

# Optically Encoded Particles as a High-Throughput Biosensor Platform

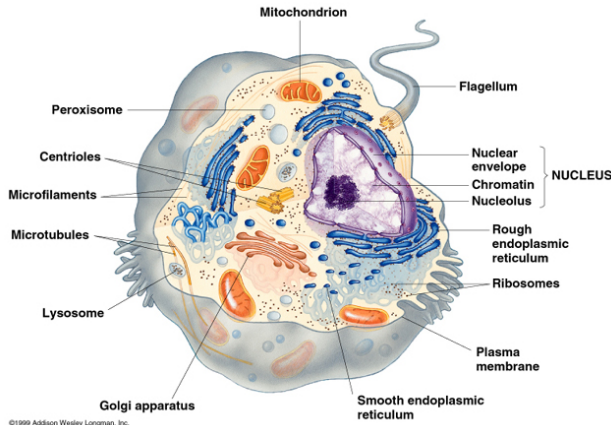
*Darby Kozak, Annie Chen, Lionel Marcon and Matt Trau*



# Biosensors & Nanotechnology

- Importance of biosensors and role of nanotechnology
- Optically barcoded particle biosensors
  - Advantages in high throughput multicomponent analysis
  - Improving assay performance via polymer modified surfaces
- Application of barcoded particle biosensors
  - Antibody 'sandwich' assay on two ovarian cancer biomarkers in serum
  - A protease 'mapping' assay of West Nile and Dengue Virus' NS3 proteases

# Biosensor Applications

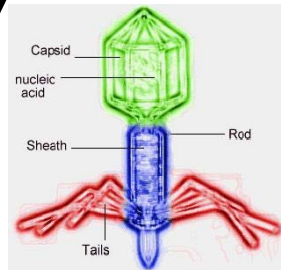
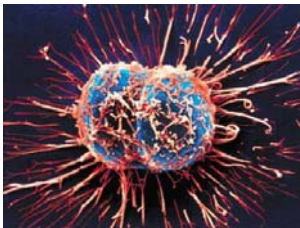


