Micromachined multi-analyte sensors: towards an "electronic tongue"

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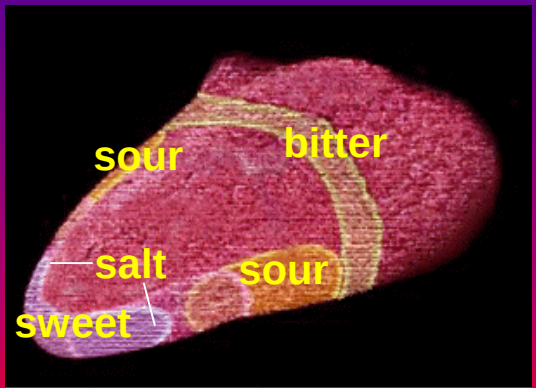
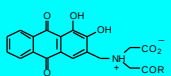
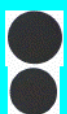
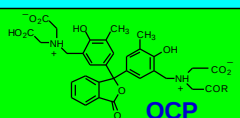
New sensing technology: What can we learn from nature??

- What about the sense of taste?
  - sense of taste is not based on highly specific receptors, but instead on pattern recognition
  - with "smart chemistry" we can make both general and selective receptors
- What might we sense?
  - foods, but also
  - things you don't want to taste!
    - blood, urine, biological and chemical warfare agents



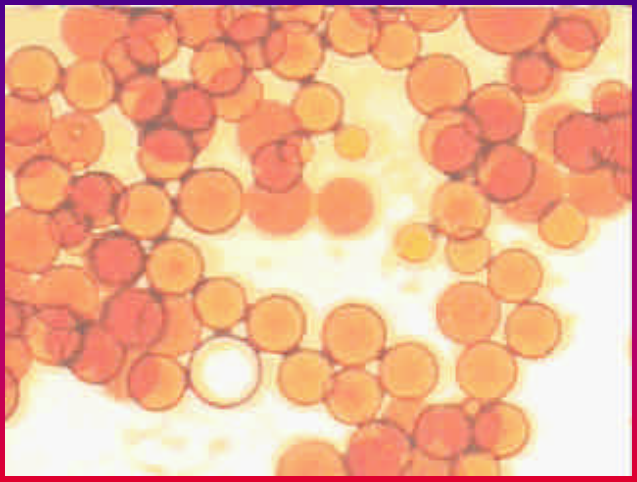
Indicator molecules interfaced to beads

- "solid phase" support for receptor chemistry
  - PEG/polystyrene, agarose, glass "beads" all convenient supports
  - "micro-beads" support the chemistry

R =	pH 3	pH 7	pH 11	Analyte
				H^+
fluorescein 				H^+
 alizarin complexone				H^+ H^+, Ce^{3+}
 OCP				H^+ H^+, Ca^{2+}

- each receptor changes color in a distinct way when exposed to different environments

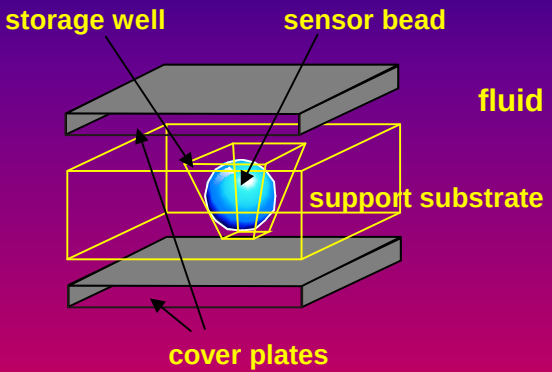
What happens when liquids flow across the beads?

