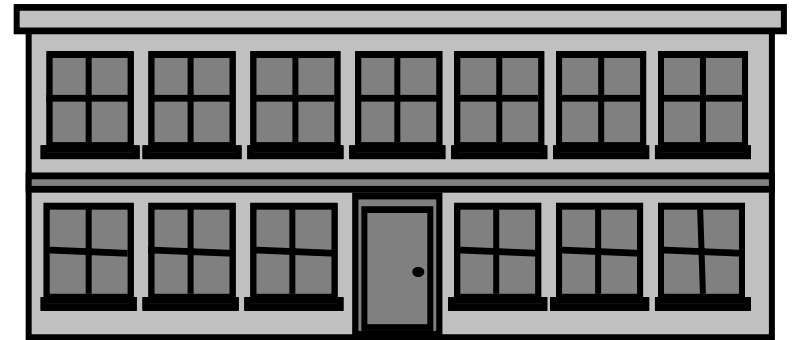


# Immune Building Demonstration



Implement, optimize, and demonstrate a full-scale building protection system at a US military site

- **FY03: Site selection**
- **FY04: System design and testing; on-site characterization**
- **FY05: Demonstration**





# Integrated Systems Experimentation Team



Fort McClellan, Anniston, AL

- **Battelle**  **Battelle**  
... Putting Technology To Work

- **Auburn University** 



- **EnSCO, Inc.**



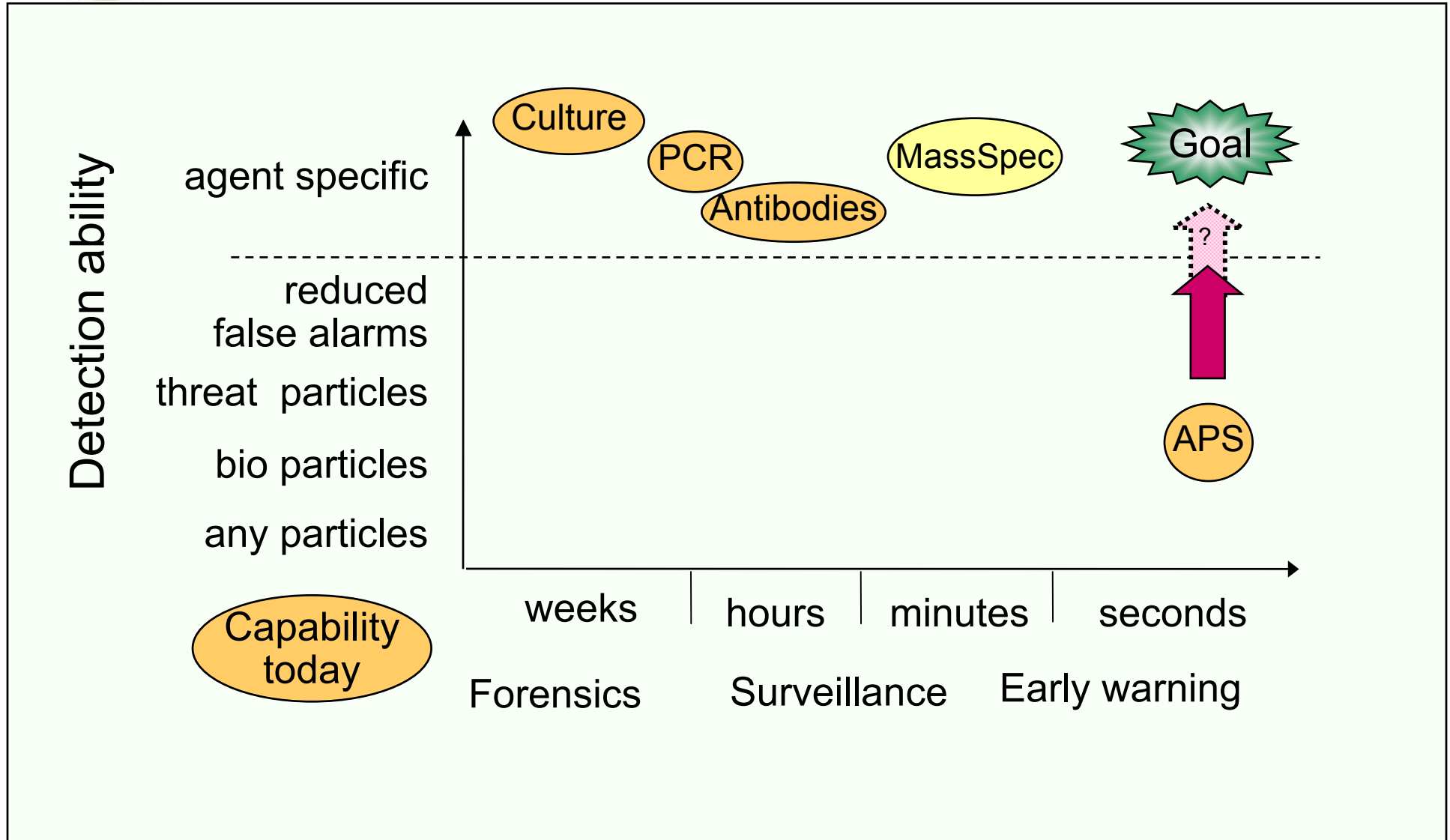
- Gage-Babcock & Associates 

- **Fidelity Engineering Corp.** 

Contact: James E. Risser, [risserj@battelle.org](mailto:risserj@battelle.org)



# Bio Sensors Context







# Biosensor Technologies



## Upconverting Phosphor Technology

### (UPT)

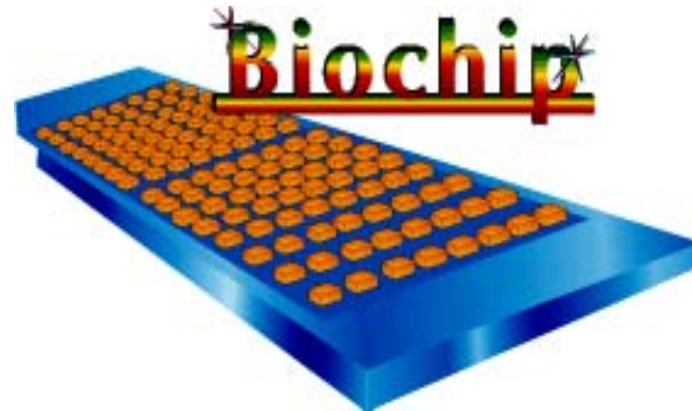