**Molecular Detection:  
Genetic, Epigenetic & Proteomic assays**

Cancer

Infectious  
Disease

Biosecurity

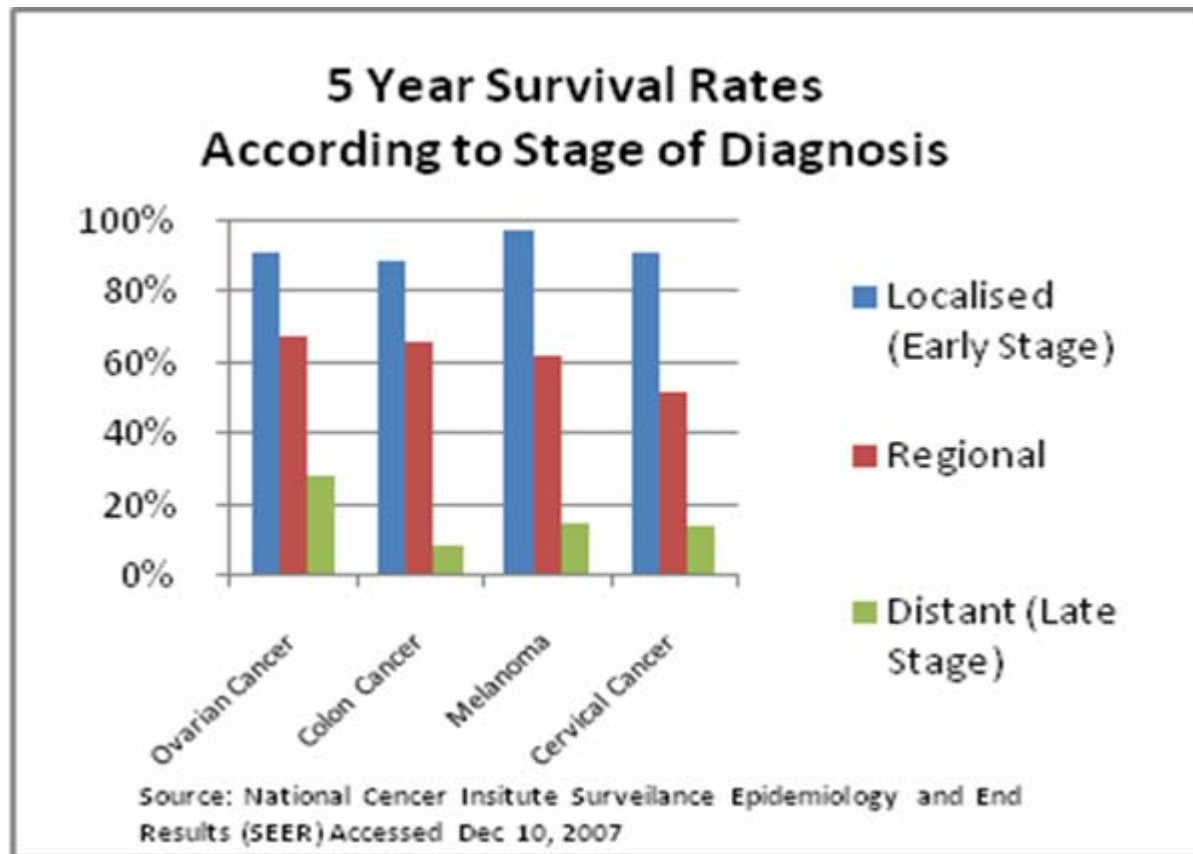


**In-the-Field Diagnostics:  
Point of care, Quarantine, Export**

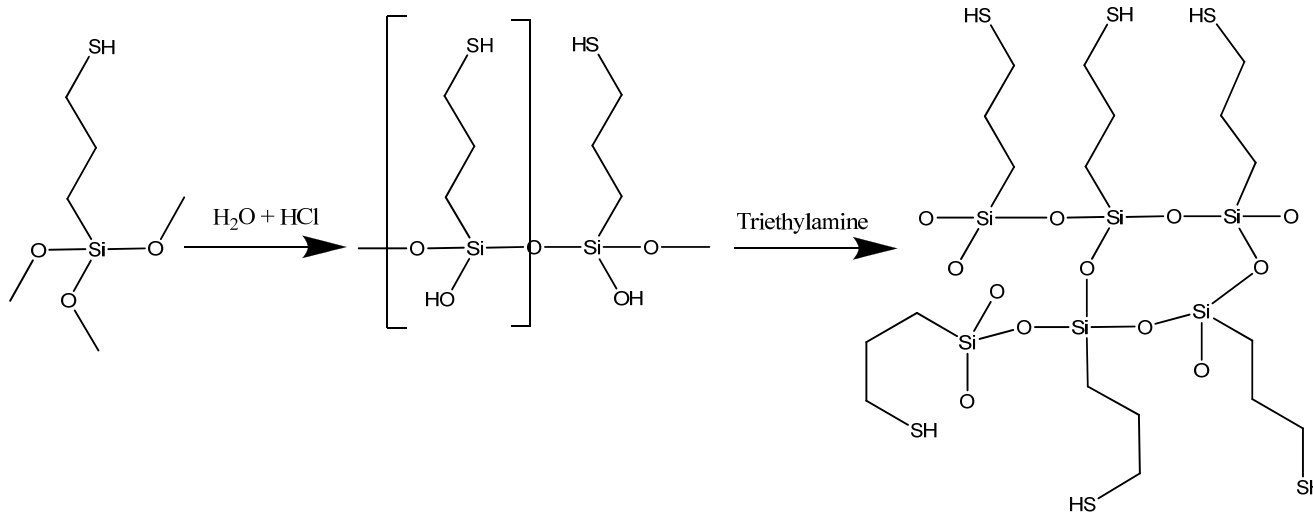


# Biosensors

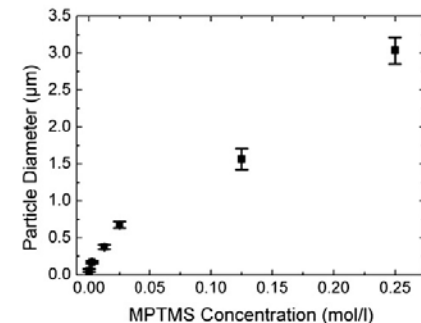
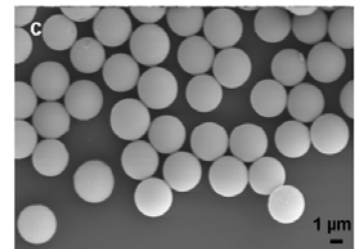
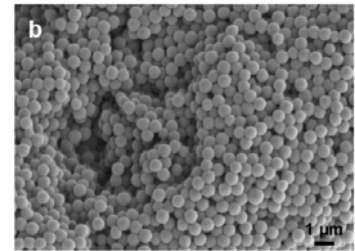
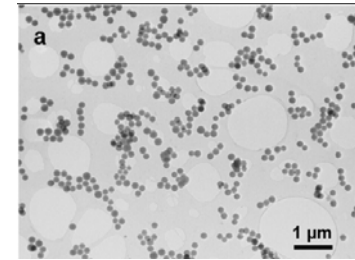
The earlier the diagnosis the better chance of successful treatment and disease remission



# Chemistry of Particle Biosensors

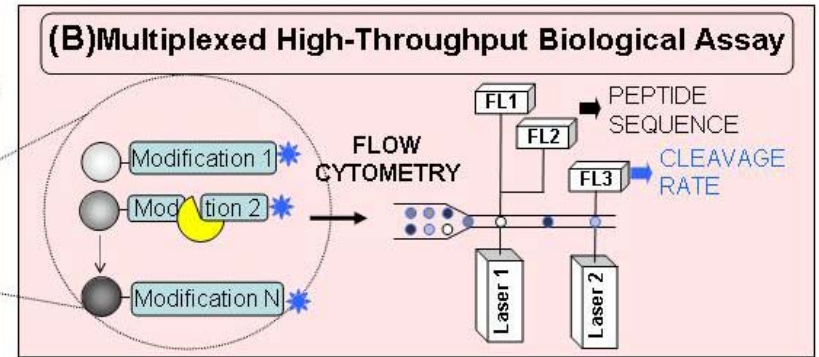
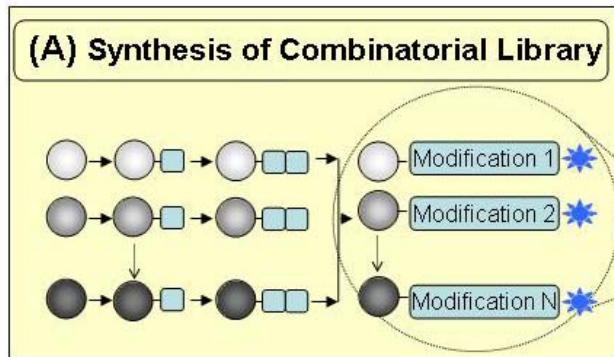


- Spherical, monodisperse particles of tailorable size (50nm to 5 $\mu$ m)
- Initially porous and swellable to allow in dyes or smaller materials
- Functional interior and exteriors



