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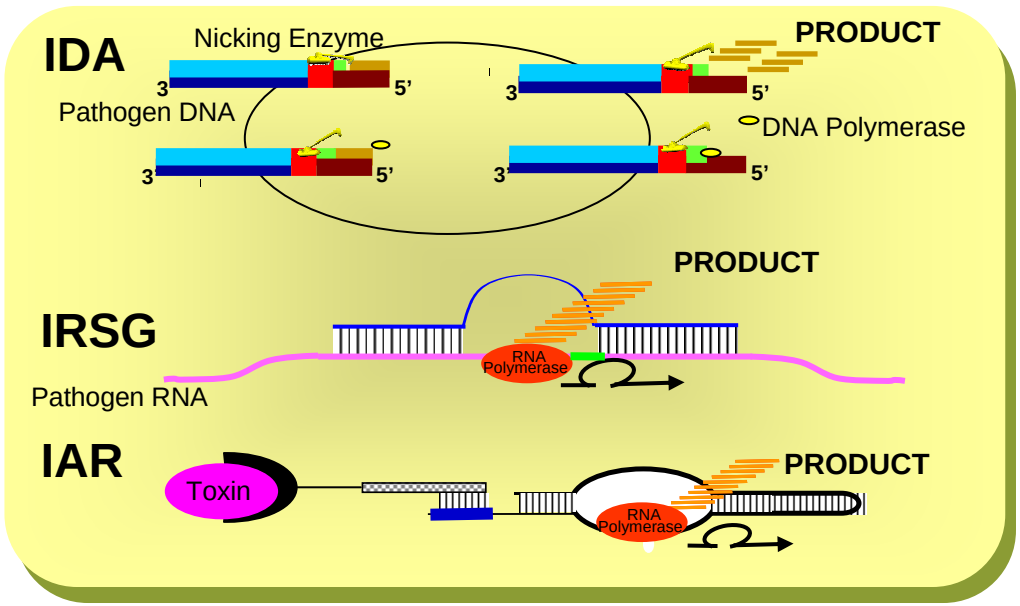
Handheld Isothermal Silver Standard Sensor (HISSS)

HISSS Goal

The goal of the Handheld Isothermal Silver Standard Sensor (HISSS) program is to develop a handheld sensor that is capable of identifying biological weapon threats across the entire threat spectrum including bacteria, viruses and toxins. The HISSS sensor will be based on novel high-speed isothermal detection methods for DNA, RNA and protein toxins.

Detection Method	Today: Laboratory Testing	Tomorrow: Handheld Testing
DNA – based	PCR	Isothermal DNA Amplification (IDA)
RNA – based	RT-PCR	Isothermal RNA Signal Generation (IRSG)
Toxin – based	ELISA	Isothermal Antibody Recognition (IAR)