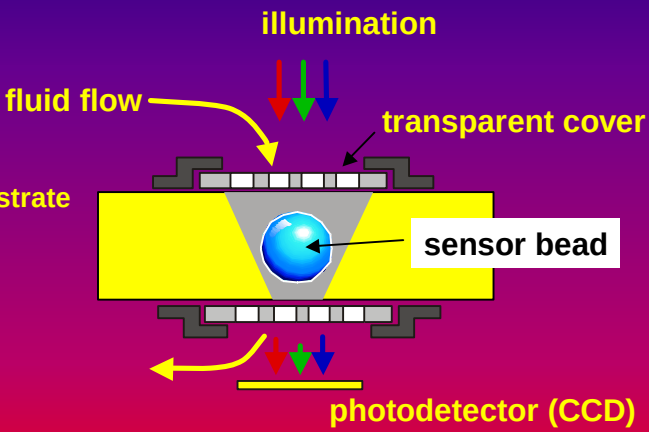


pH ramp (up and down)

- a BIG problem with PEG beads
  - dry state ~ 100 mm diameter
  - "wet" state 200 mm diameter
  - diameter a function of chemical environment

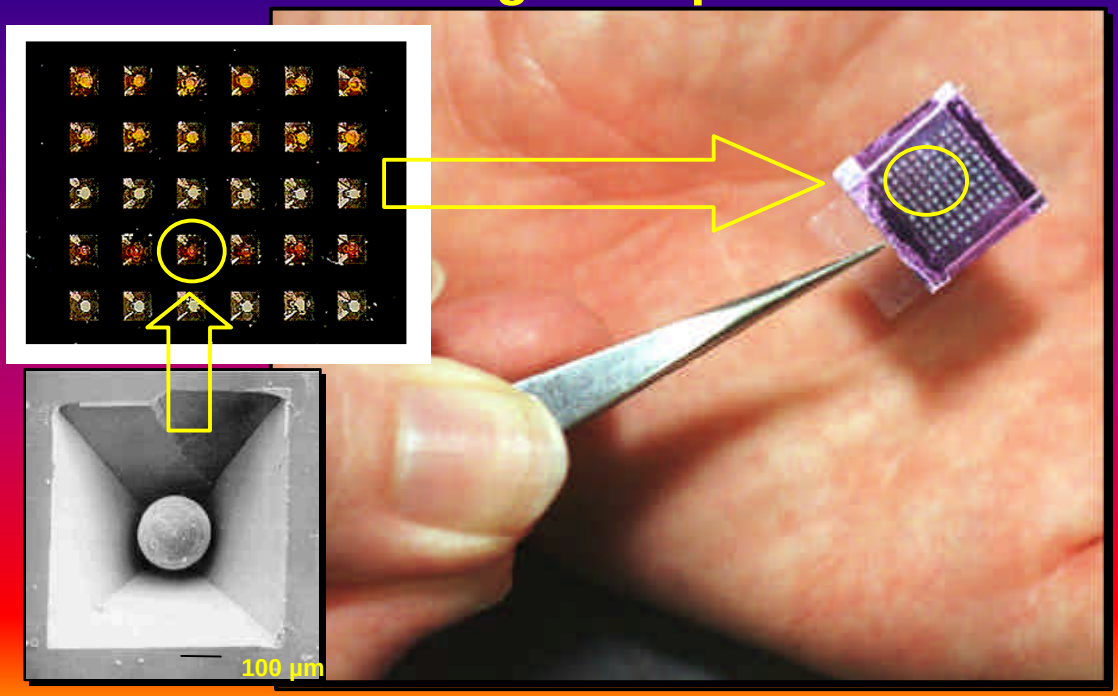
Bead sensors in micromachined storage wells





- use micromachining to form a microscopic “test-tube”
  - storage well for the bead “tastebuds”
- cover layer used to keep beads in place