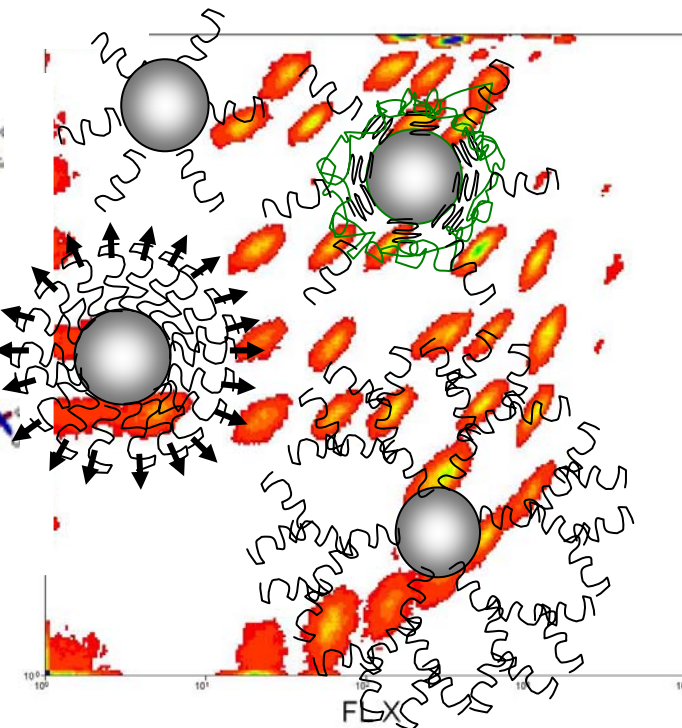
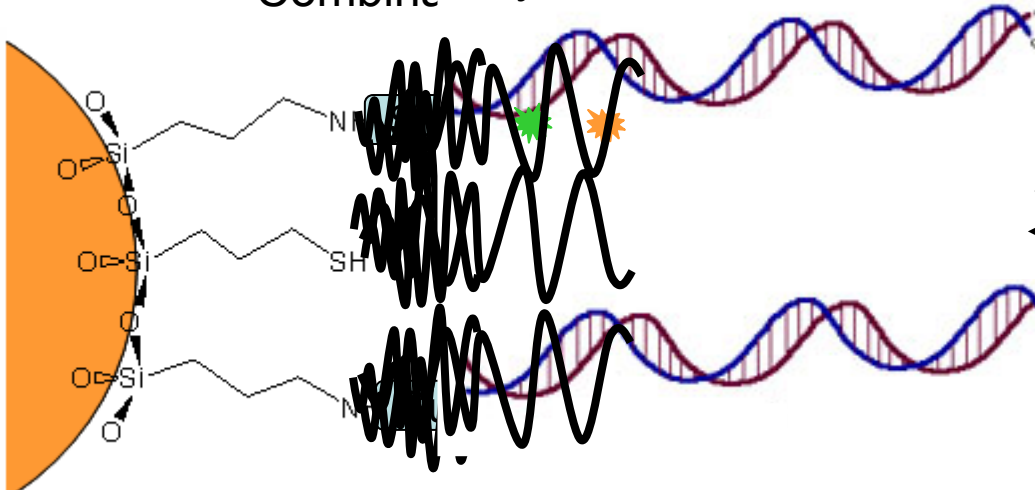
Battersby *et al.*, 2002, *Chem Commun.* 1435.  
Miller *et al.*, 2005, *Langmuir*, 21, 9733.  
Vogel *et al.*, 2007, *J Coll & Inter Sci.* 310, 144.