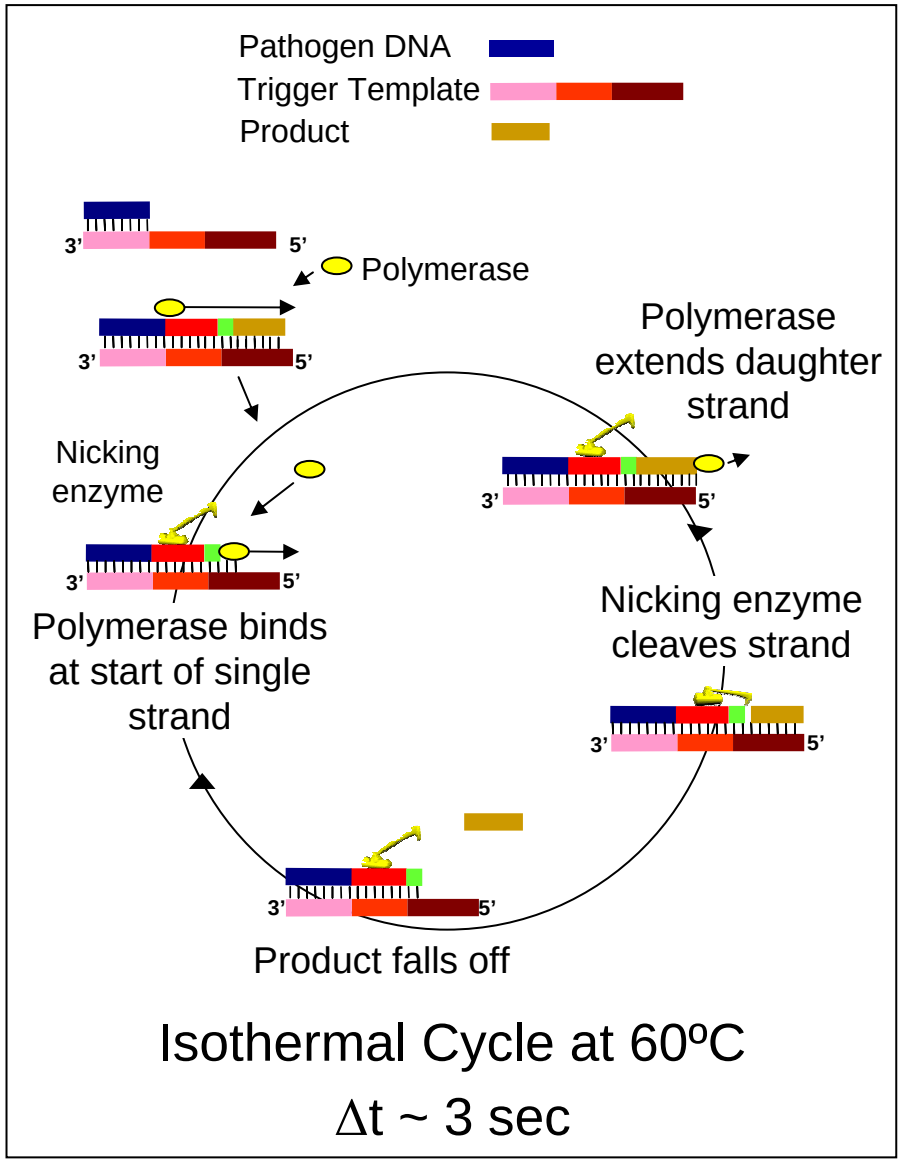
Why Can We Make it a Handheld?

- Handheld device requirements
  - Low power
  - Lightweight
  - Small size
- Low power
  - Isothermal DNA, RNA and protein detection
    - Laboratory level accuracy
    - No temperature cycling allows for far less power
    - Novel methods increase reaction speed require less power
  - Microfluidics
    - Smaller fluid volumes allows for less power
- Lightweight
  - Weight driven by battery requirements
  - Lower power requirements reduces device weight
- Small size
  - Microfluidics reduce the size of a laboratory to a cartridge
  - Small sample size reduces reagent storage requirements