Current generation of electronic tongue chip

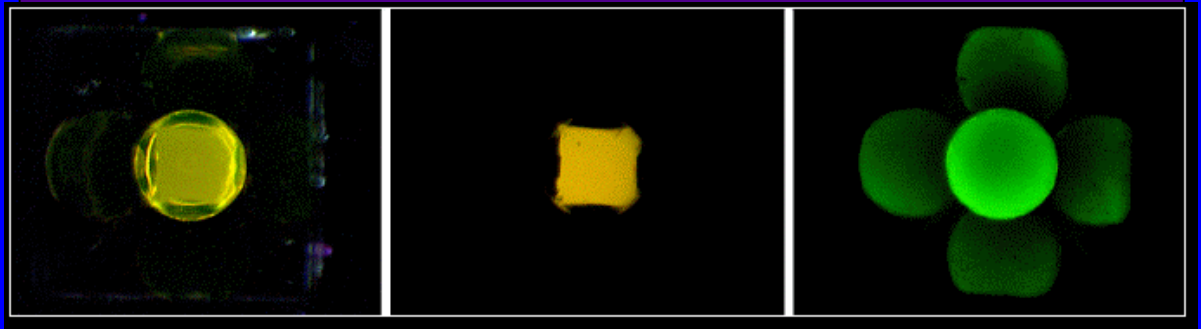


Pick-and-place loading of beads

- process and placement requirements similar to pcb assembly
  - rates of 10,000 parts placed per hour may be achieved using moderately priced assembly systems

manual pick and place of a bead

Illumination Conditions (5-carboxy fluorescein Bead)



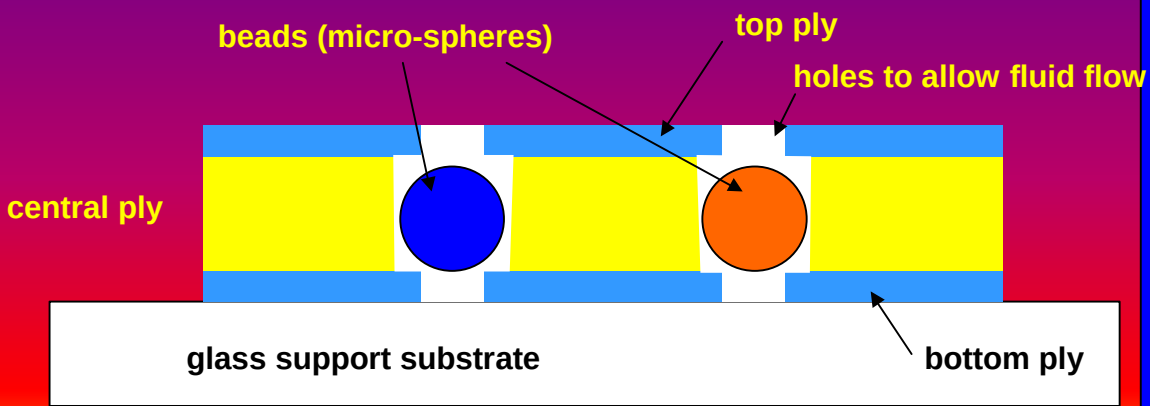
Reflected White Light: Top Illumination

Transmitted White Light: Bottom Illumination

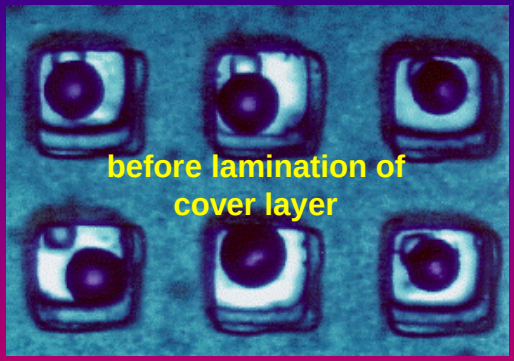
Epi Fluorescence: GFP Filter set

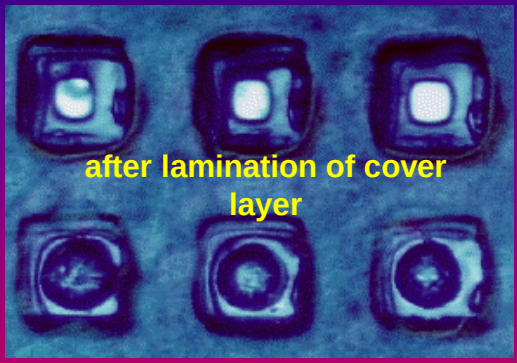
Other methods of array fabrication

- only common glass and polymer materials used
  - holes could be made many ways
    - drilled, embossed
    - photolithographically using photo-imagable polymers