# Principal of Dual Purpose Supports

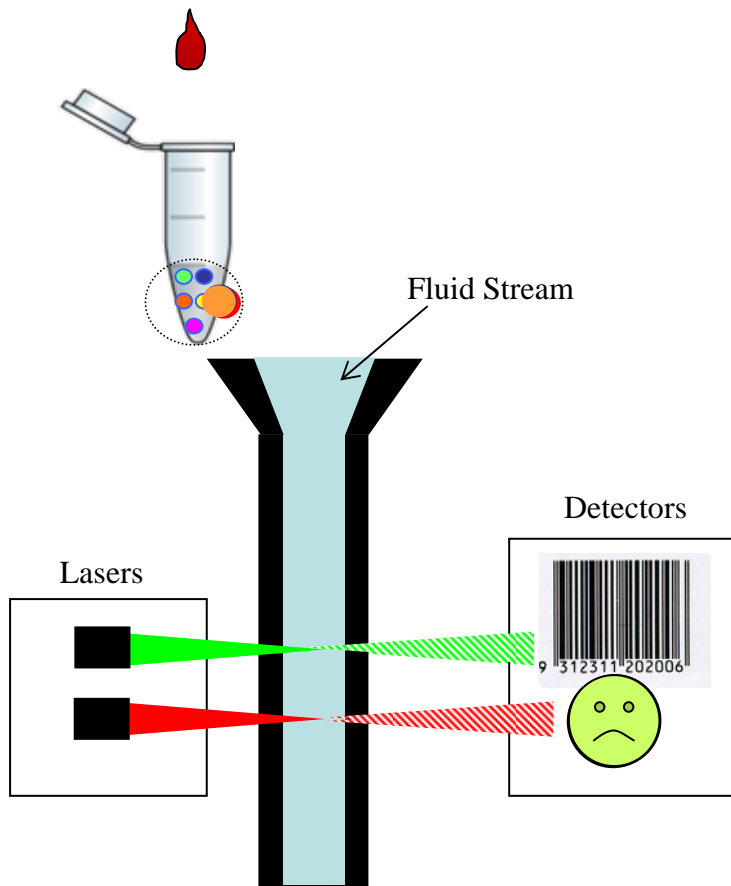


## Bio-Assay

Combine Polymer Modification



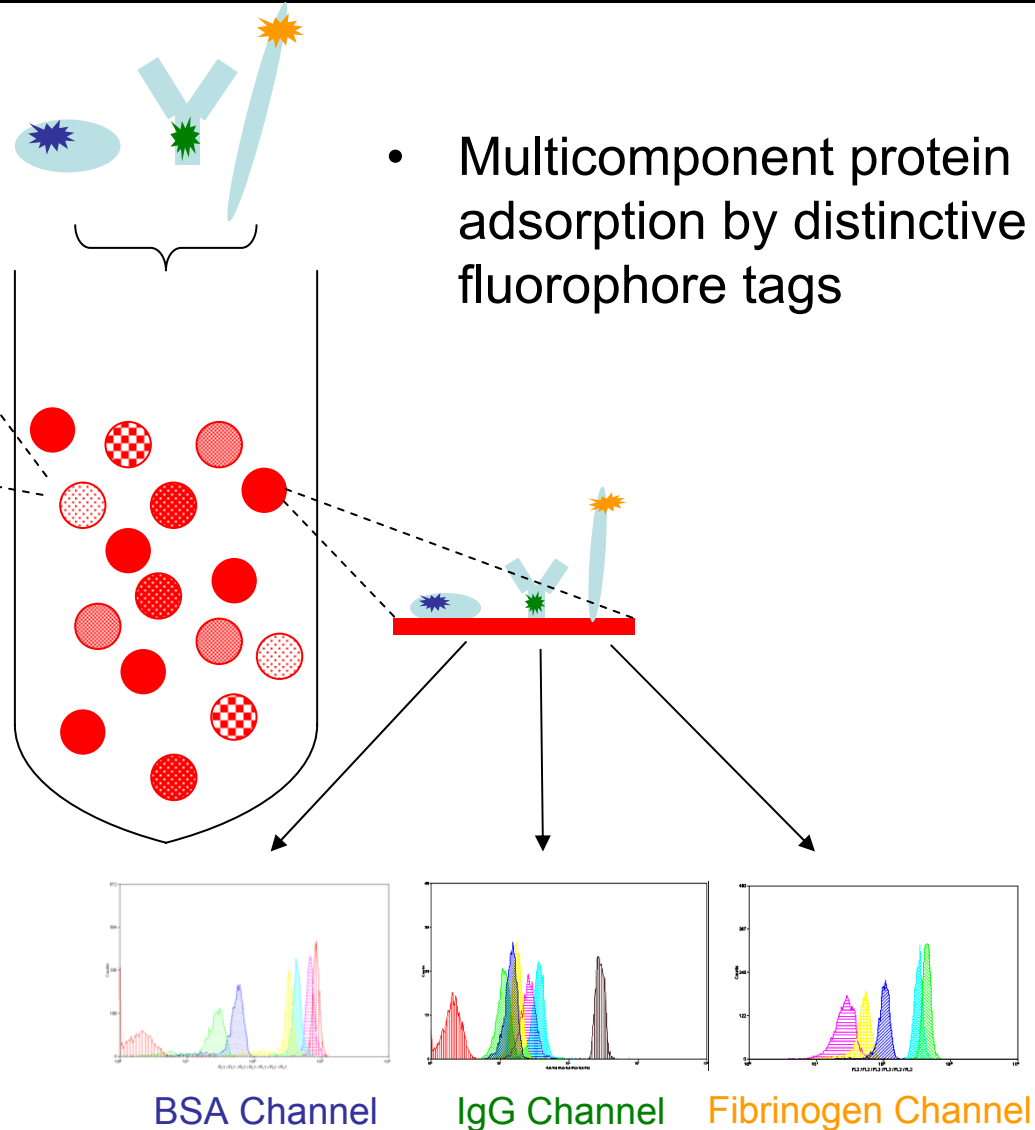
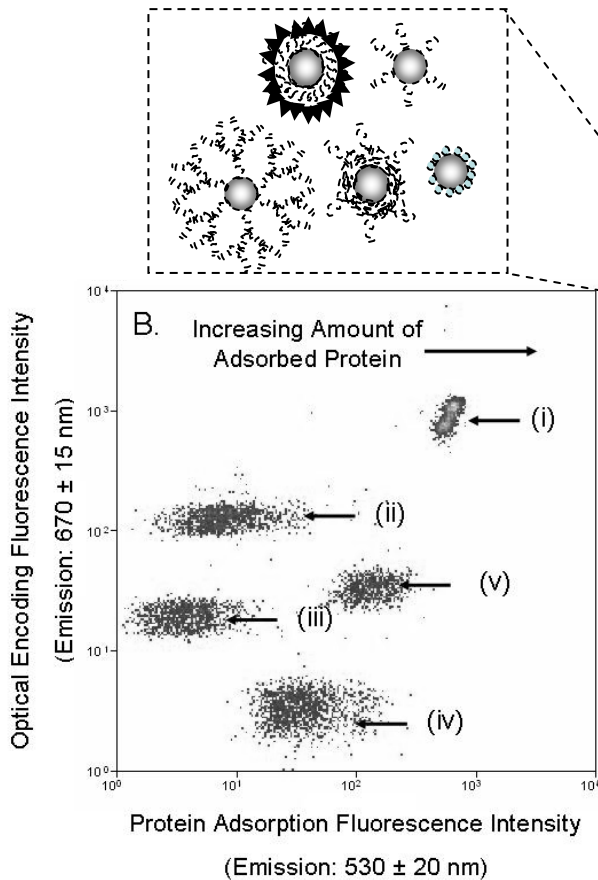
# Flow Cytometric High-Throughput Analysis



- **Single Particle Analysis**
  - >1,000 particles per second
- **Multi-Parametric Analysis**
  - Multiple Spectral Detectors from far-UV to near-IR
  - Enables encoded particle libraries and quantification of multicomponent adsorption
- **Low Sample Volume**
  - 50 to 250  $\mu\text{L}$  and good mixing
  - Small adsorbent (10,000 particles) and adsorbate (ng's protein) quantities

