

Ultrasensitive detection of DNA and proteins for bloodscreening



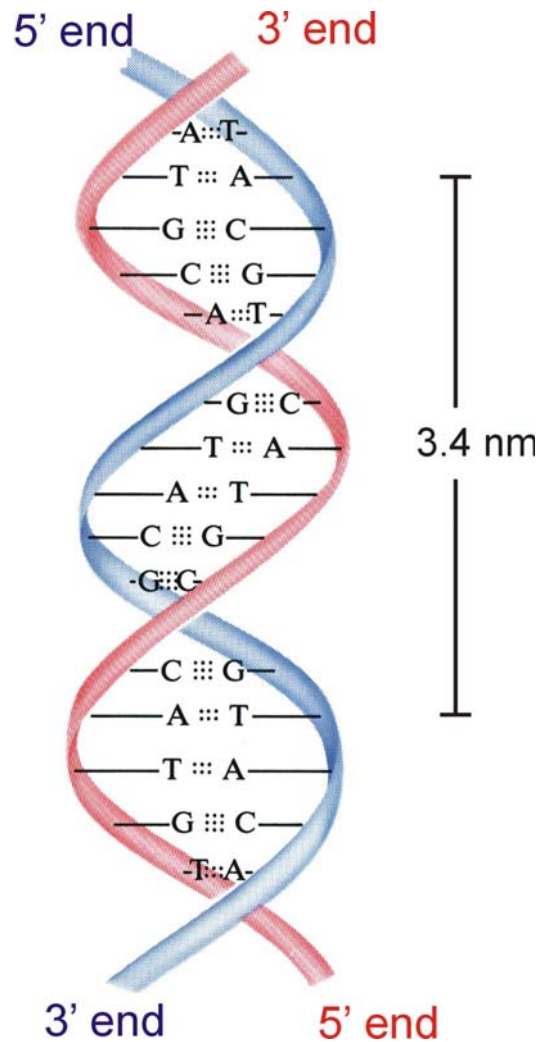
Chad A. Mirkin

Dimitra Georganopoulou

Department of Chemistry and
Institute for Nanotechnology
Northwestern University
2190 N. Campus Drive
Evanston, IL 60208-3113



Biological Labeling/Detection Methods



1. Radioactive isotopes
2. Colorimetric detection
3. Chemiluminescence
4. Fluorescence (dye molecules)
5. Nanoparticle-based labeling (DNA detection)

Potential Advantages:

- Selectivity
- Sensitivity
- Multiplexing Capabilities
- Ratioing Capabilities
- Cost

