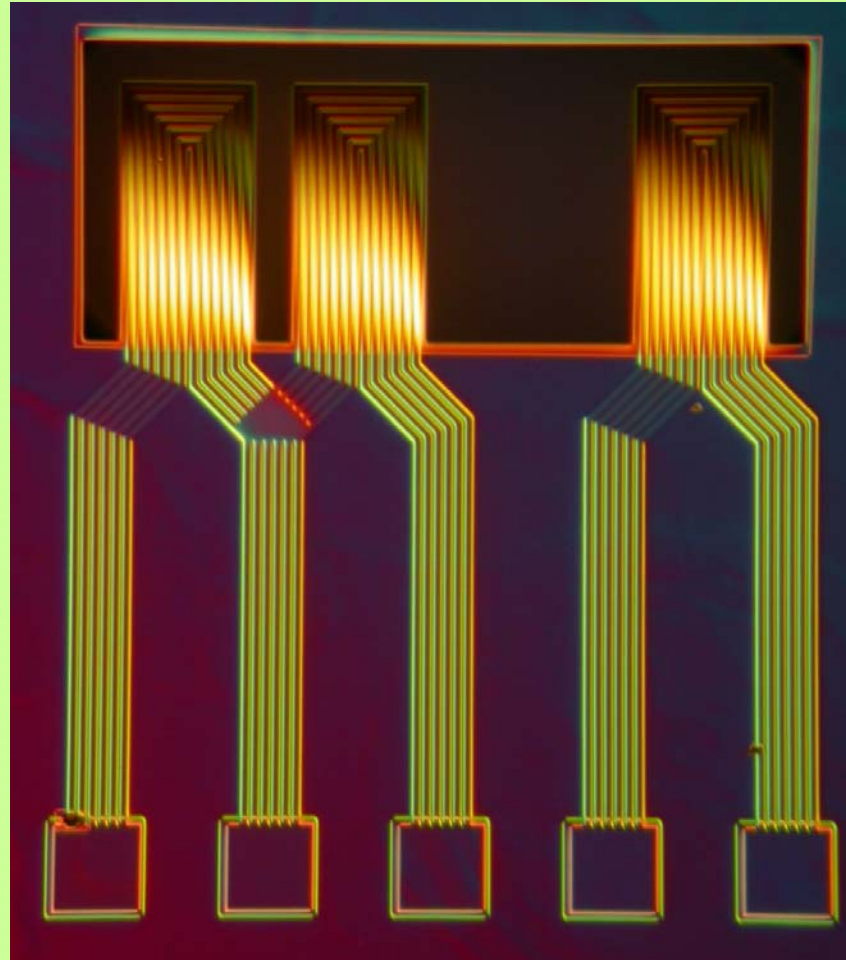


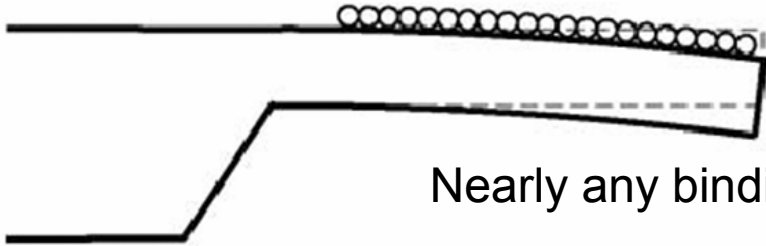
Microfabricated devices for biomolecular detection



Scott Manalis

*Associate Professor
Biological Engineering and Media Arts & Sciences
Massachusetts Institute of Technology*

Mechanical detection with microcantilevers



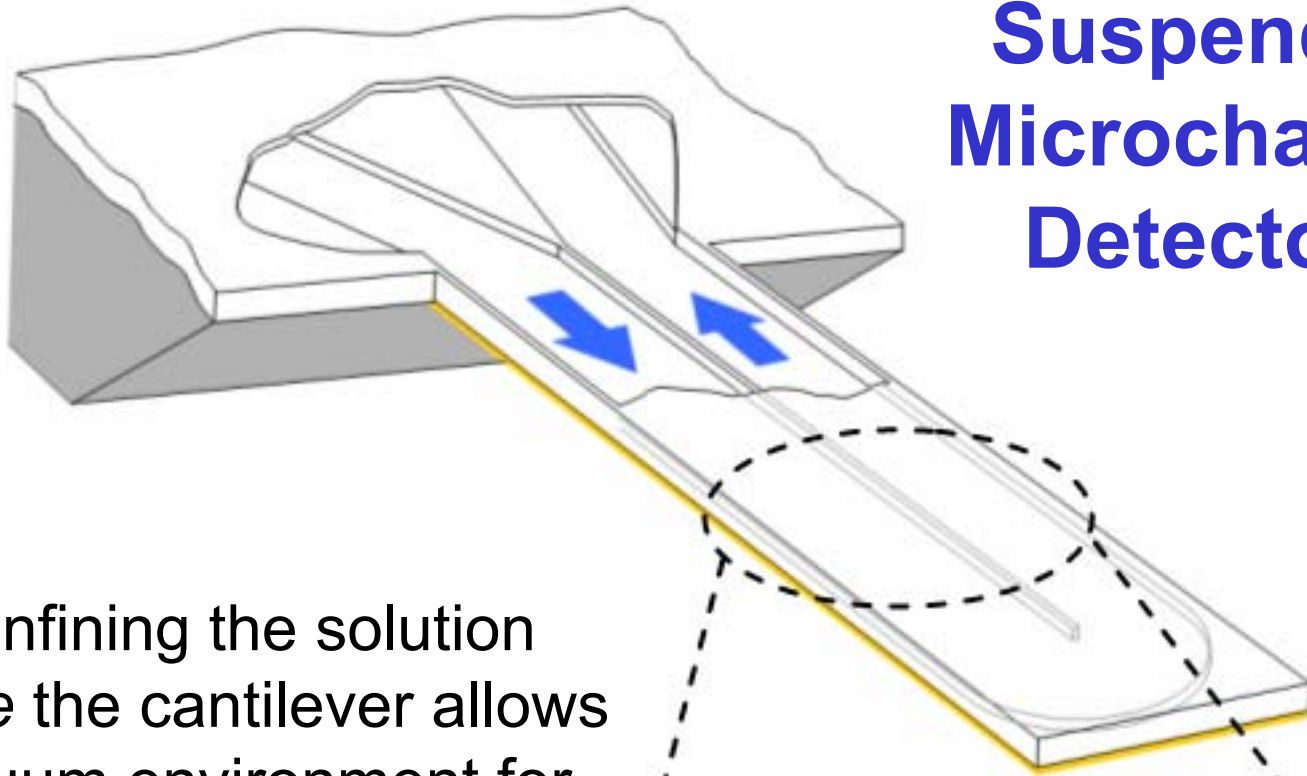
Adsorption – surface stress – bending

Nearly any binding reaction on cantilever surface results in bending

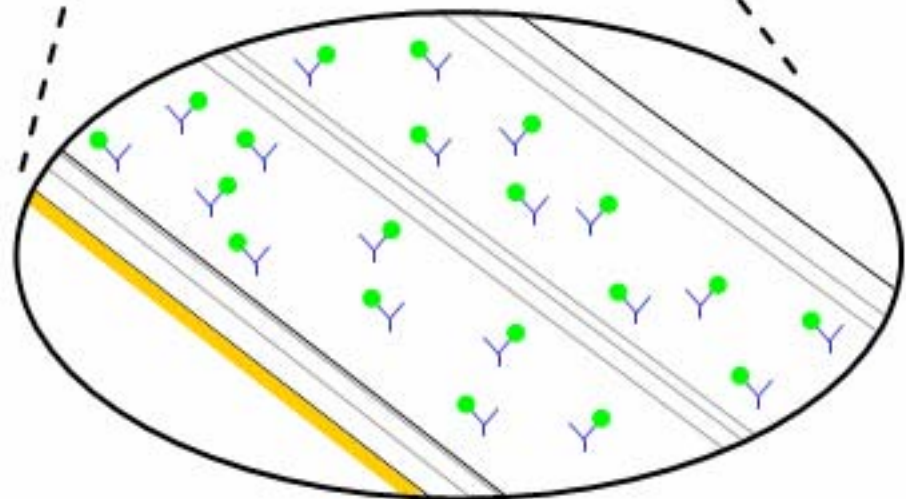
Gimzewski et al. measures DNA hybridization (Science 2000)