Pathogen DNA Detection with IDA

Pathogen DNA Detection with IDA

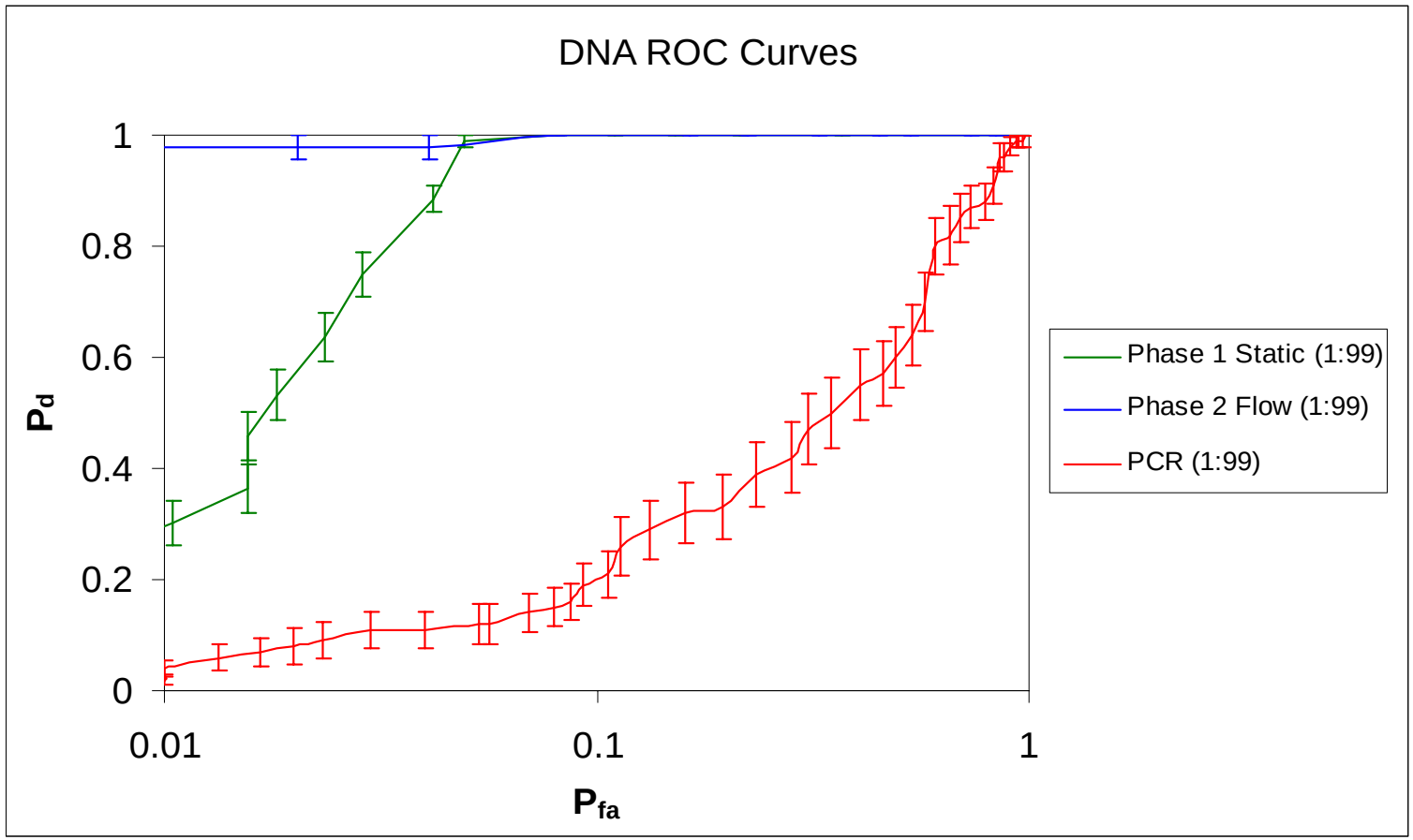
- Isothermal DNA amplification delivers faster cycling times and lower false alarm rates than comparable assays
  - IDA reaction enables higher specificity and greater sensitivity than traditional PCR
  - Existing primers are used
    - No new bioinformatics
  - "Thermodynamic switch"
    - Reaction temperature is chosen so that extended strand is stable and cleaved strand is unstable
    - Cycle time is based on the speed of the enzymatic reaction



ROC Curves for DNA

DNA: Phase I static assay vs. Phase II flow through assay vs. PCR

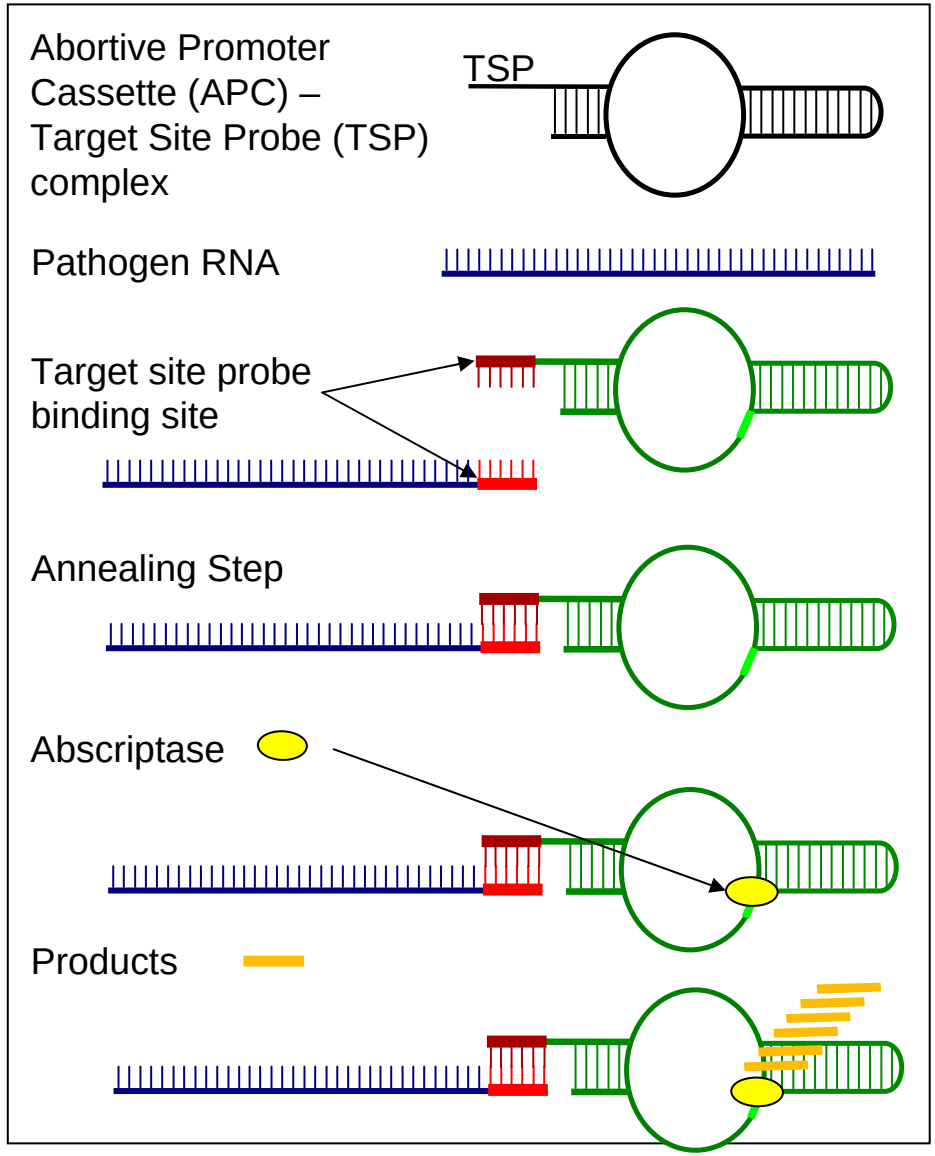
- Go/No Go: Demonstrate that the flow through false alarm rate for IDA is equivalent or better than static conditions
- Results: IDA has statistically the same FAR under static and flow through conditions