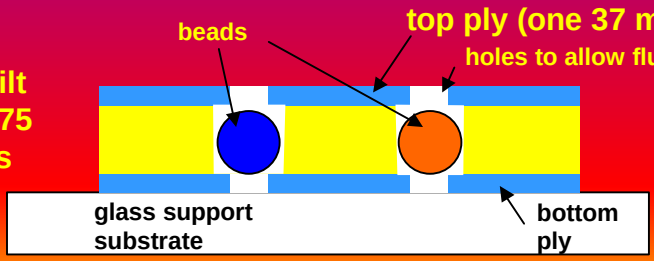


Initial demonstration of array using dry film resist



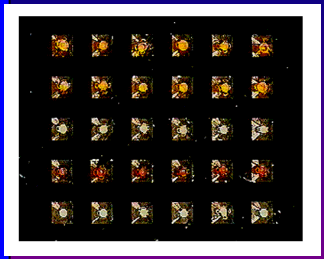


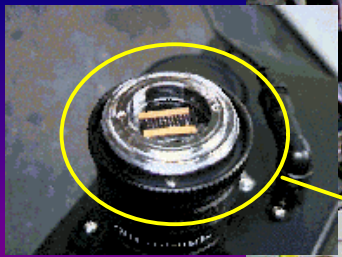
central ply built up from three 75 micron layers



Component integration

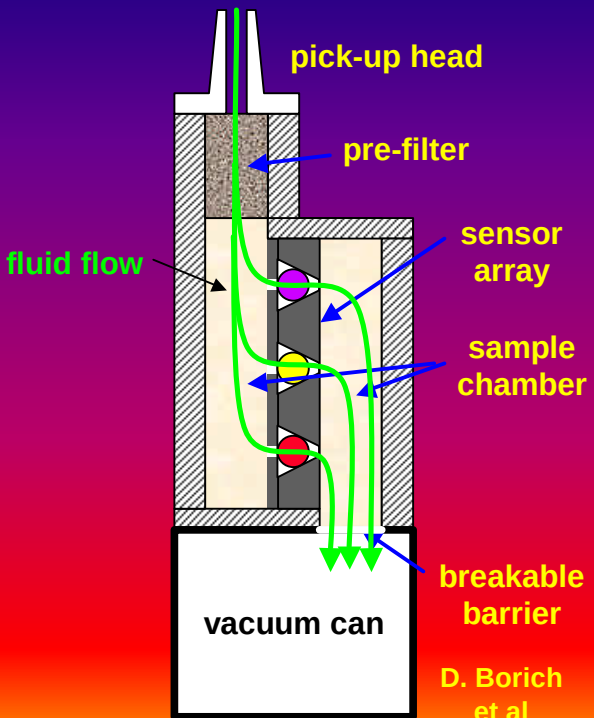
The University of Texas at Austin





Array package and sample introduction

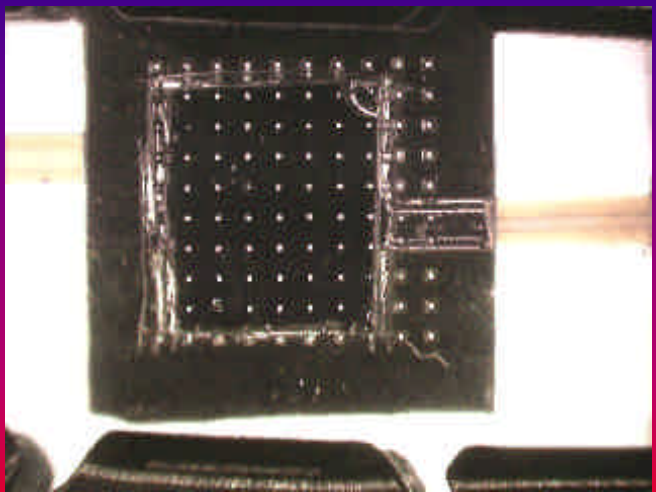
- sensor chip / fluid container / sampler as one unit
  - minimizes total volume of bio-haz waste
  - "pre-filter" between pick-up and sensor/sample chamber
    - removes particulates, whole blood cells, etc.
    - can be impregnated with analytes as necessary for assay
  - use vacuum "can" to pull sample into chamber
    - precise sample volume
    - if beads stored in buffer, simultaneously removes buffer