Nucleic Acid Detection

Concentration/
of molecules

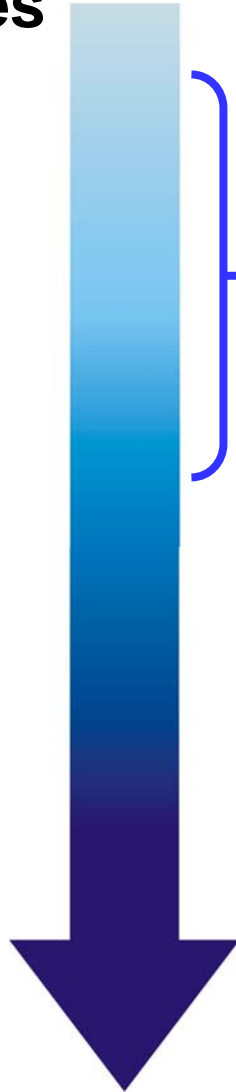
$10^{-6} / \sim 10^{12}$

$10^{-9} / \sim 10^9$

$10^{-12} / \sim 10^6$

$10^{-15} / \sim 10^3$

$10^{-18} / \sim 10^0$



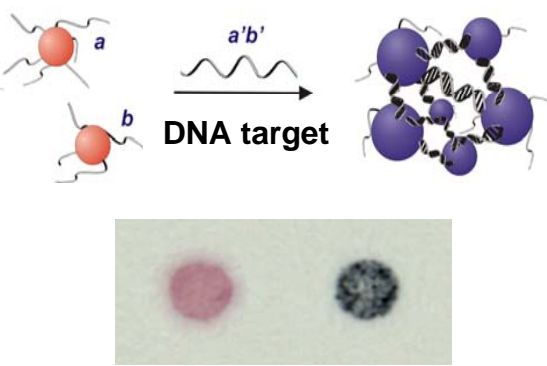
**Molecular
Fluorophore-Based
Assays/Gene Arrays**

**Polymerase Chain
Reaction**

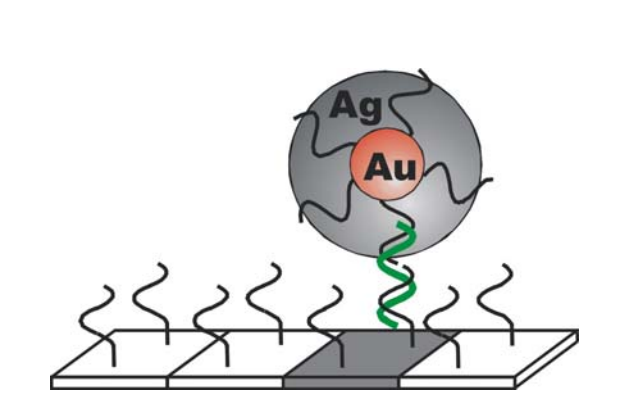
Limitations

- Speed
- Complexity
- Multiplexing Capabilities
- Cost

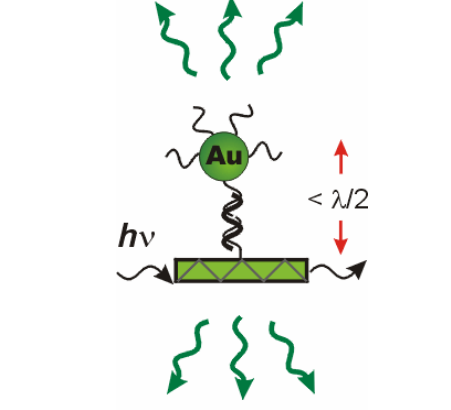
One Platform: Many Detection Methods and Capabilities