Majumdar et al. measures antibody – antigen binding (PNAS 2001)

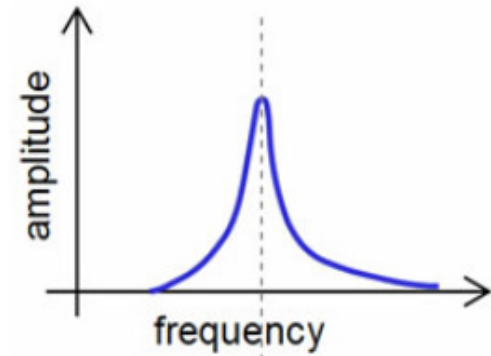
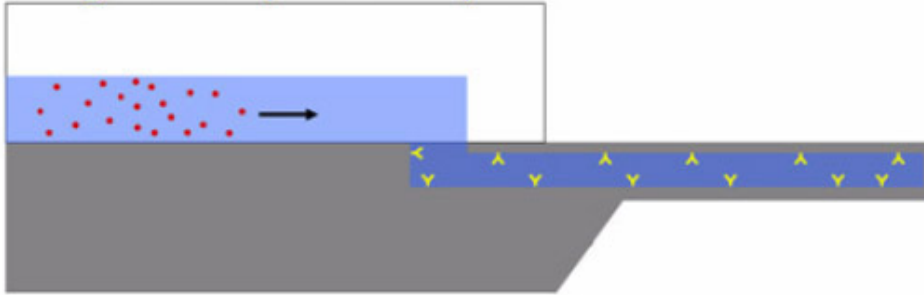
Suspended Microchannel Detectors



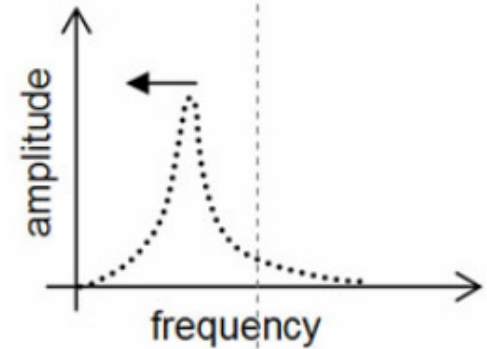
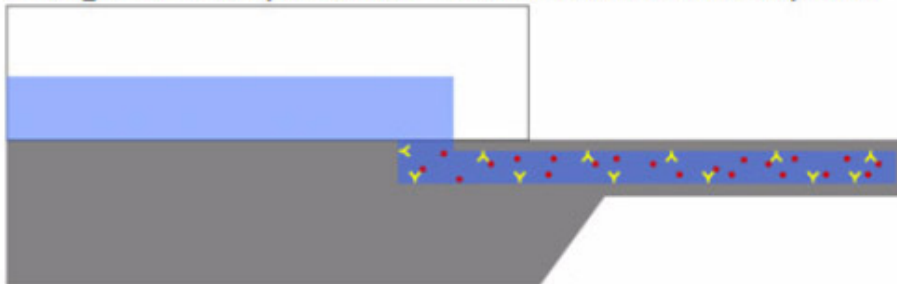
Confining the solution *inside* the cantilever allows vacuum environment for resonator and aqueous environment for biomolecules



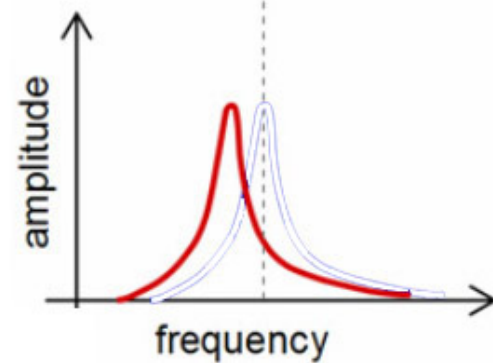
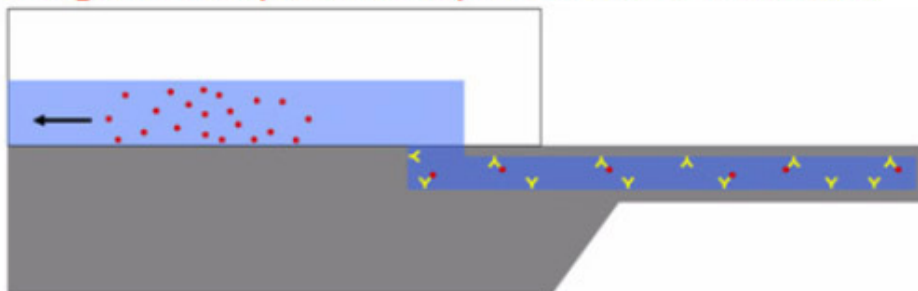
Stage 1: Sample is transported into U-channel