Pathogen RNA Detection with IRSG

Pathogen RNA Detection with IRSG

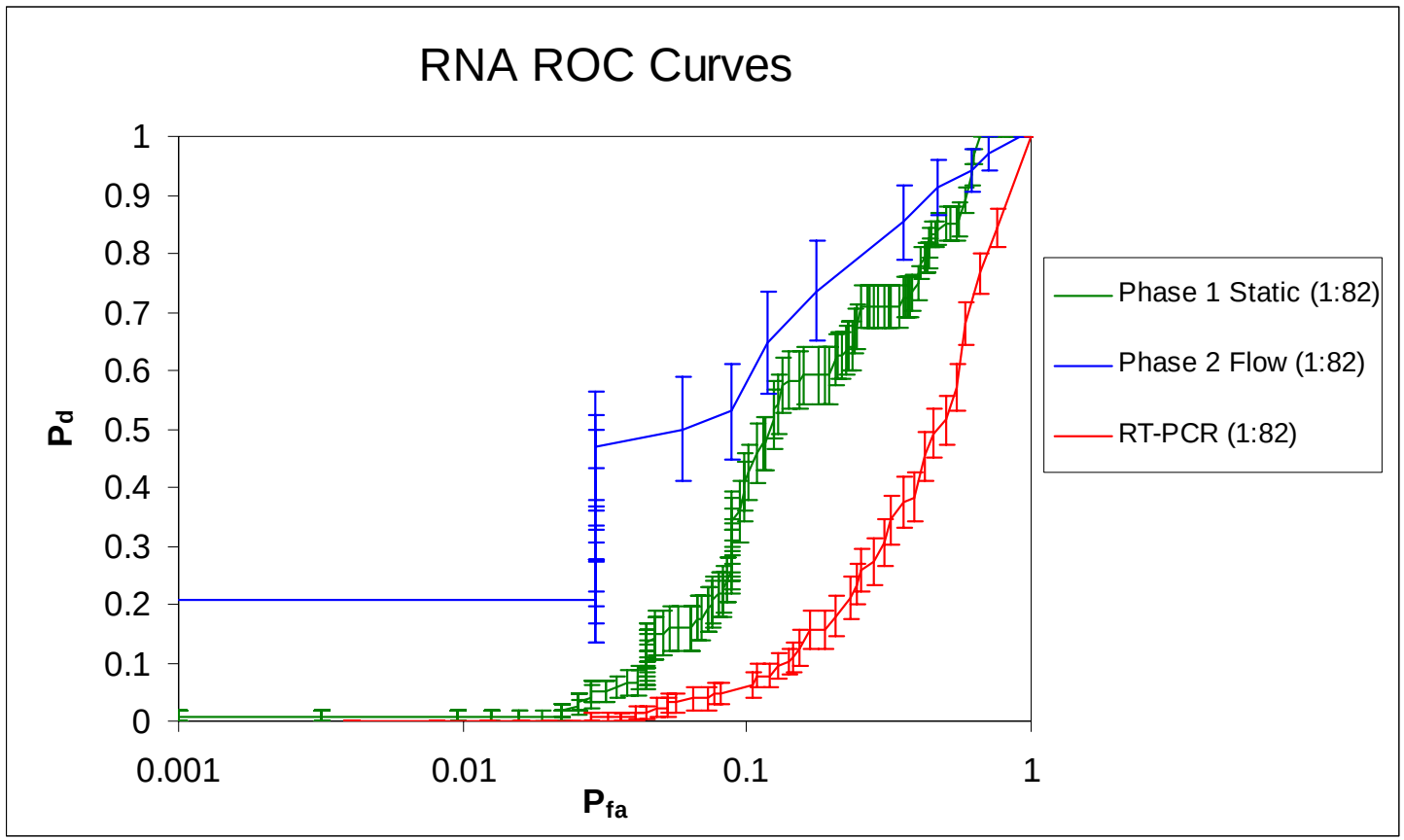
- Isothermal RNA amplification delivers faster cycling times and lower false alarm rates than comparable assays
  - Don't need to convert RNA to DNA before carrying out specific detection reactions
  - Existing primers are used
    - No new bioinformatics
  - Uses novel abscription process such that once a binding event has occurred signal products are generated at a very fast rate