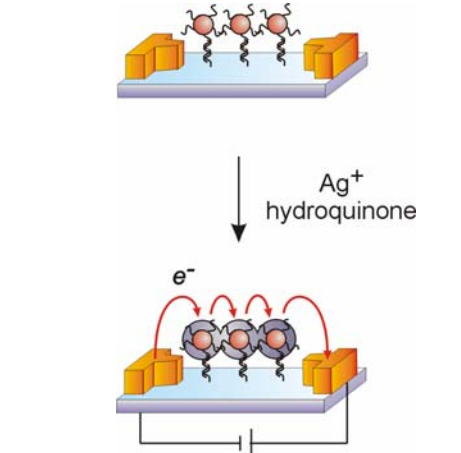
Spot Test
Science, 1997
JACS, 1998



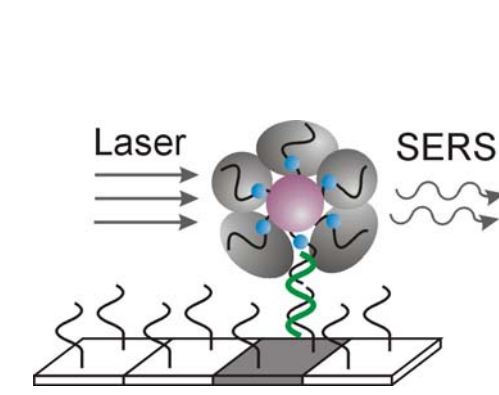
Silver-Staining
Science, 2000



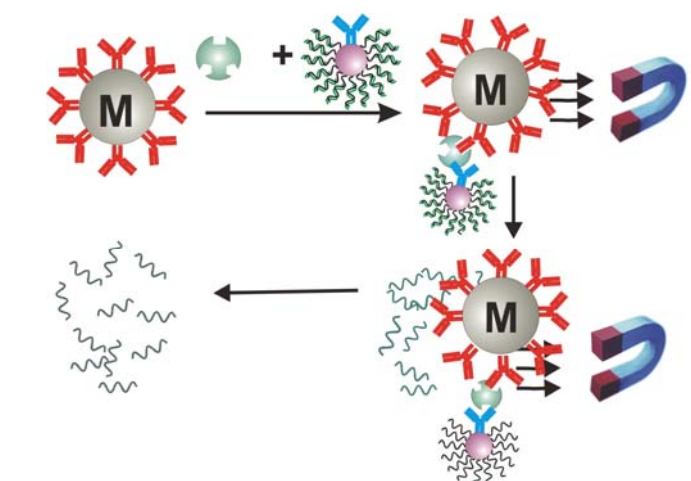
White Light
JACS, 2000



Electrical
Science, 2002



Raman
Science, 2002



Bio-Barcode Assay
Science, 2003

Experimental Set-up



Multifunctional equipment

- ❖ Direct genomic detection
- ❖ Multiplexed targets
- ❖ Automated assay process
- ❖ Ease of use
 - ❖ Minimal training required
 - ❖ Automated data tracking
 - ❖ No interpretation required