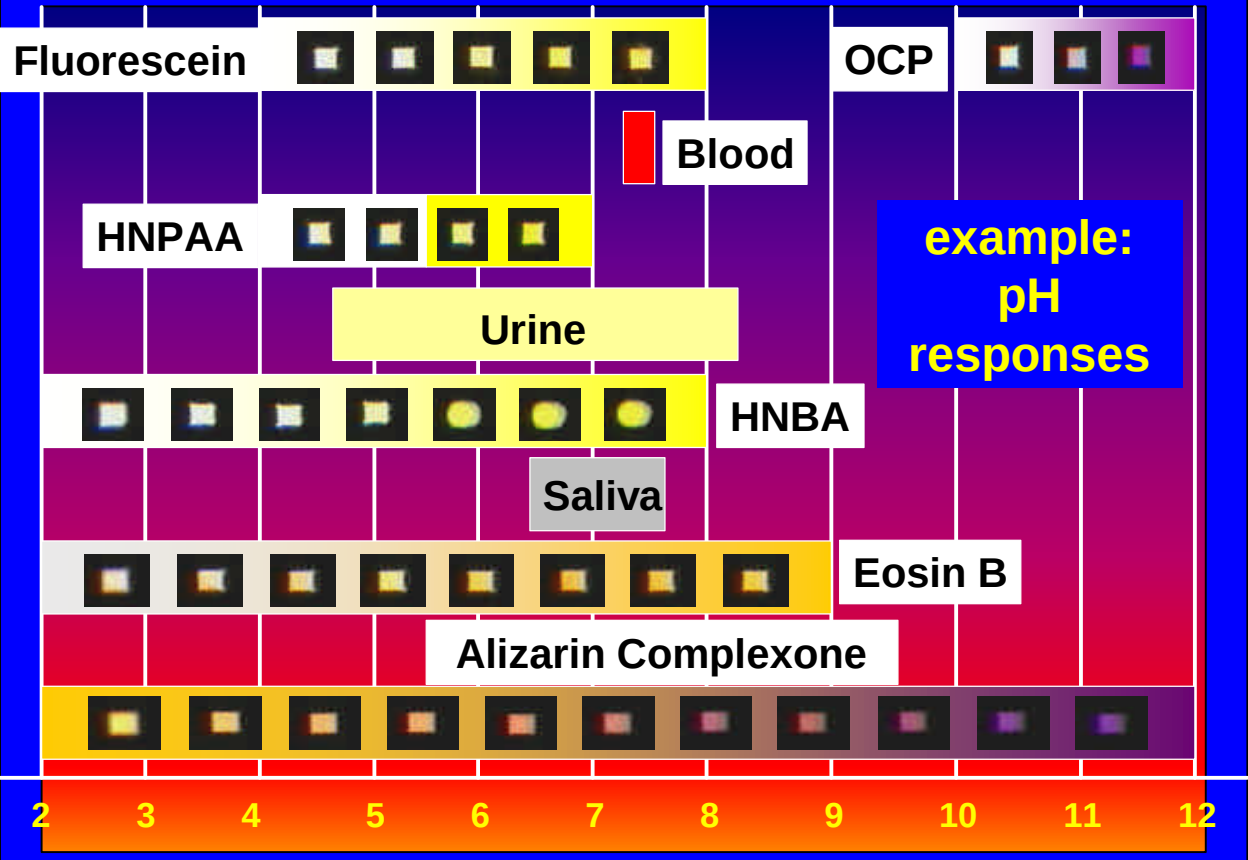
Fluid flow into a bead array

- forced (pumped) flow
- note disappearance of air bubbles in storage wells
  - flow through geometry essential for consistent bubble elimination