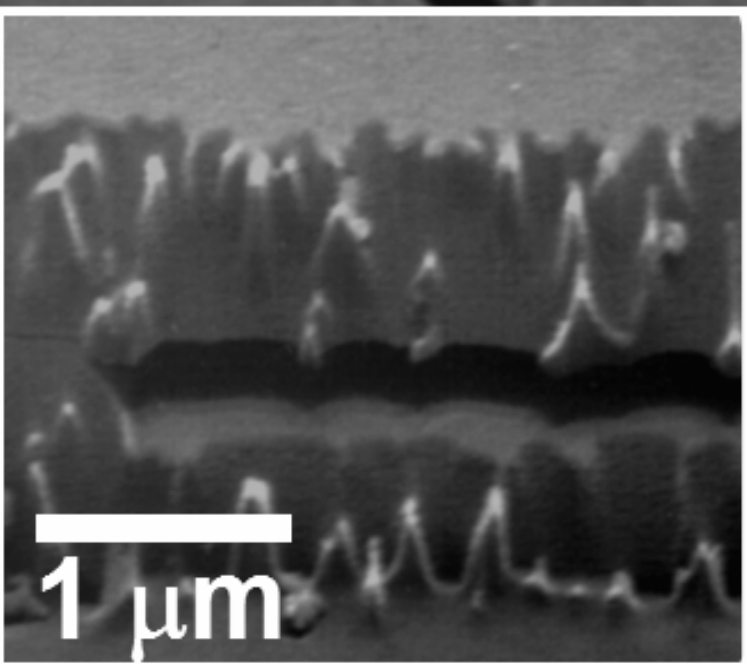
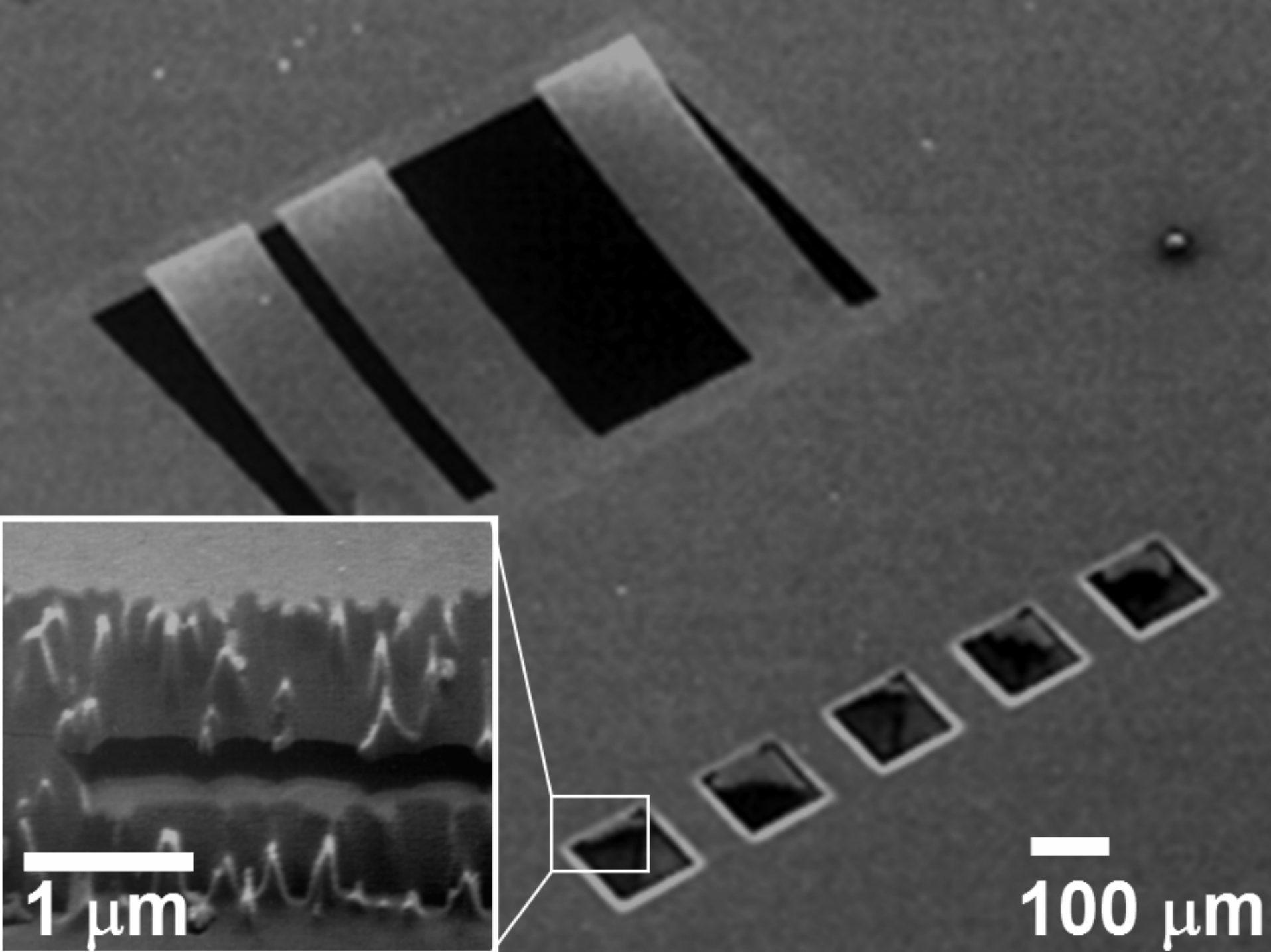