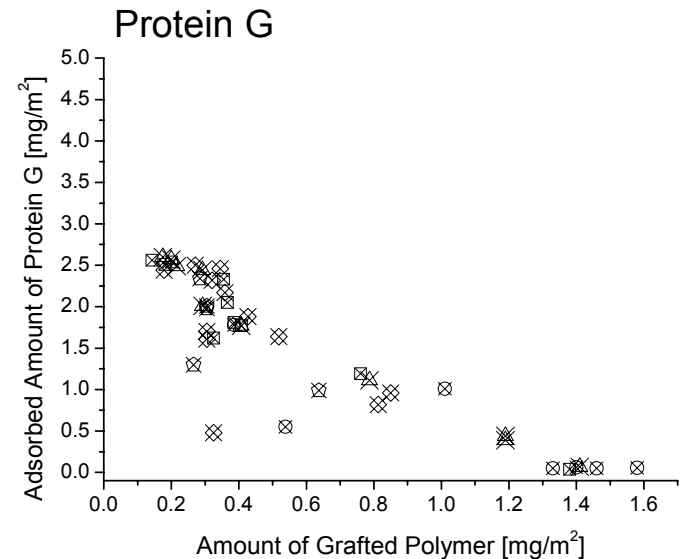
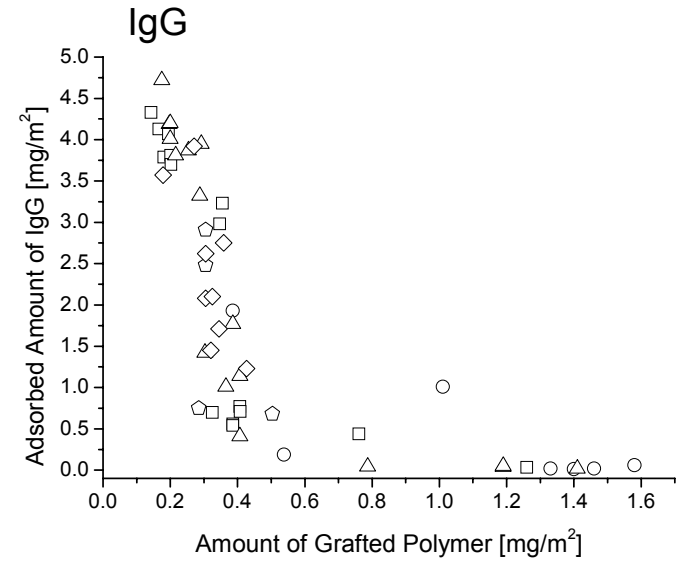
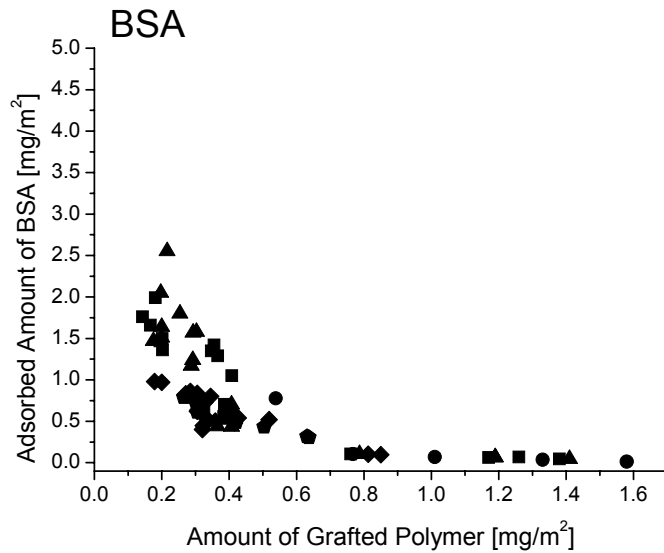
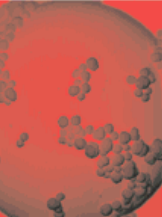
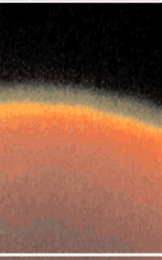
# Simultaneous Multiplexed Surface and Multicomponent Protein Adsorption

- Optical Encoding for multiplexed surfaces





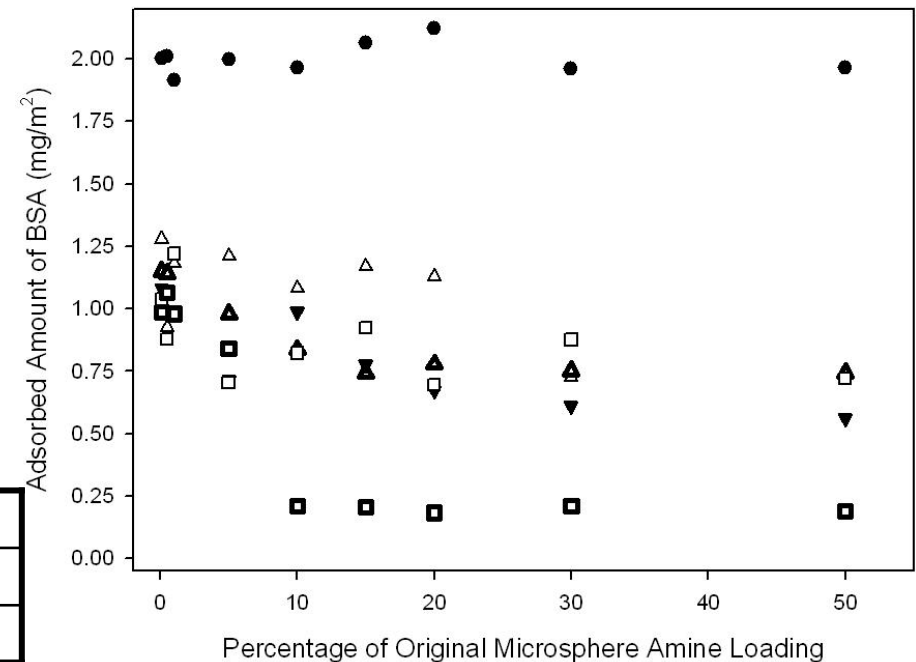
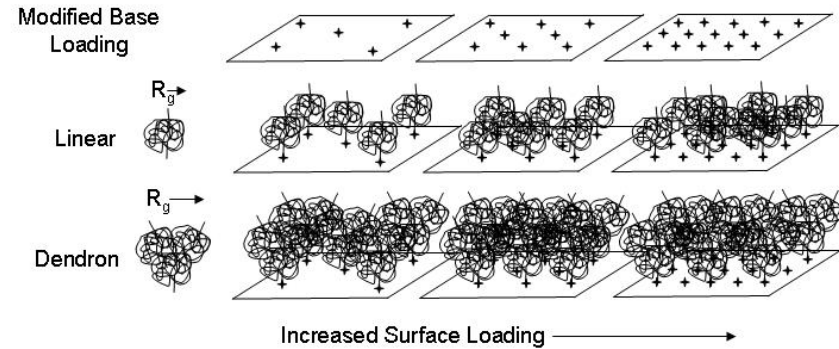
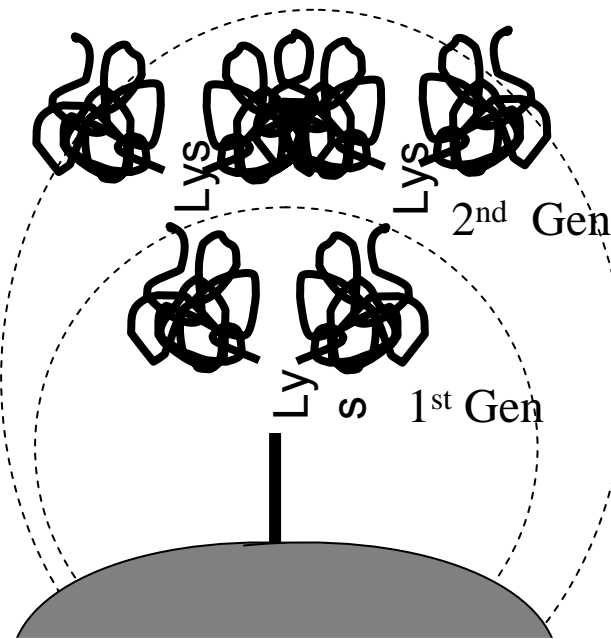
# Improving Biosensors through Protein Resistant Surfaces