Go/No Go for RNA

RNA: Phase I static assay vs. Phase II flow through assay vs. RT-PCR

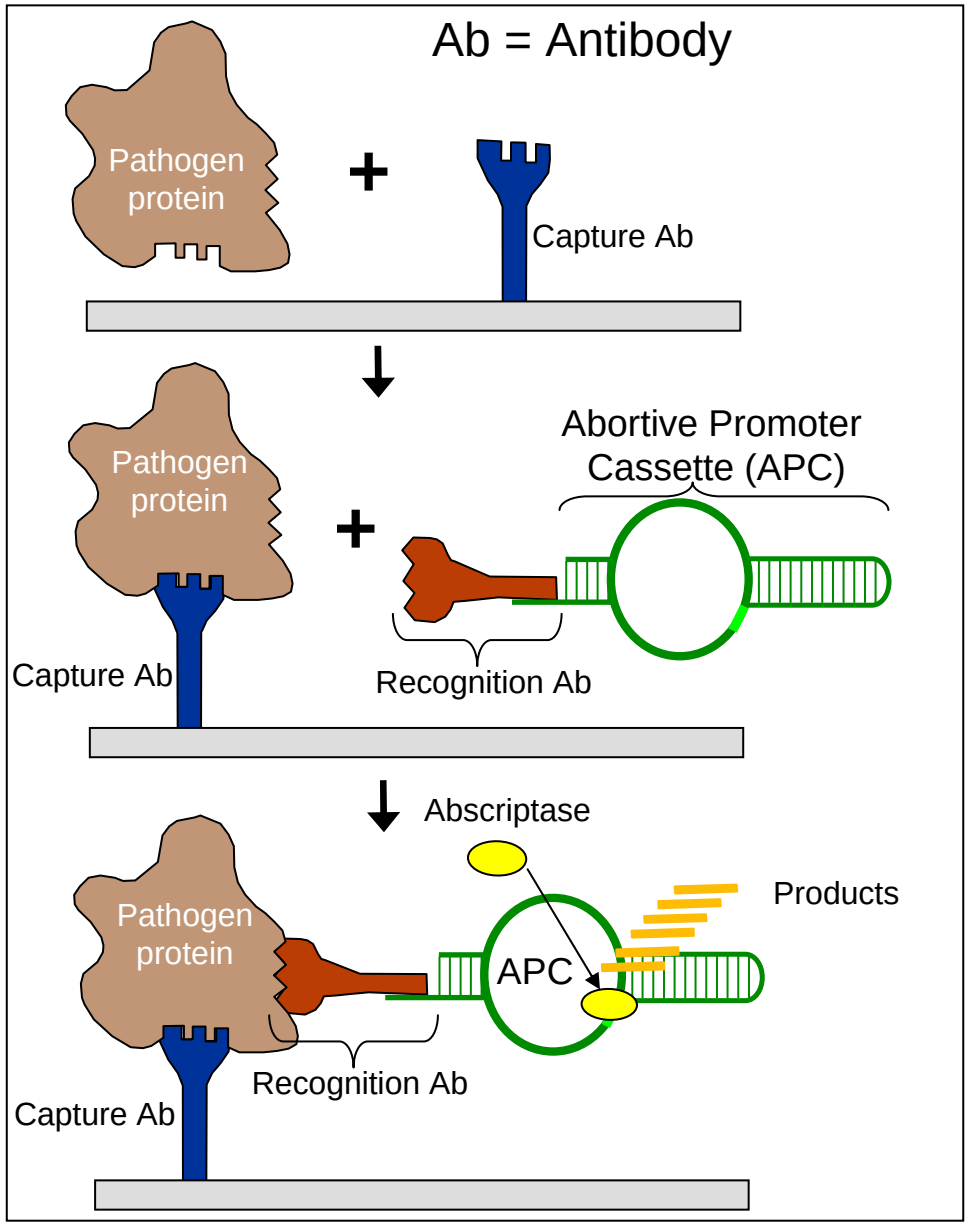
- Go/No Go: Demonstrate that the flow through false alarm rate for IRSG is equivalent or better than static conditions
- Results: IRSG has statistically the same FAR under static and flow through conditions