Verigene™ System

Verigene Hybridization Unit



Lab on a Chip Technology

Protein/Small Molecule Detection

Concentration/
of molecules*

$10^{-6} / \sim 10^{12}$

$10^{-9} / \sim 10^9$

$10^{-12} / \sim 10^6$

$10^{-15} / \sim 10^3$

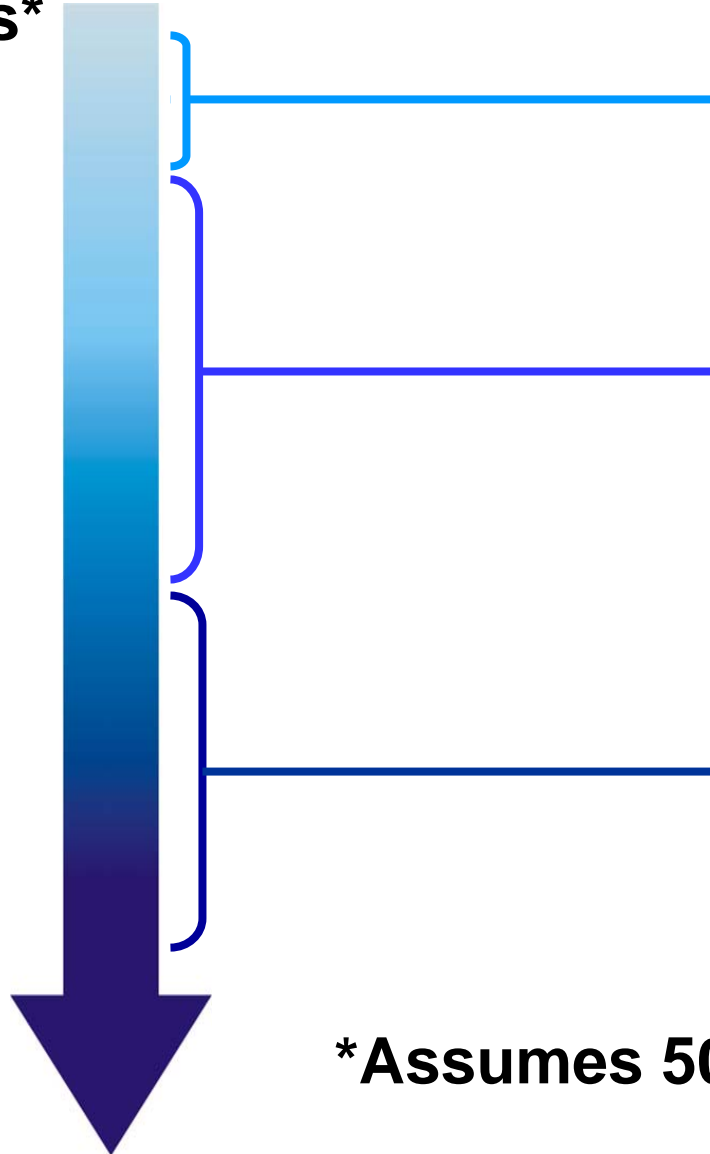
$10^{-18} / \sim 10^0$

Small Molecule:
Glucometer

Proteins:
ELISA

??????

*Assumes 50 microliter sample



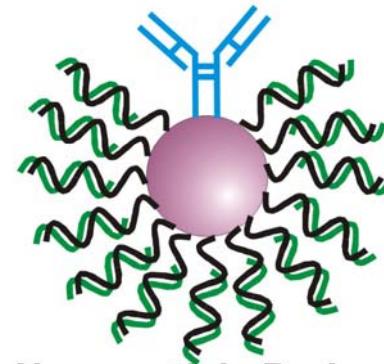
The Next Generation Nanoparticle Probe with Bio-barcodes