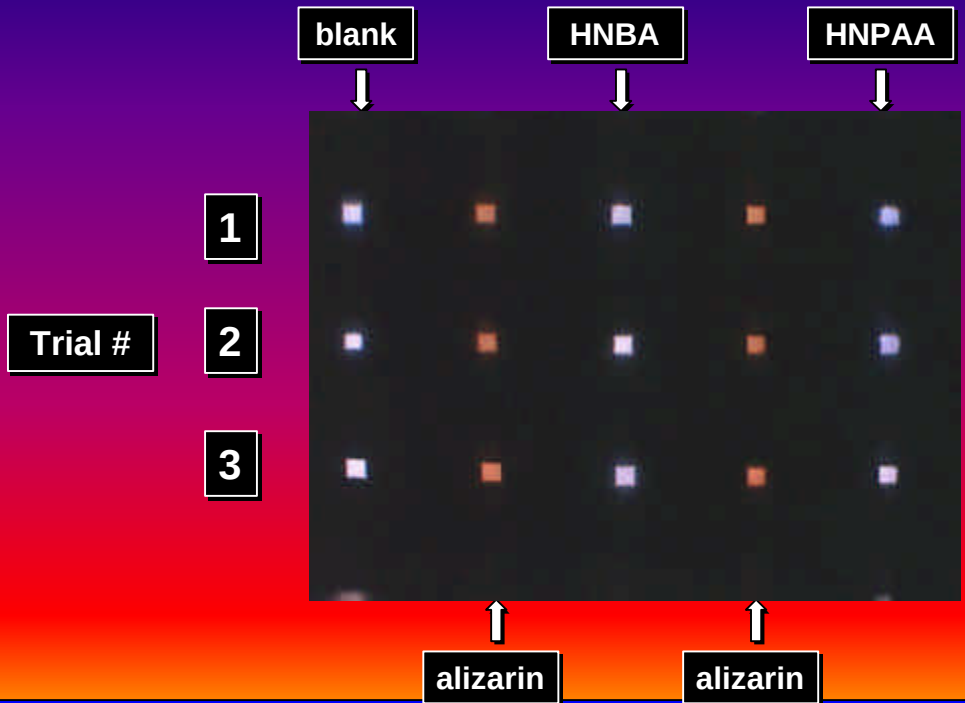
Fluid flow (pumped) into disposable plastic chip holder