Protein Toxin Detection with IAR

Protein Toxin Detection with IAR

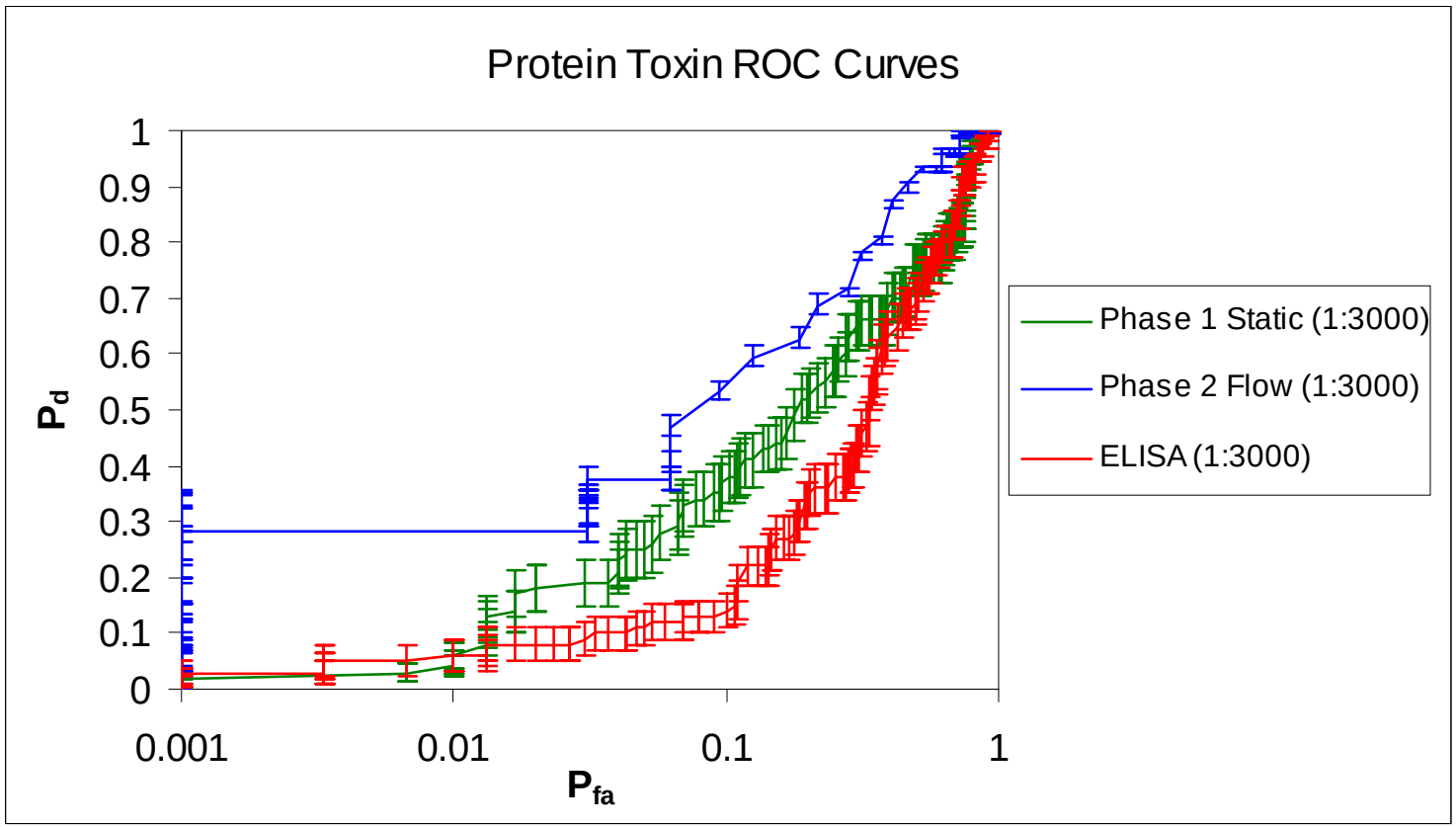
- Isothermal protein detection delivers faster cycling times and lower false alarm rates than comparable assays
  - Existing antibodies are used
    - No new bioinformatics
  - More sensitivity
    - More product per binding event
  - Measurable product using mass spectrometer