Biobarcode DNA library
by varying sequence
and length of DNA



1. SH
2. Bovine serum albumin
- 3.



Nanoparticle Probe for
Protein B Encoded with
Barcode DNA



Gold nanoparticle



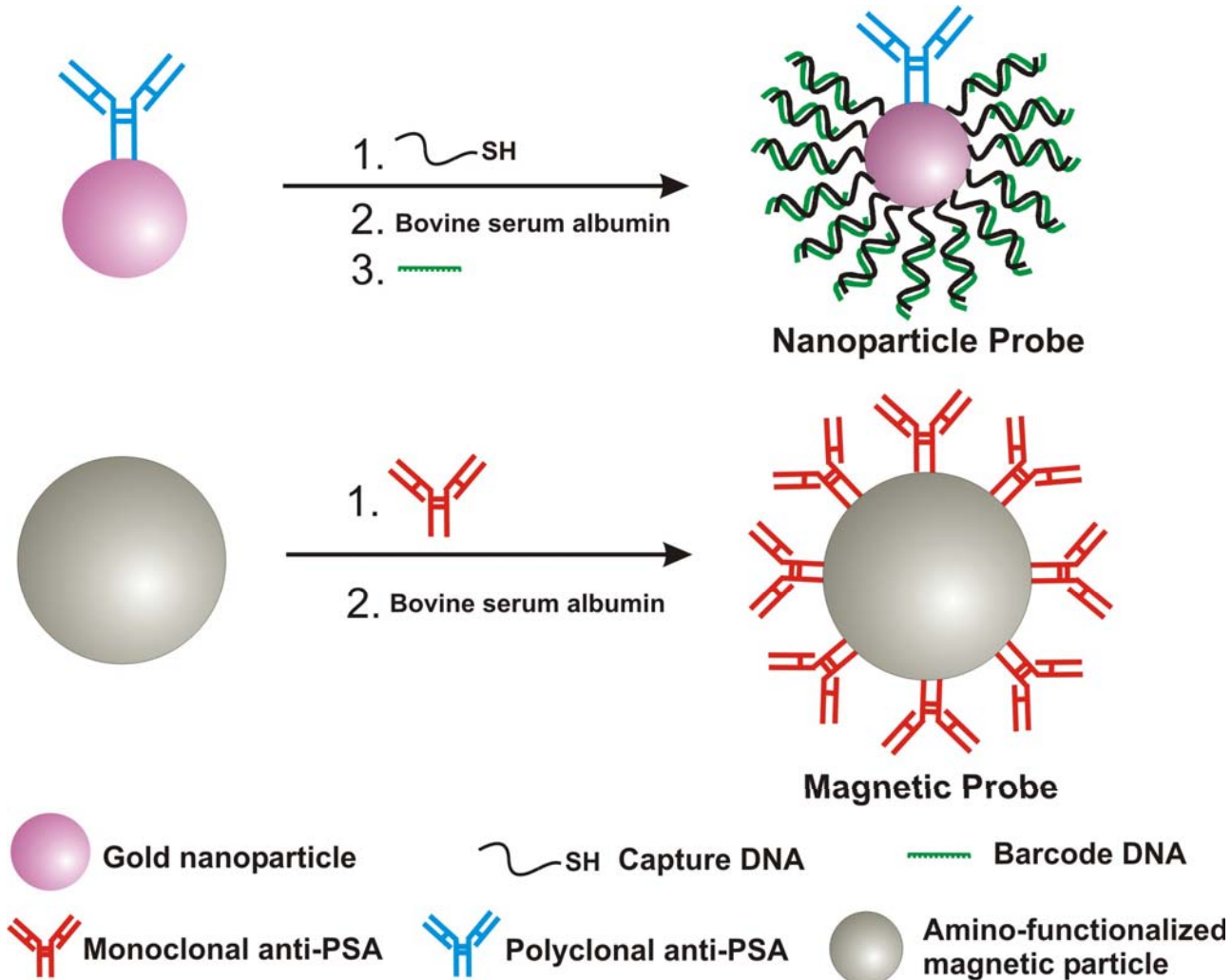
SH Capture DNA

Barcode DNA

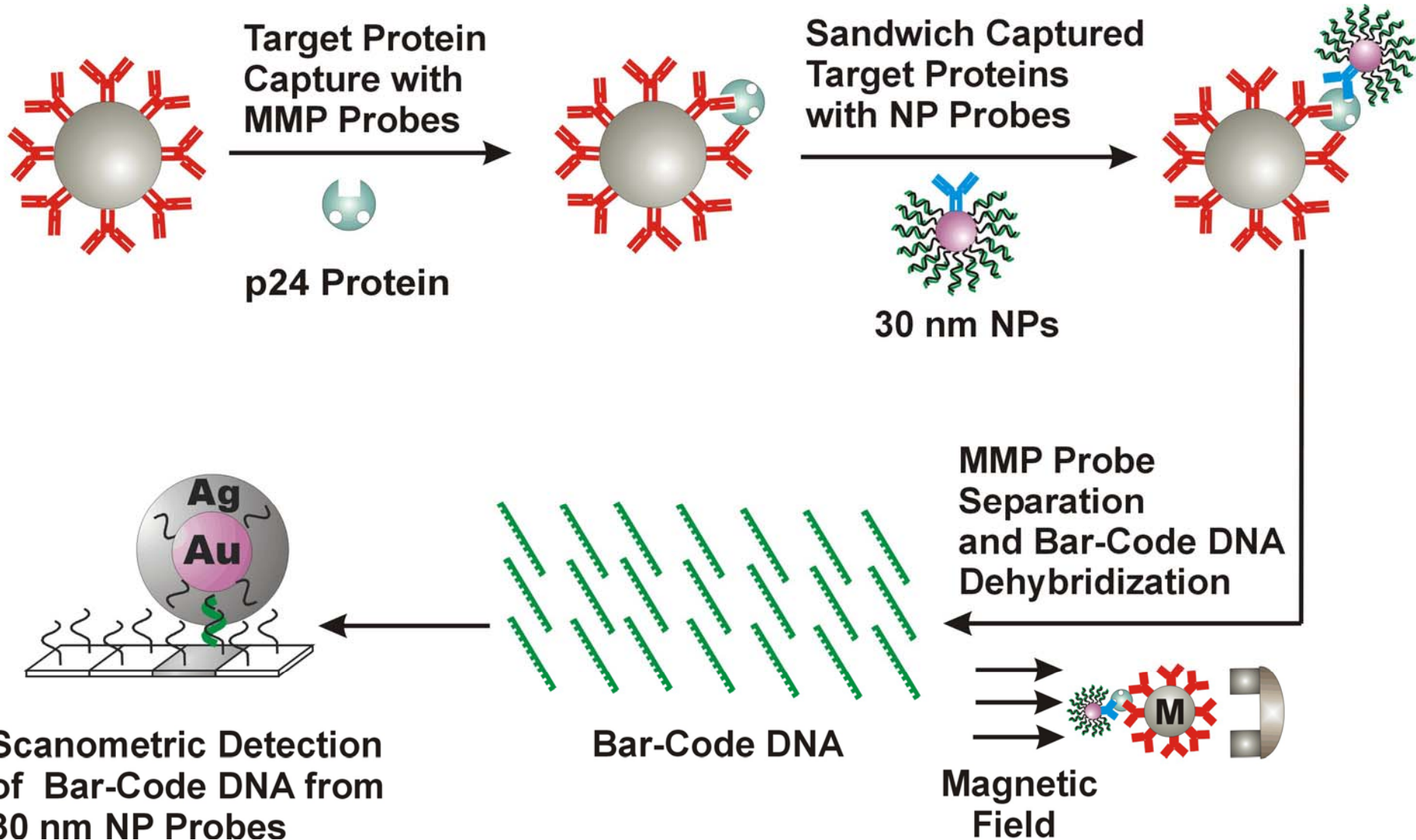


Anti-PSA

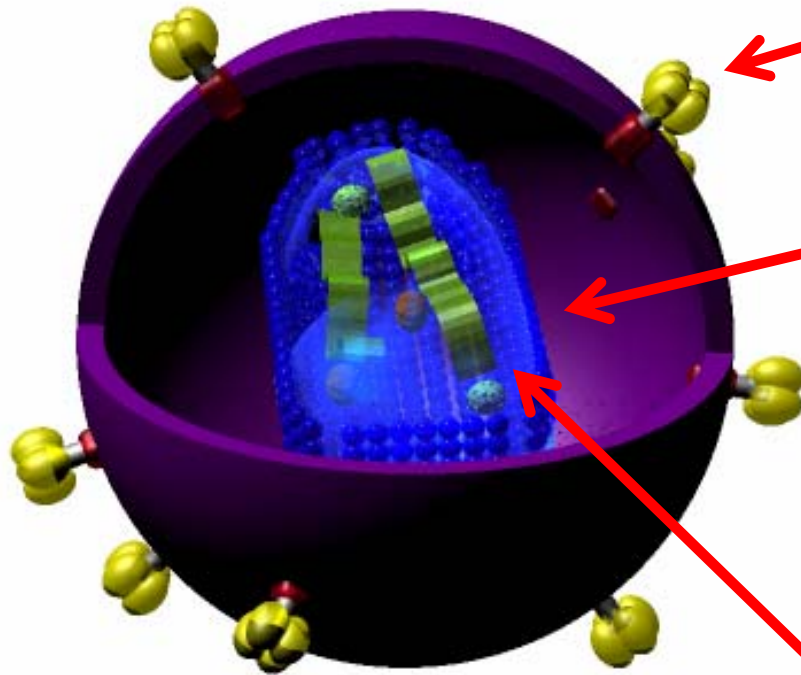
Probe Design and Preparation



Biobarcode Detection of HIV



The Human Immunodeficiency Virus (HIV)



Surface glycoprotein (gp120): highly mutable

Capsid protein (p24): ~2000 copies per virus

*p24 is a good target since there are many copies of p24 available in each virus and p24 has relatively few mutations.