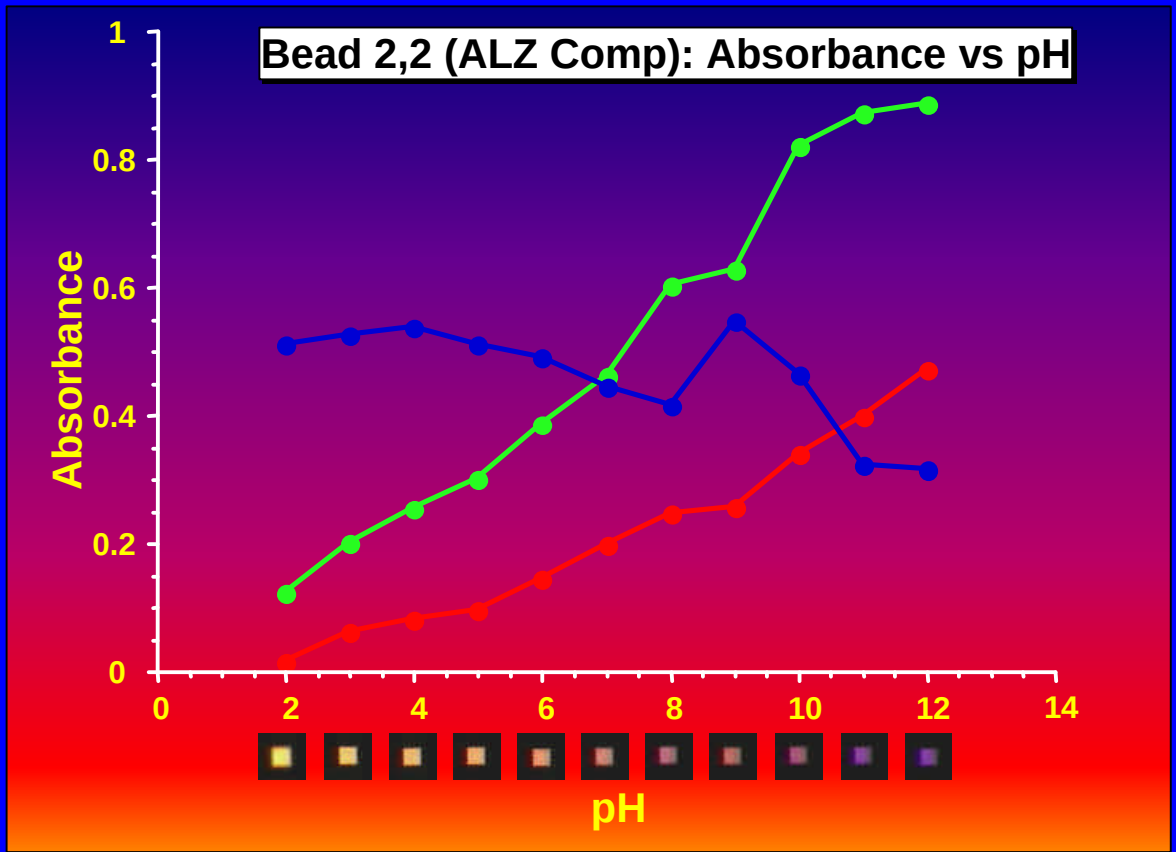


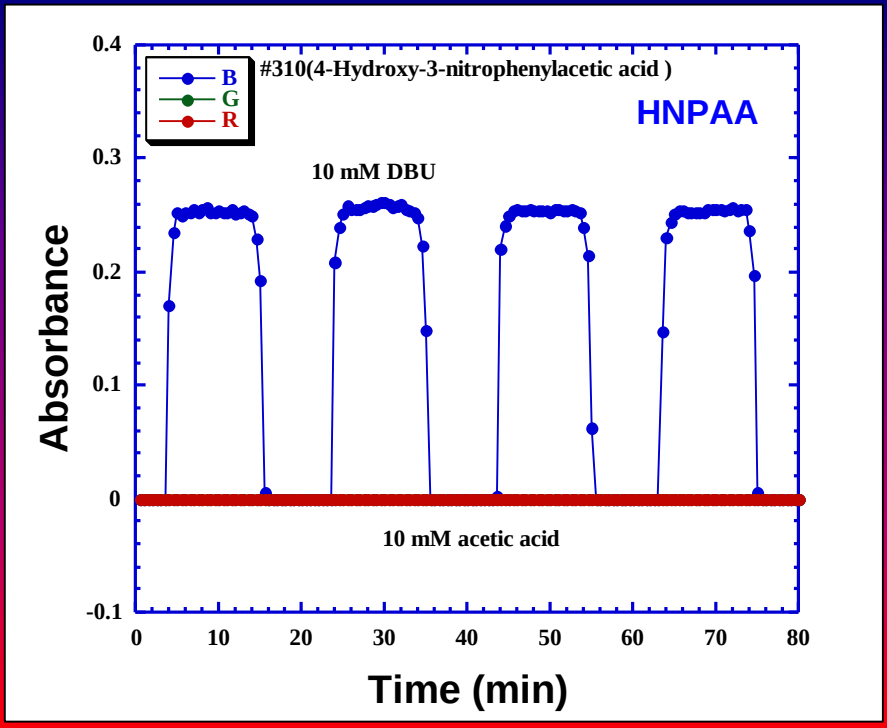
- macroscopic view


Fluorescein
OCP
Blood
HNPAA
example: pH responses
Urine
HNBA
Saliva
Eosin B
Alizarin Complexone
2 3 4 5 6 7 8 9 10 11 12