-SRI International (Menlo Park, CA)  
Handheld Biosensor



## MAGIChip™

Micro Array of Gel-Immobilized Compounds

- University of Washington
- Argonne National Laboratory (ANL)
- JHU/APL
- Food and Drug Administration (FDA)

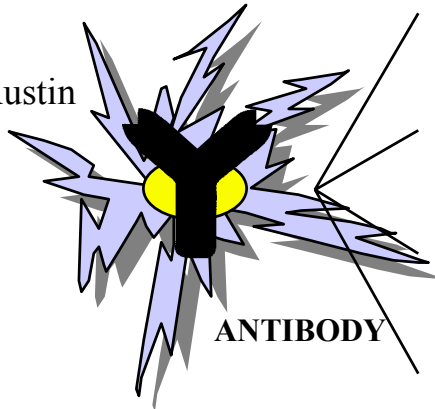


## (DARE) DARPA Antibody Replacement Enhancement Team

### Identifying Technology

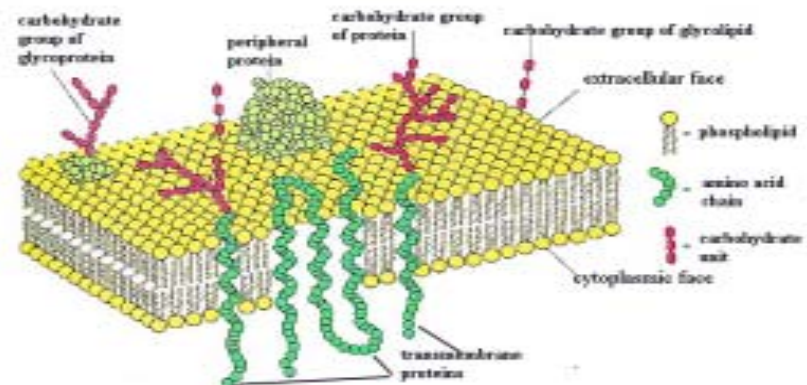
Critical Sensor Technology

- University of Alabama
- Archemix
- University of Texas at Austin
- Polytechnic University
- University of Missouri
- Auburn University



## Ion-channel Biosensor Team

- Auburn University
- Sandia National Laboratory
- Rush-Presbyterian
- Polytechnic University



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