	PEG $M_w$
□	2,000
○	3,400
△	6,000
◻	10,000
◇	20,000

# Improving Biosensors through PEG-Lys Copolymer Dendrons

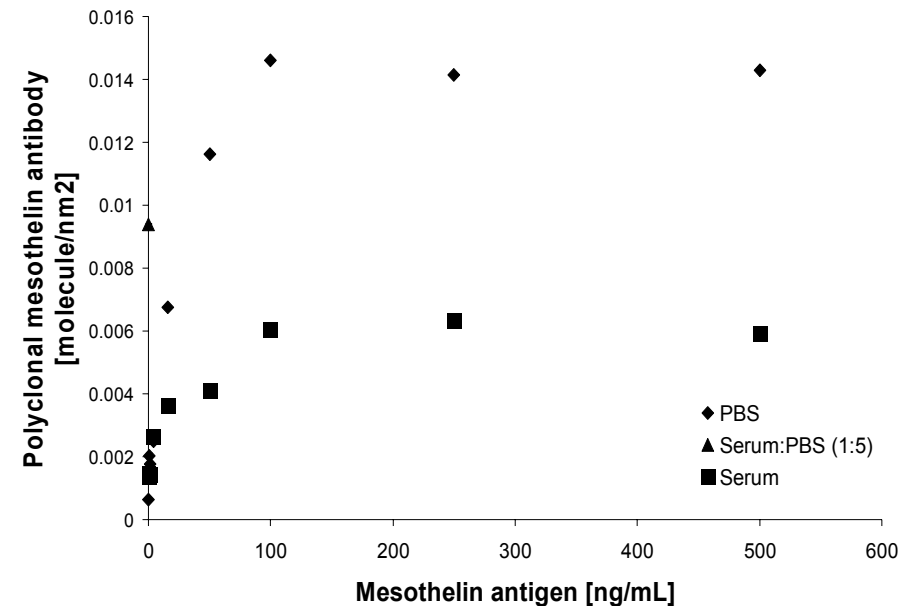
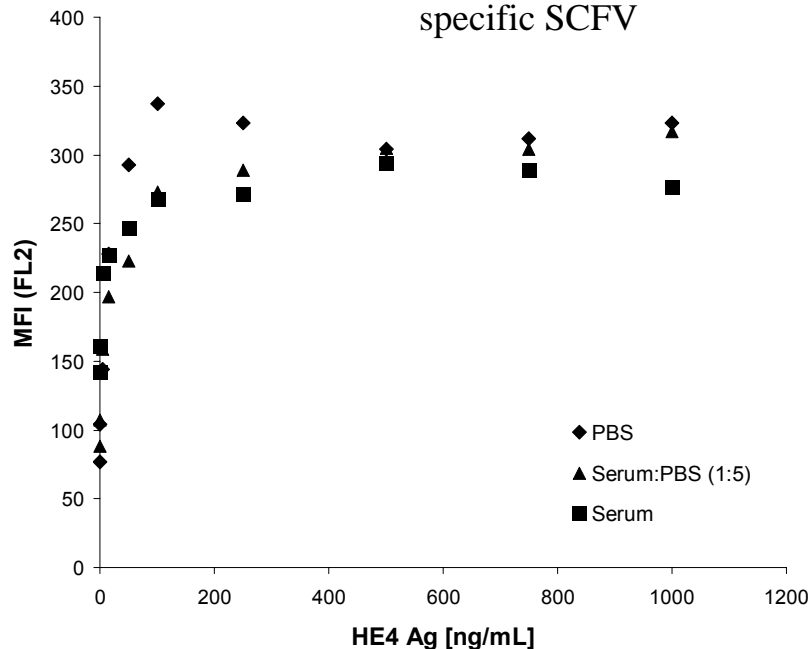
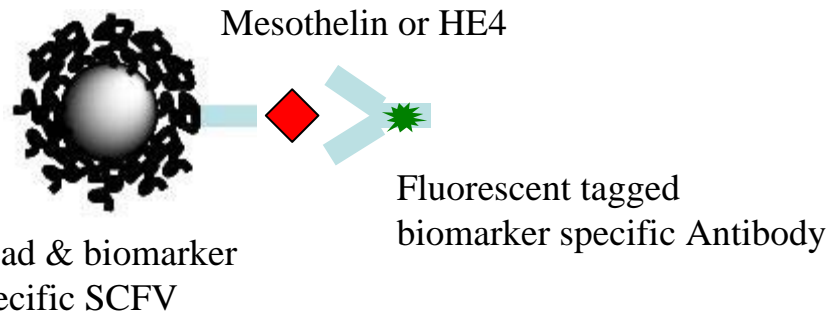
- Increasing Dendronic generation and surface loading increased protein resistivity