Stage 2: Sample binds to immobilized receptors

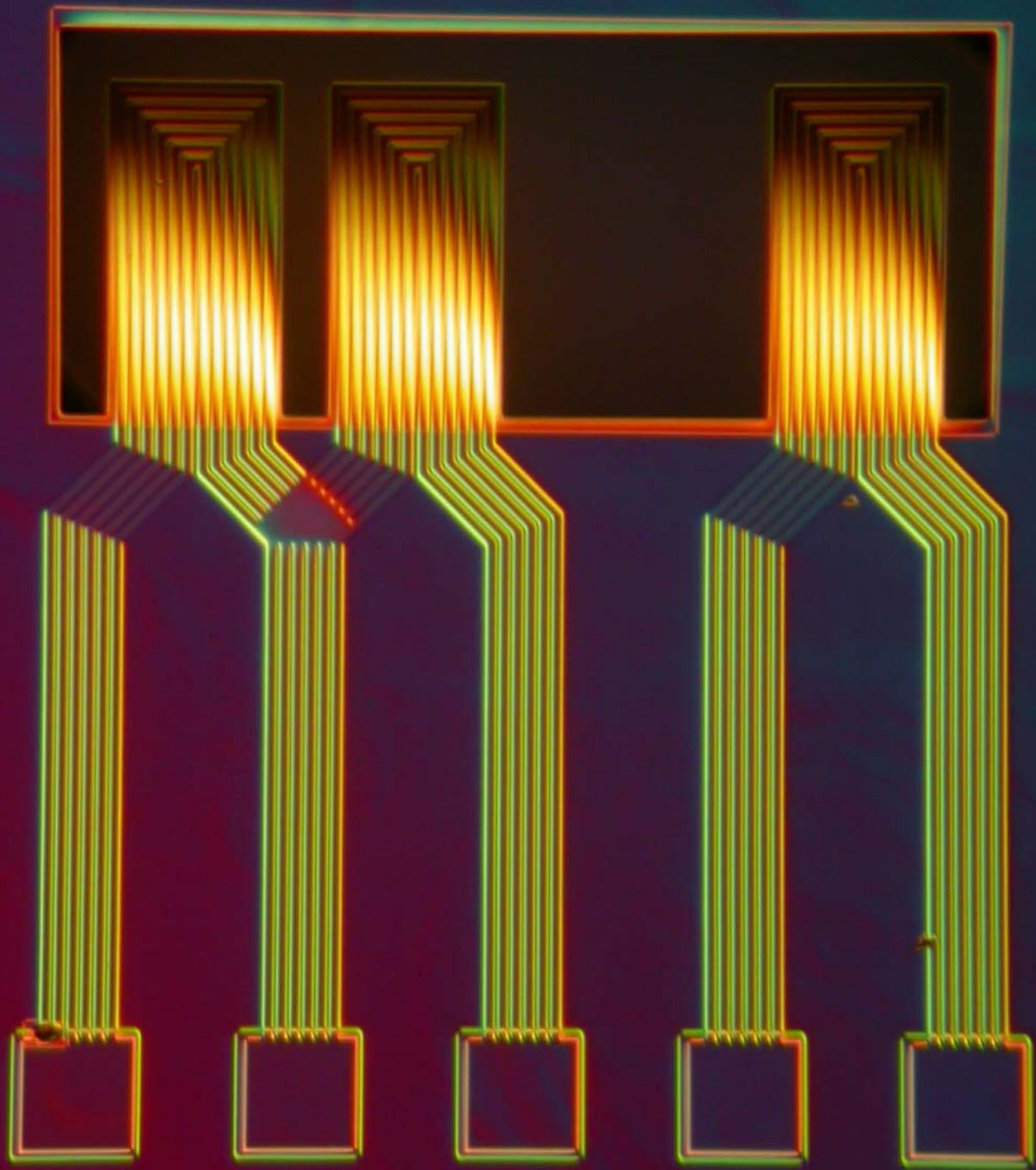


Stage 3: Sample is transported out of U-channel

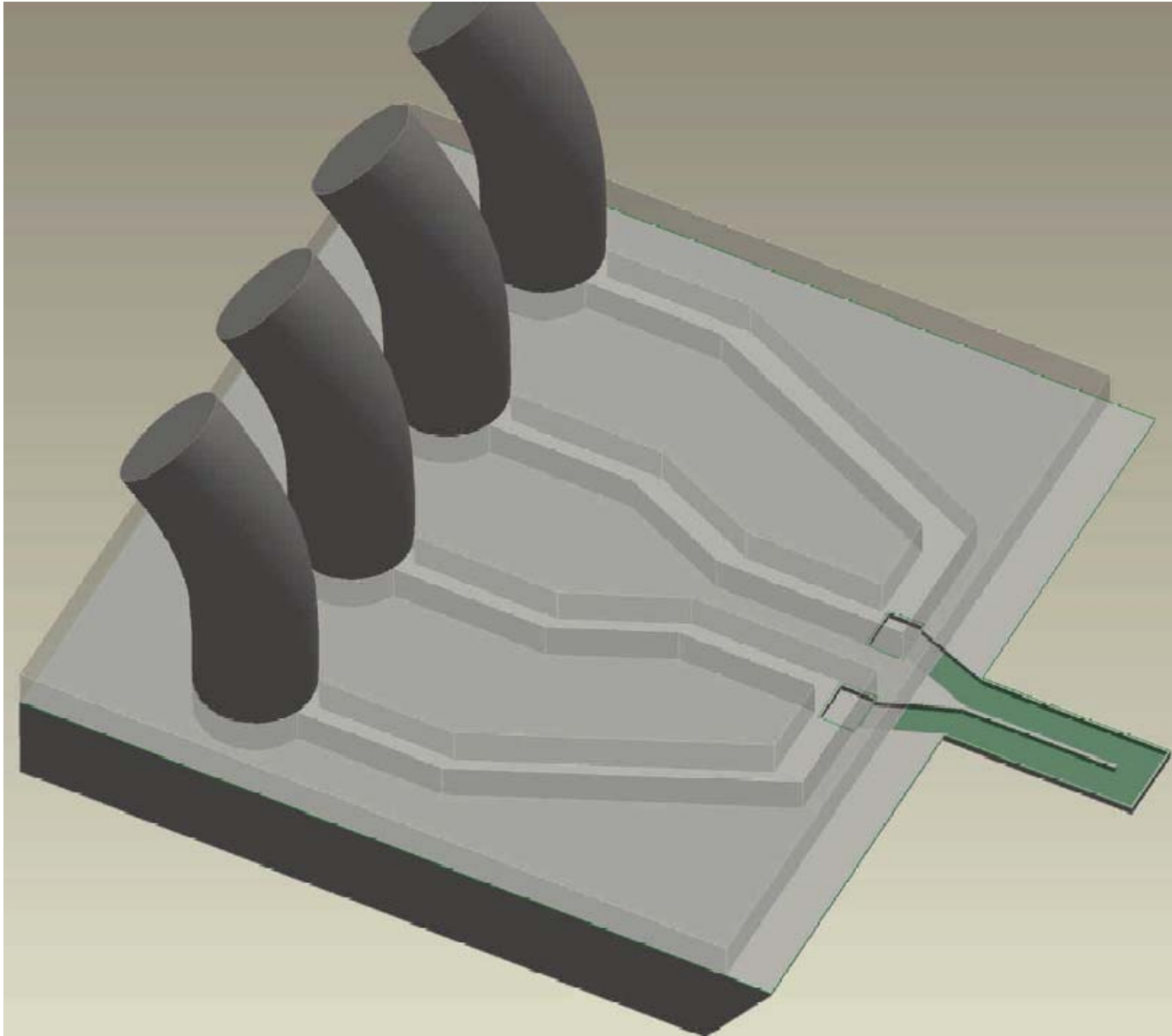


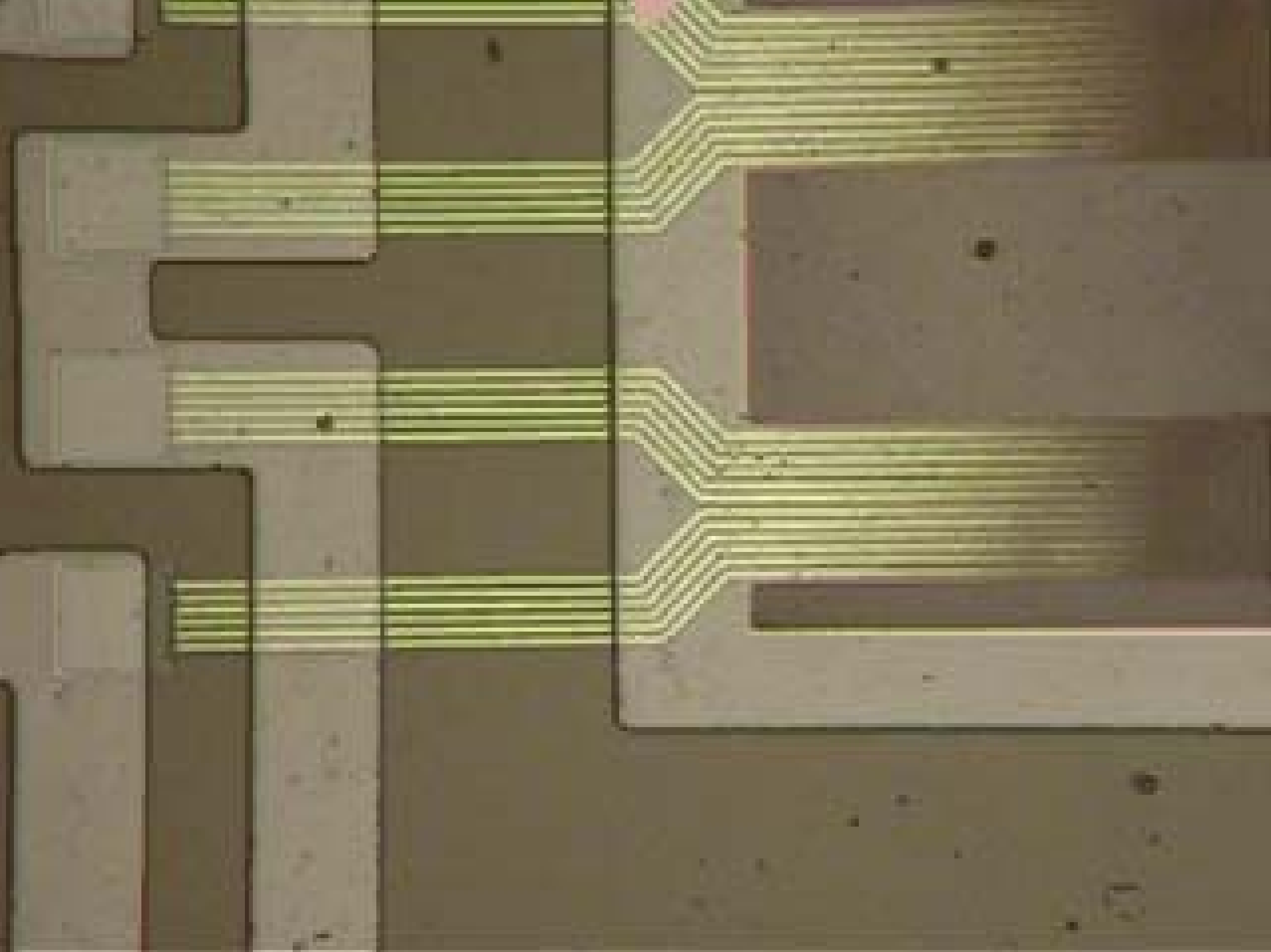


100 μm