Go/No Go for Protein Toxins

Toxin: Phase I static assay vs. Phase II flow through assay vs. ELISA

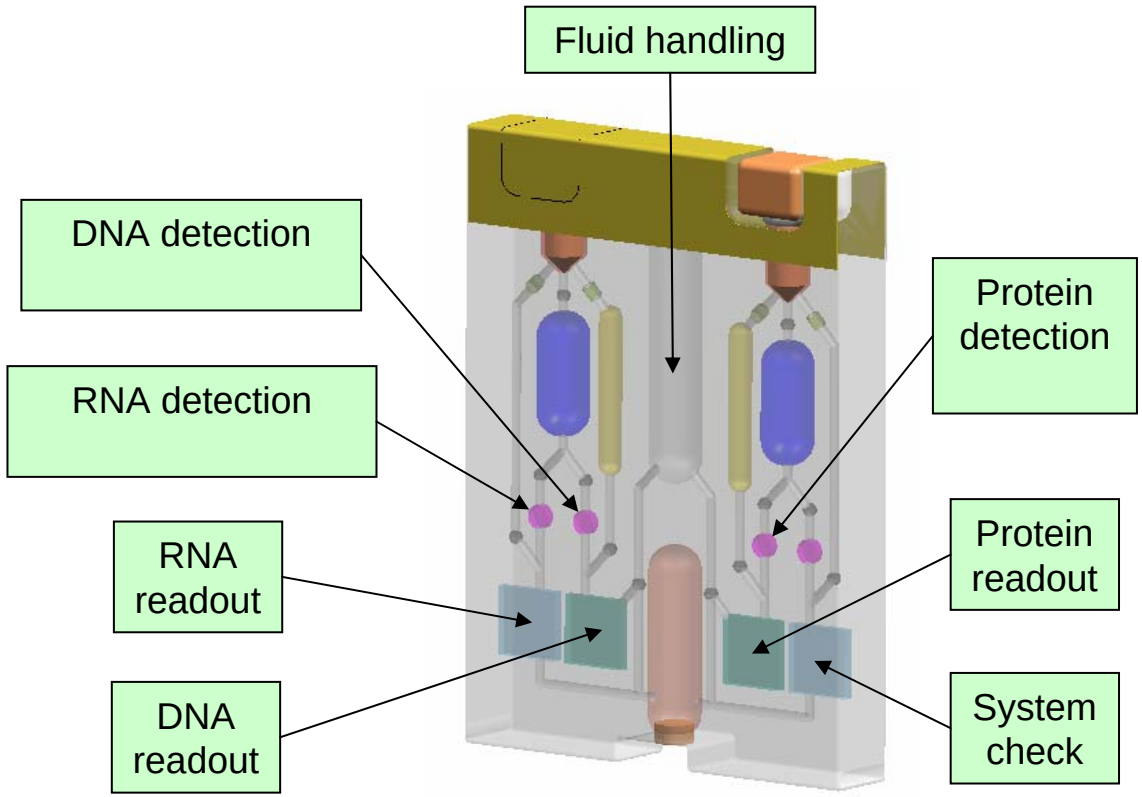
- Go/No Go: Demonstrate that the flow through false alarm rate for IAR is equivalent or better than static conditions
- Results: IAR has statistically the same FAR under static and flow through conditions