●	Unmodified	△	1-PEG
▲	2-PEG Linear	□	1st Gen PEG Dendron
▼	3-PEG Linear	◻	2nd Gen PEG Dendron

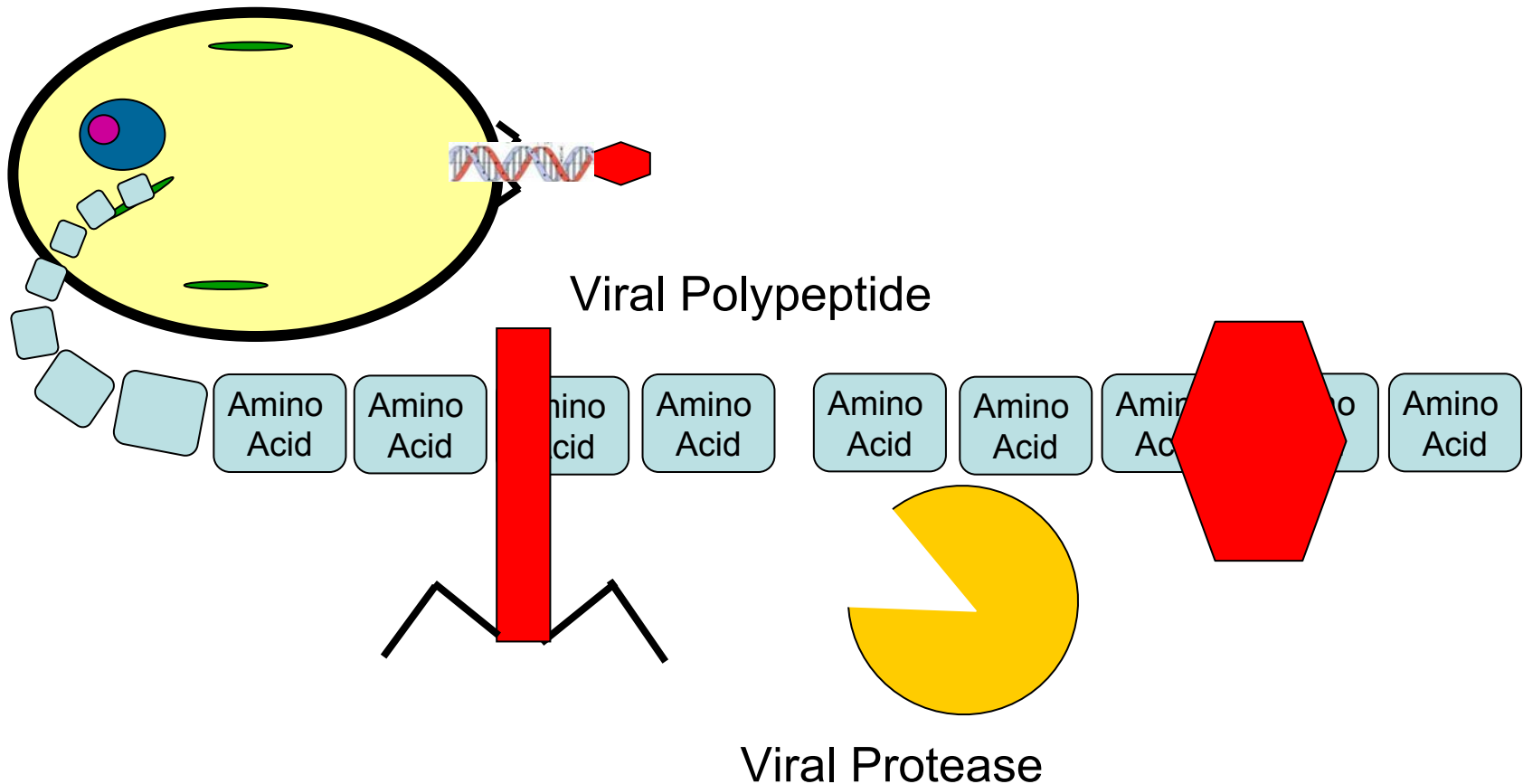
# Ovarian Cancer Biosensor

- Detection of HE4 and Mesothelin ovarian cancer biomarkers in spiked serum samples.