Two unspliced viral genomes

Detection of p24 possible with Biobarcode assay. Calibration curve with detection limit of high aM, and correlation of patient samples with PCR results.

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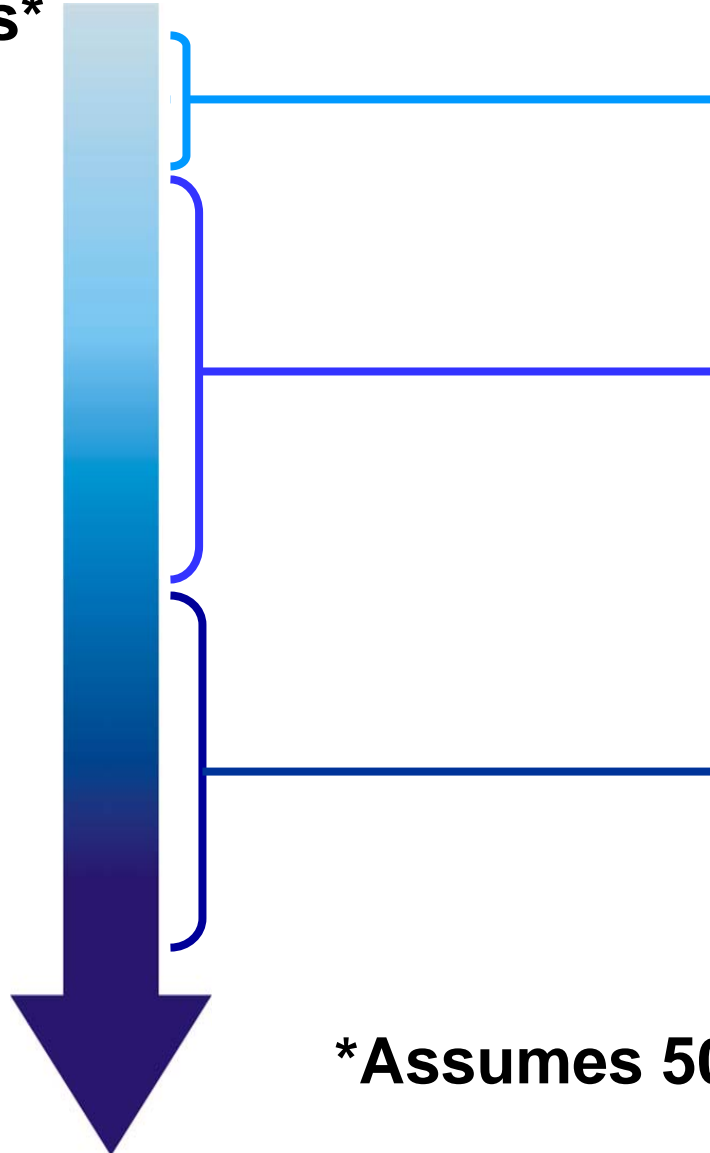
$10^{-18} / \sim 10^0$

Small Molecule:
Glucometer


Proteins:
ELISA

Biobarcode
Assay

*Assumes 50 microliter sample



Field Defining Technologies

	Concentration	Molecule/Drop	Detection/ Targets/Disease
	10^{-3} - Millimolar	Quadrillions	Colorimetric/ Enzymatic Chemistry Blood Sugar (Diabetes)
	10^{-6} - Micromolar	Trillions	
	10^{-9} - Nanomolar	Billions	ELISA & Chemiluminescence Troponin, CK-MB, BNP, β HCG
	10^{-12} - Picomolar	Millions	
	10^{-15} - Femtomolar	Thousands	Bio-barcode Technology Alzheimer's Disease, Mad Cow, Ovarian, Breast, and many other cancers, Pulmonary Disease, Cardiovascular Disease, HIV
	10^{-18} - Attomolar	Tens	
	10^{-21} - Zeptomolar	<1	



Acknowledgements

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