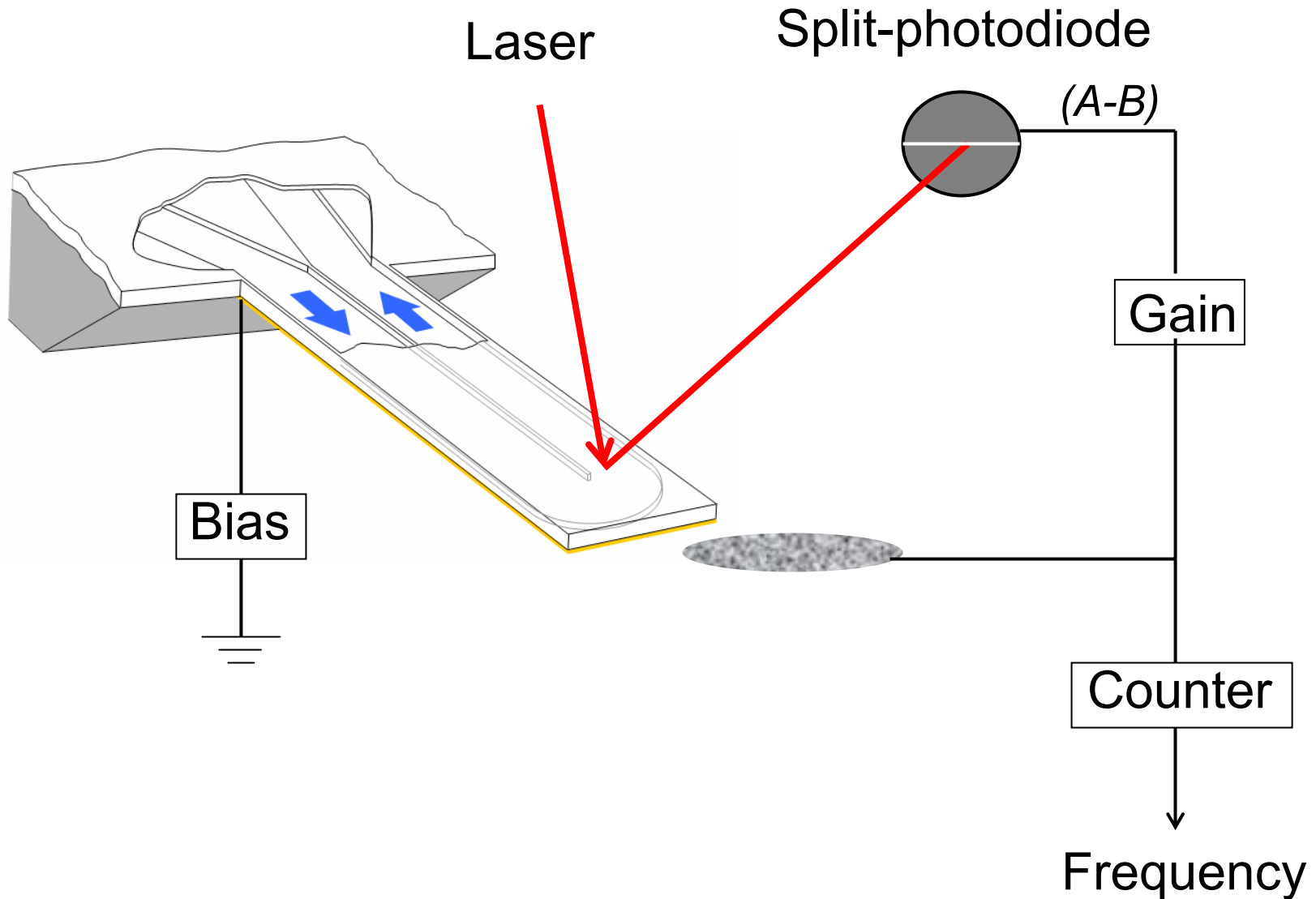


Device packaging

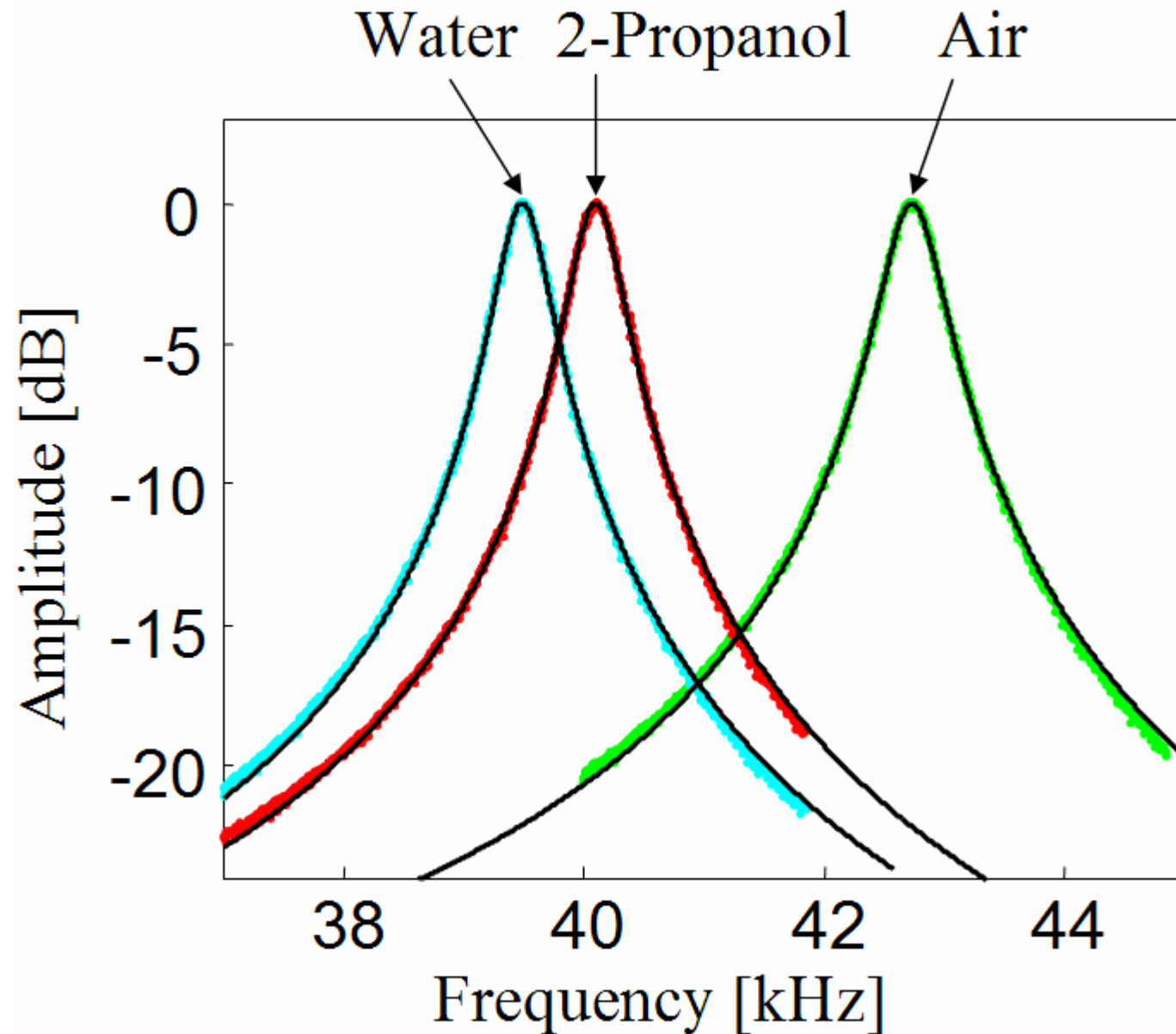




Measurement Schematic





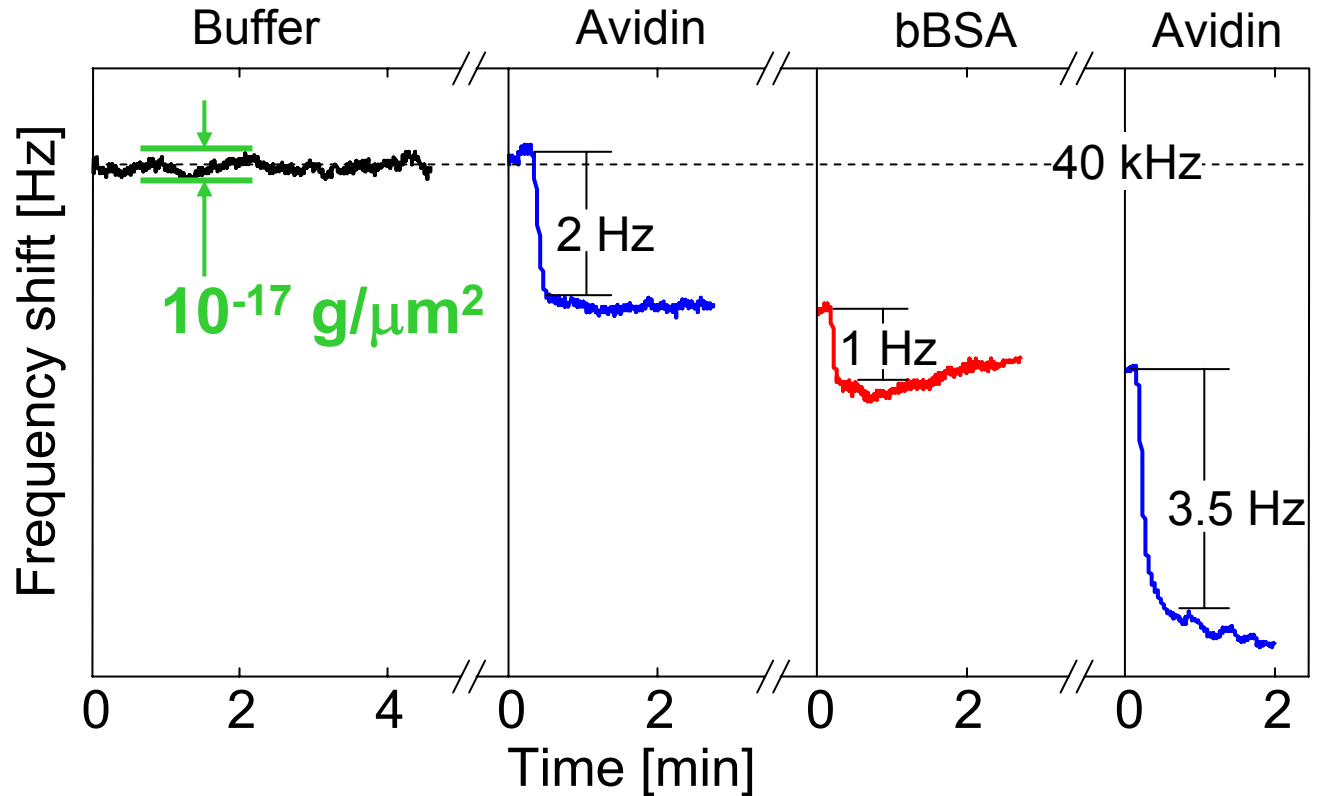
No viscous damping



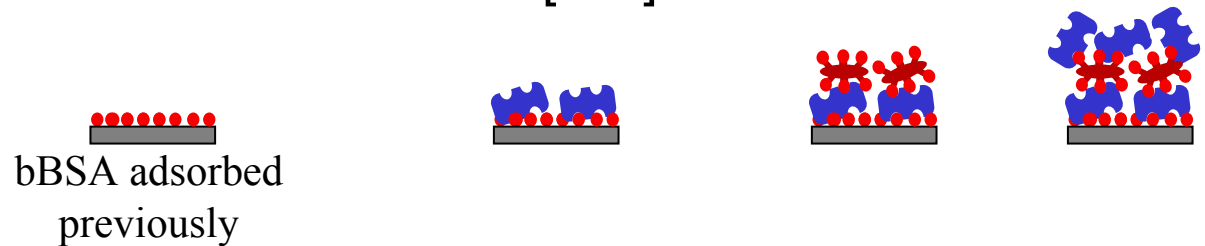
Quality factor
is independent