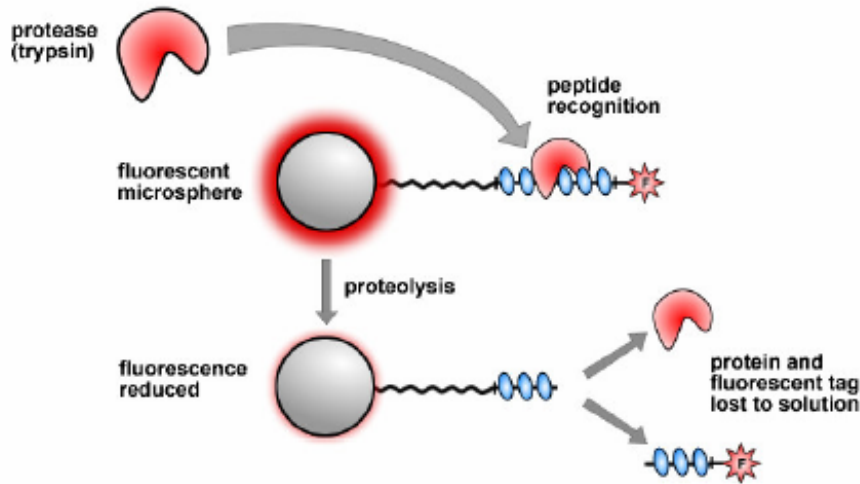


# Protease Mapping Assay

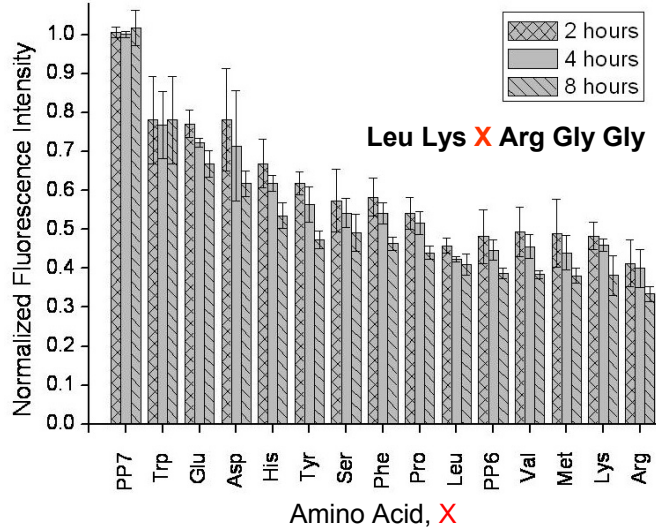
- Protease inhibitors are a highly specific and effective means of treating infectious diseases



# Infectious Disease Assays

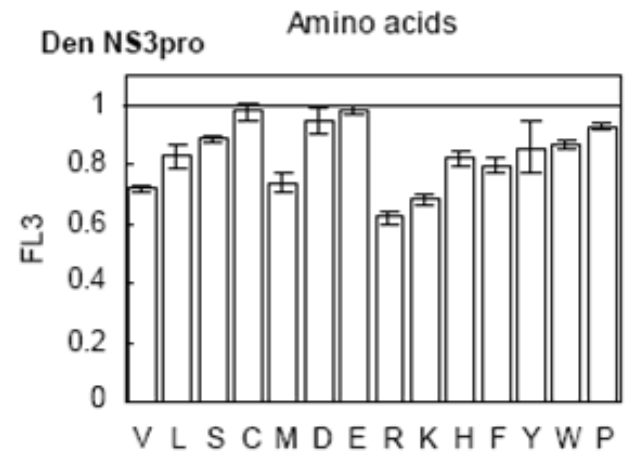
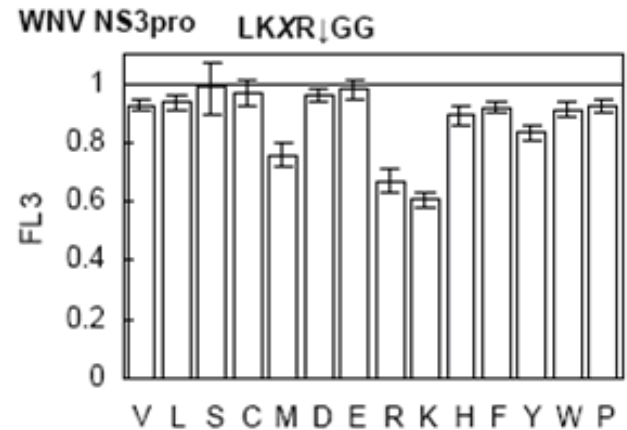


## Model: Trypsin protease



Surawski et al., *Mol. BioSyst.*, 2008, 4, 774-778.

## West Nile Virus & Dengue Fever



Marcon et al., *Analytical Biochemistry*, 2008, 376, 151-153.

# Summary

- Optically barcoded particles as biosensors
  - Ability to fluorescently encoded libraries of discriminate particles
  - Chemically modifiable surfaces – peptide, DNA, polymers, etc.
  - Simultaneous multicomponent adsorbate and multiplexed adsorbent ability.
  - Immunoassay results for two ovarian cancer biomarkers in serum
  - Mapping of two viral protease cleavage sites

# Acknowledgements

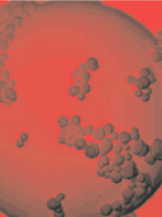
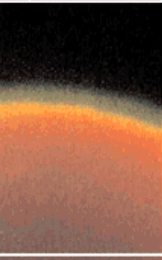


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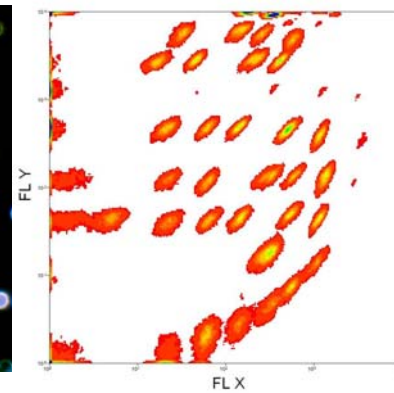
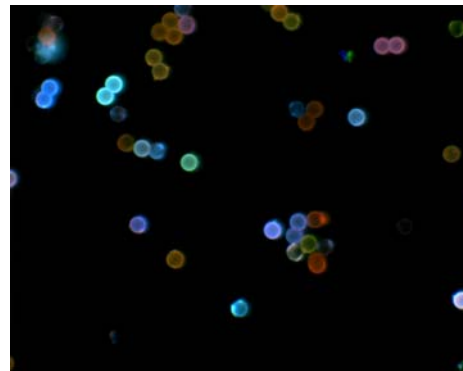
Centre for Microscopy  
and Microanalysis



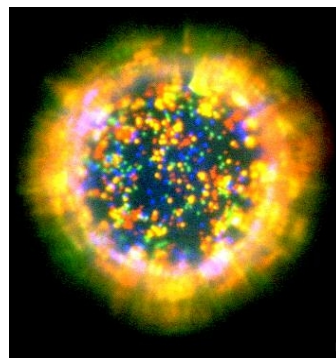
# Creating Barcoded Particle Biosensors



## 1) Fluorescent Dyes



## 2) Bead-on-Bead



## 3) Light Scattering