Conceptual Design of Handheld Instrument

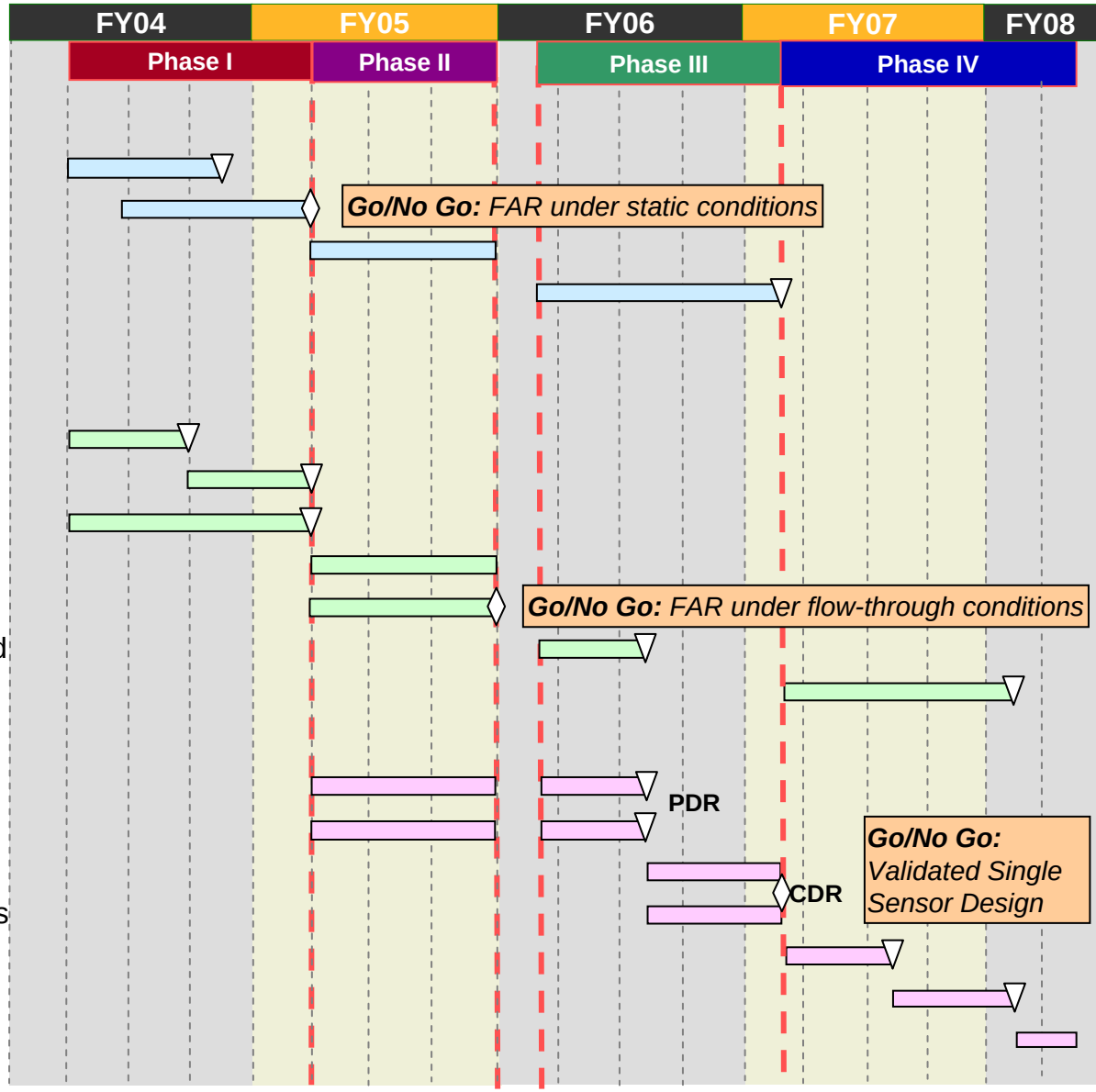
Notional Handheld Instrument

Notional Sample Cartridge



The handheld sensor will be capable of being operated by military personnel in the field environment

HISSS Program Schedule



Reaction Developers

- Optimize Static Reactions with Simulants
- Demonstrate Static FAR with Challenge Sets
- Optimize Flow-Through Reactions
- Develop Stable Reagents for Fieldable Device

System Integrator

Flow-through Testbed

- Design and Build Flow-Through Testbed
- Initial Flow-Through Testing
- Reaction Models
- Optimize Flow-Through Reactions
- Demonstrate Flow-Through FAR
- Integration of all Detection Reactions in Testbed
- Testbed Live Agent Tests

Handheld Sensor

- Sensor Design
- Sensor Models
- Validate Sensor Design using Model
- Validate Sensor Design in Testbed w/ Simulants
- Build Prototype Sensor
- Test Prototype Sensor
- Sensor Field Trials