of medium

Biotin/Avidin multilayer formation

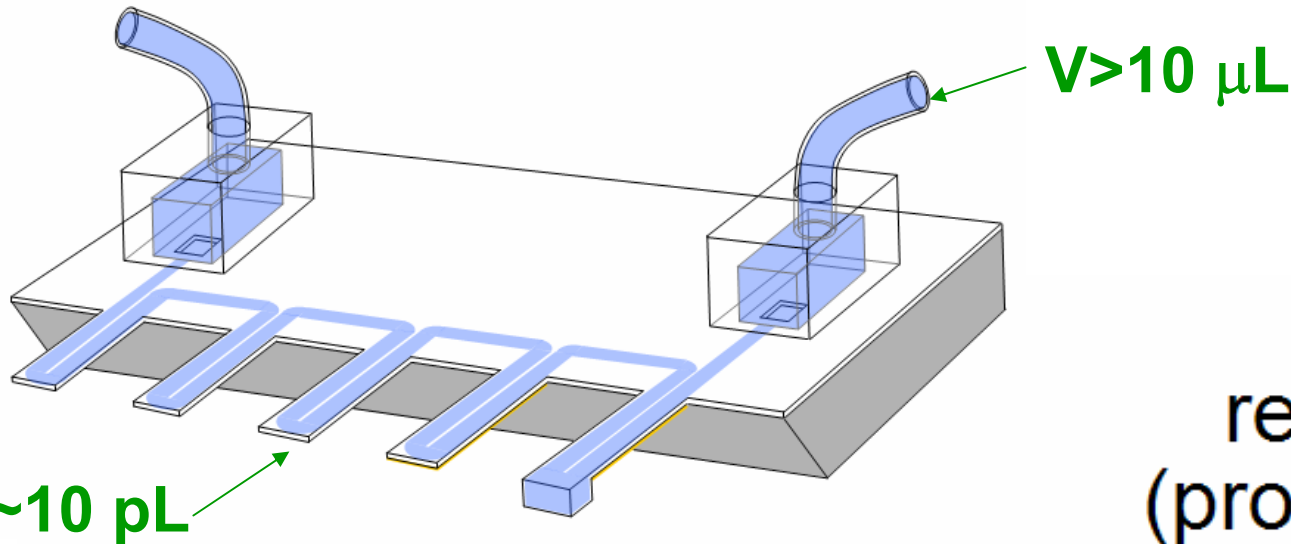
-  Avidin
(500 $\mu\text{g}/\text{mL}$)
-  bBSA
(1 mg/mL)



Channel wall:



How sensitive is the suspended microchannel detector?



Mass
resolution
(proteins/ μm^2)

