The Role of Detection in Biodefense

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Dr. Bernadette Johnson
(781) 981-1902
bernadette@ll.mit.edu

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### Title and Subtitle

**The Role of Detection in Biodefense**

### Authors

MIT Lincoln Laboratory 244 Wood Street Lexington, MA 02420-9108

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### Abstract

See also ADM001576., The original document contains color images.

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Overall Biodefense Strategy

Prevent attack
  YES  → Prevent/minimize exposure

• Advance intelligence*
• Terrorist tracking*
• Surveillance/interdiction*
• Limit/control supplies

NO  → Prevent/minimize infection

• Evacuation/Avoidance
• Filtration/Overpressurization
• Standoff/perimeter sensing*
• Active HVAC manipulation*
• Personal protection gear
• Neutralization

YES  → Prevent/minimize casualties

• Vaccination/prophylaxis
• Exposure assessment*
• Presymptomatic treatment*

NO  → Effective/appropriate treatment*

• Decontamination*

* Detection required
The Challenge of Biological Agent Detection

• Protection requires rapid detection of pathogens in the environment (no false negatives, few false positives)
• Treatment and retaliation require accurate determination of the agent and its source
• Why is this so difficult?
  – Even low concentrations can be lethal
  – Aerosol are small (1 - 10 microns)
    Low scattering cross section
  – Signatures can be non-specific
    Very different from chemical agents
  – Biological technologies widespread that may mask signature
  – Competing backgrounds
    Natural and man-induced substances
    Indigenous bioaerosol, including pathogens
Sensing Requirements Driven by Understanding of Infectious Dosage

No sensing systems currently exist that offer continuous, real-time organism-identification capability.

Minimum infectious dosages based on normal breathing rate

Current medical laboratory techniques

Illness onset (hours to days)

Exposure duration

Bioagent Concentration (particles/liter of air)

- Botulism
- Anthrax
- Plague
- Smallpox
- Q fever
- VEE

1 min 10 min 1 hr 6 hr 1 day

10^5 10^4 10^3 10^2 10 1
Generic Biosensor Architecture

- Particle count/sizing
- UV Laser-induced-fluorescence
  - Point
  - Standoff
- Air-to-liquid collection
- Impaction
- Electrostatic separation
- Culture
- Immunoassay
- Cell-based
- PCR/DNA based
- Mass Spectrometry
Examples of Trigger Sensing Technologies

- **Particle counting/sizing**
  - Simple, inexpensive, portable
  - Not specific to biologicals

- **UV Laser-Induced Fluorescence**
  - Offers biologic/nonbiologic differentiation
  - Has been developed for both point and standoff sensing

[Images of various sensing technologies are shown, including BAWS (MIT LL), UV APS (TSI), and Short Range Biological Stand-off Detection System (Fibertek).]
BAWS Principle of Operation

Pulsed Ultraviolet Laser (266 nm)

Spectral Filter

Photo-detector

Fluorescence Emission and Elastic Scattering

Agent Containing Particle

Detected Signals

UV

Visible

Elastic

Particle Discrimination

Particle Emission Spectrum

Relative Signal

Wavelength (nm)

Fluorescence

Elastic Scattering

Tryptophan

NADH

Flavins

Dirt

Agent

UV - Visible

UV - Elastic

UV - Elastic

UV - Visible
Example of BAWS Response to Simulant Releases

March 17, 1999
Dugway PreBLWE

Referee Data
- 2 - 10 \( \mu \)m particles (TSI APS)
- \textit{Bacillus globigii} (STA sampler)

BAWS III Data
- Alarm window
- Agent

Particle counters would alarm here but not here

March 17, 1999
Dugway PreBLWE

Trial 3
Release

Trial 4
Release

Trial 5
Release
Collection of a Sample Following a Trigger

- Collection systems can also be used for continuous monitoring
  - Periodic sampling and assay offers detect-to-treat for many threat agents

Air-Liquid Collection
- Wetted Wall Cyclone (Battelle)

SpinCon (MRI)

Dry Impaction
- BioVic (MesoSystems)

Dry Filter Unit

Collection systems can also be used for continuous monitoring
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Current Bioagent-Identification Technologies

Rapid ID

**Immunoassays**
- Selectivity from high affinity binding of antibody to agent-specific structures

**Polymerase Chain Reaction (PCR)**
- Selectivity from sequence-specific DNA/RNA recognition
- Enzymatic amplification provides superb sensitivity

Orthogonal ID Confirmation Technologies

Culture-based assays
- Traditional method since Pasteur – still “gold standard” for ID
- Viable organisms replicated in culture and identified using biochemical assays and microscopy

Response Time

Sensitivity/Accuracy
Examples of In-Use Rapid Identification Techniques

Ticket cartridges and reader for lateral-flow immunoassay in Joint Biological Point Detection System (JBPDS)

Commercially available LFI tickets and reader (Tetracore/Alexeter)

• Immunoassay-based tickets are relatively fast and require minimal sample preparation but their sensitivity is often poor and readout fairly subjective for low concentrations
Concept

B cell emits ~200 photons within 30 seconds after bioagent binding

Prototype microcentrifuge device

Tests Against Killed Tularemia
(Collab. with NMRC)

\[
\begin{align*}
\text{Photons/sec} & \\
0 & 10 \quad 100 \quad 1000 \quad 10000 \\
\text{Time (sec)} & \\
0 & 100 \quad 200 \\
\end{align*}
\]

# Inactivated Tularemia Particles
- 600
- 60
- 0
Confirmation Identification Technology

- Systems being developed (and deployed) that provide agent ID within 30 minutes of introduction of prepared sample

- Challenge remains in automating sample preparation and analysis

![Semi-automated field-portable PCR devices](image1)

- **RAPID - Idaho Technologies**
- **SmartCycler XC System - Cepheid**
- **Bioseeq - Smiths**

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Examples of Integrated Systems

Biological Integrated Detection System (BIDS)

Portal Shield

Immunoassay ticket reader
Sample collection
BAWS trigger

Joint Biological Point Detection System (JBPDS)
Military versus Civilian Detection Systems

• Military systems developed primarily for outdoor force protection
  – Emphasis has been on preserving functionality during assault (i.e., put masks on) and minimizing exposure (avoidance)

• Technology limitations on real-time detection and identification have driven users to multi-stage architectures
  – Fast non-specific trigger sensors followed by sample collection and multi-tiered assay

• Civilian Biodefense can borrow from military investment but requirements do differ
  – The most successful technologies will offer benefits above and beyond those given by Biowarfare protection (e.g., better infectious disease control, early diagnostics, exposure assessment, treatment, etc.)