Quartz Crystal μ Balance commercial

100

**Suspended
microchannel**

Version 1

100

Predicted

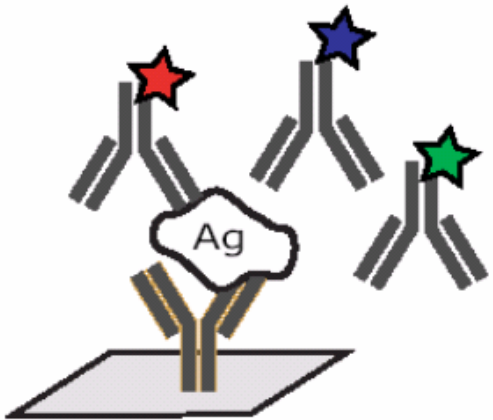
1

Fluorescence

microarrays

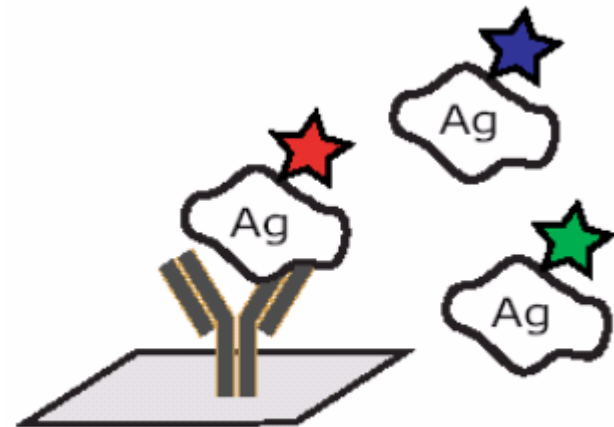
1

Comparison to Fluorescent Protein Microarray



sandwich detection

- Highly selective
- Highly sensitive



direct labeling

- Less selective
- Labeling is difficult for low abundant proteins

Label-free provides real-time binding kinetics

Target molecule

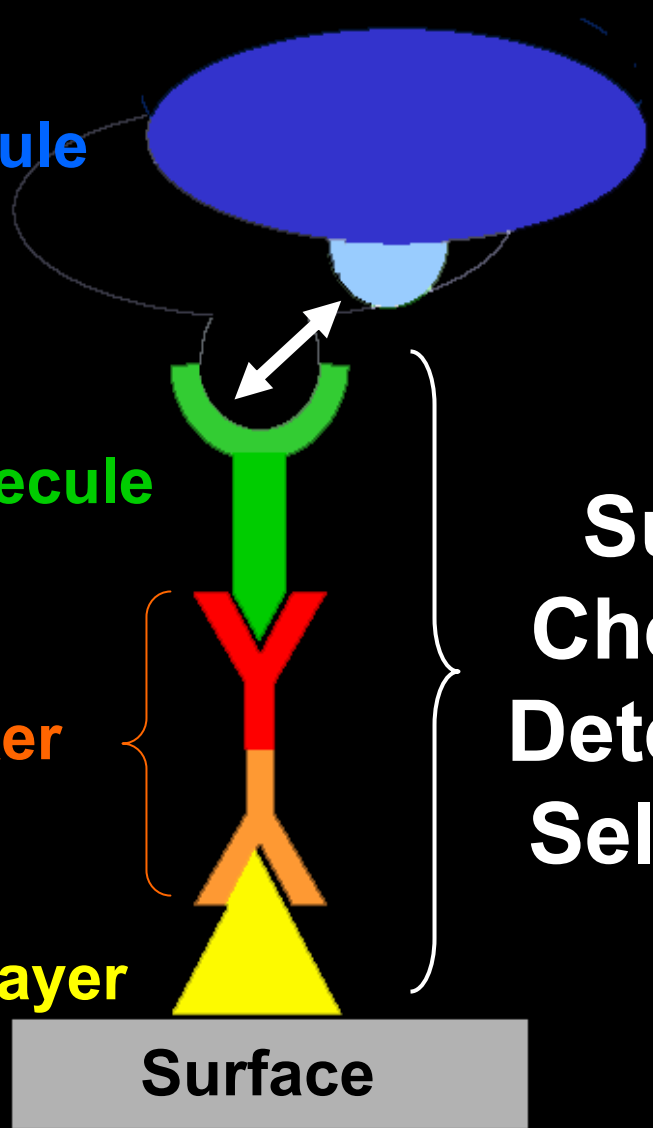
Receptor molecule

Crosslinker

Silane monolayer

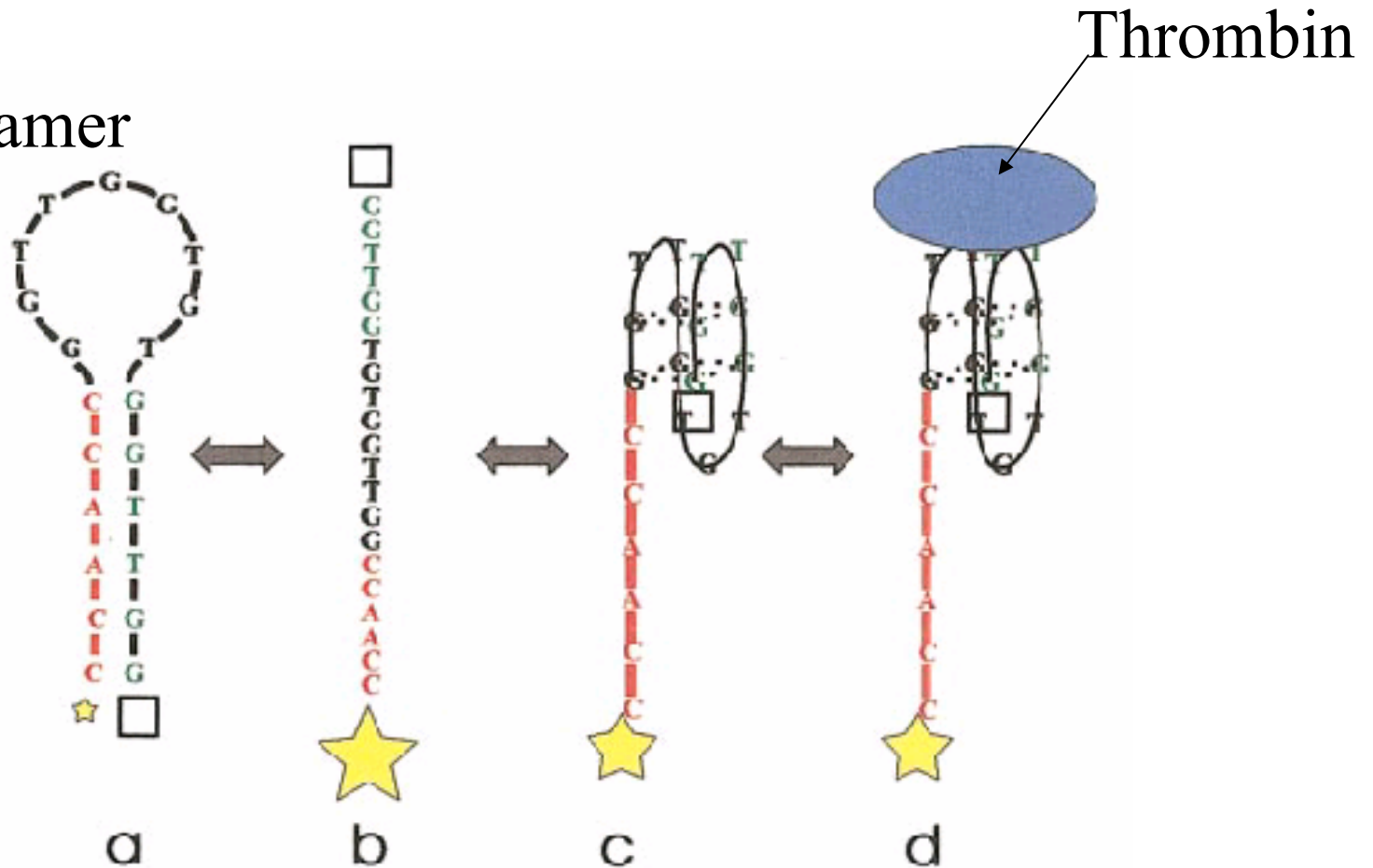
Surface

**Surface
Chemistry
Determines
Selectivity**

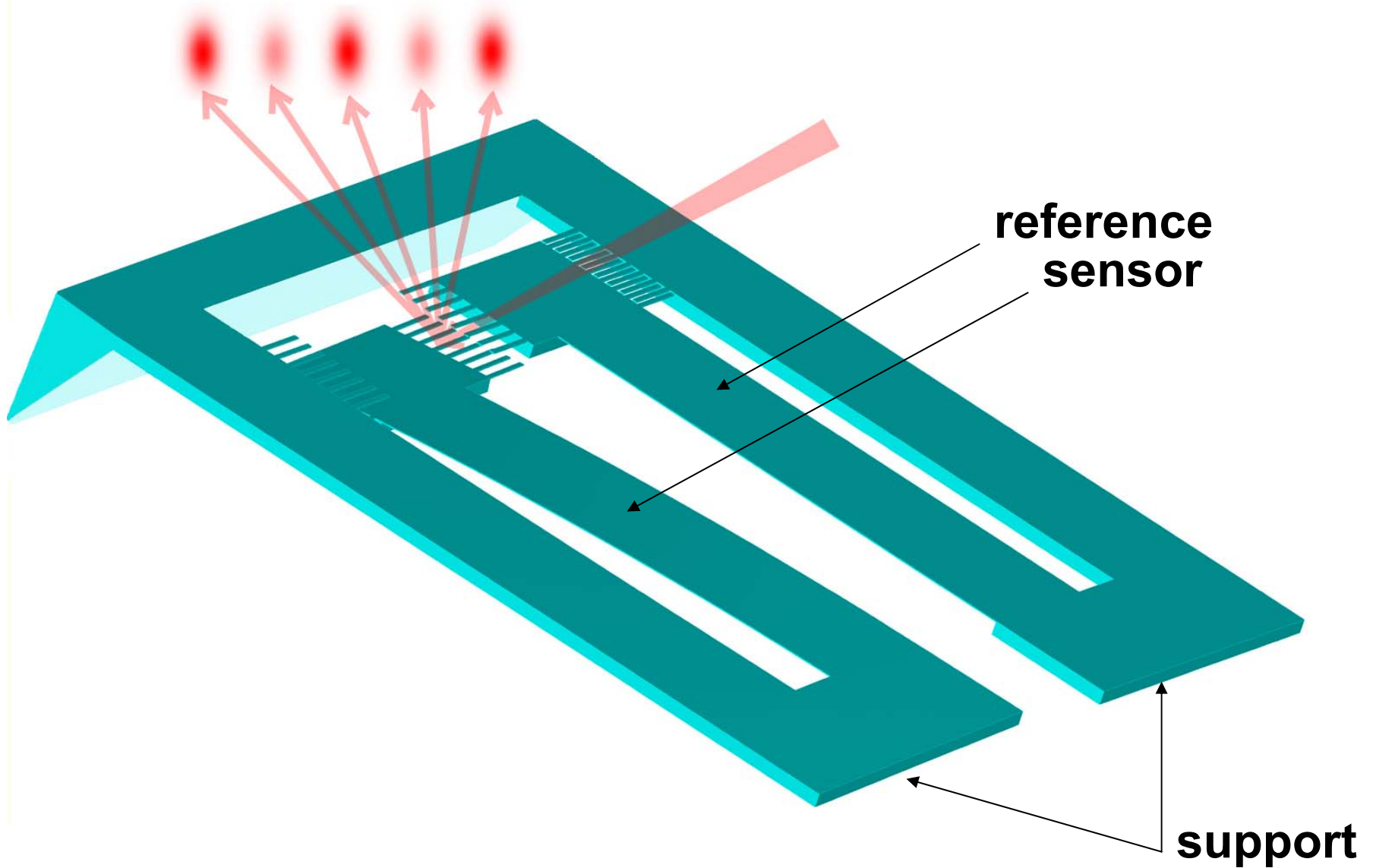


Example: Thrombin binding aptamer

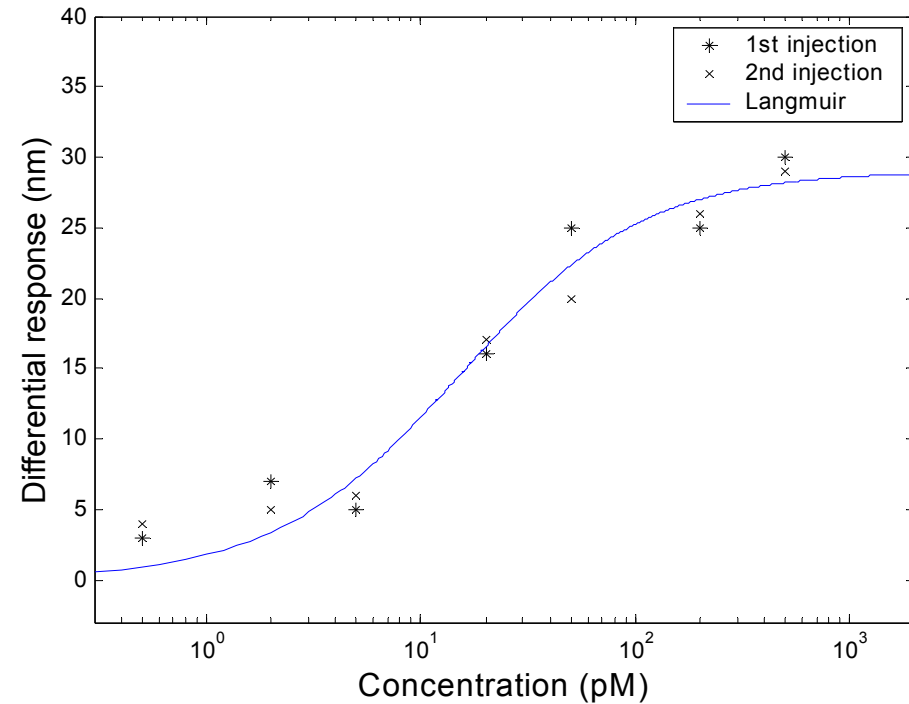
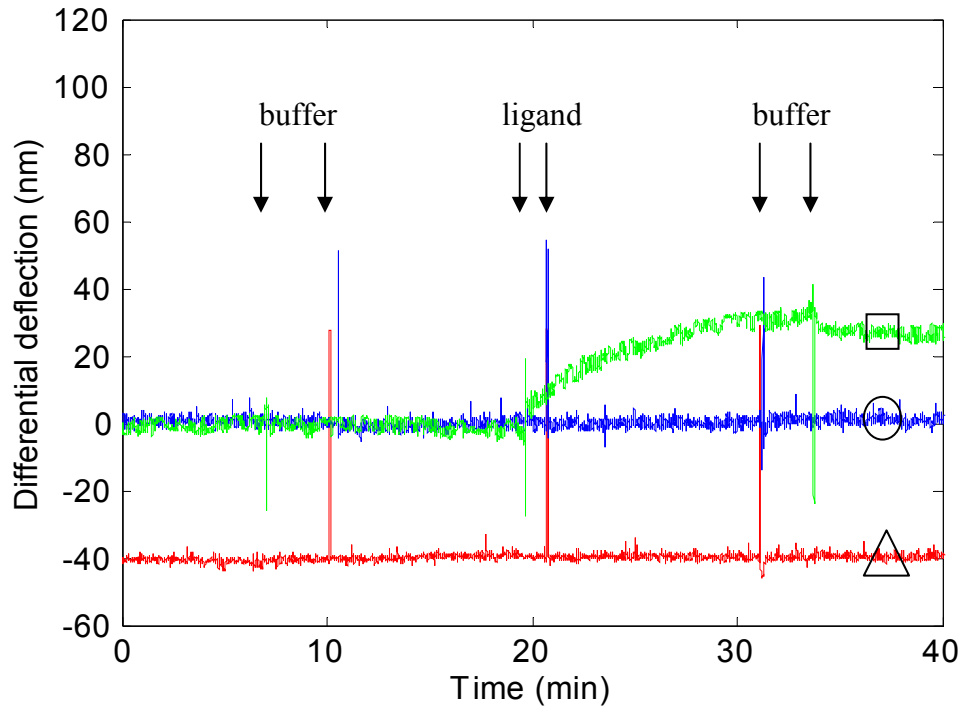
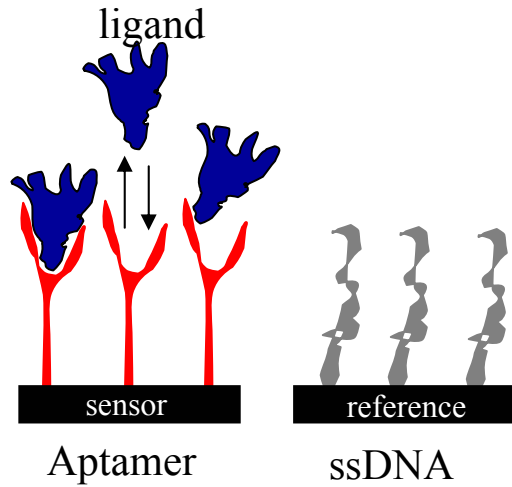
DNA Aptamer



Micromechanical stress sensor



Aptamers – ligand binding induces surface stress



Savran et al, Anal. Chem. 2004

The Team...

Suspended microchannel resonator (SMR)

Thomas Burg

Vacuum packaged SMRs on 6" wafer scale

John Foster and Amir Mirza

Innovative Micro Technology, Santa Barbara CA

Aptamer-based protein detection

Cagri Savran in collaboration with **Scott Knudson** and **Andy Ellington** (*UT Austin*)

Scanning probe microscopy with disturbance suppression

Andrew Sparks

Funding

DARPA bio:info:micro

AFOSR

NIH Center for Cell Decision Process

NSF Center for Bits and Atoms