Movie Showing the Cycling of Four pH Indicators Between pH=2 and pH=12



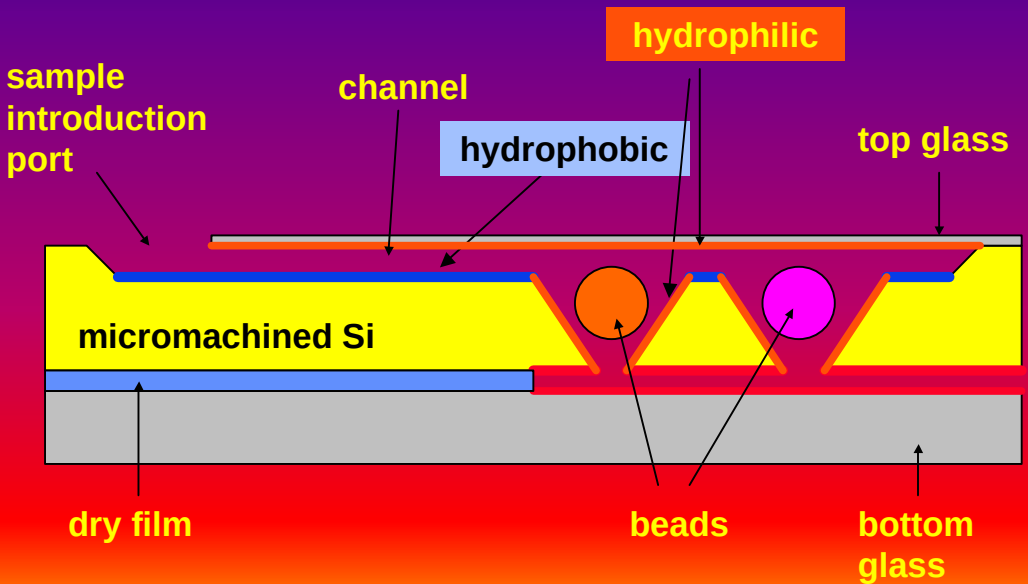

Bead 2,2 (ALZ Comp): Absorbance vs pH
Absorbance
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
12
14
pH



Flow rate: 1 mL/min;
Image captures one point at every 30 sec.

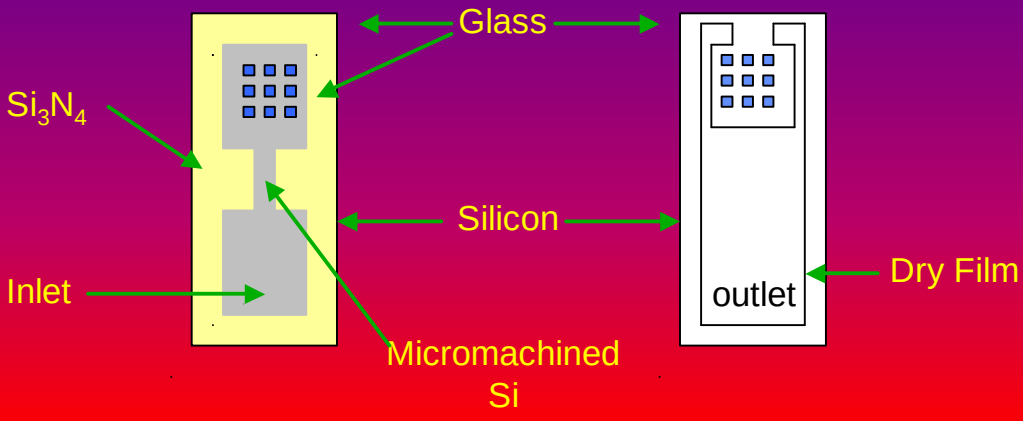
Passive fluid introduction

- Cross sectional view

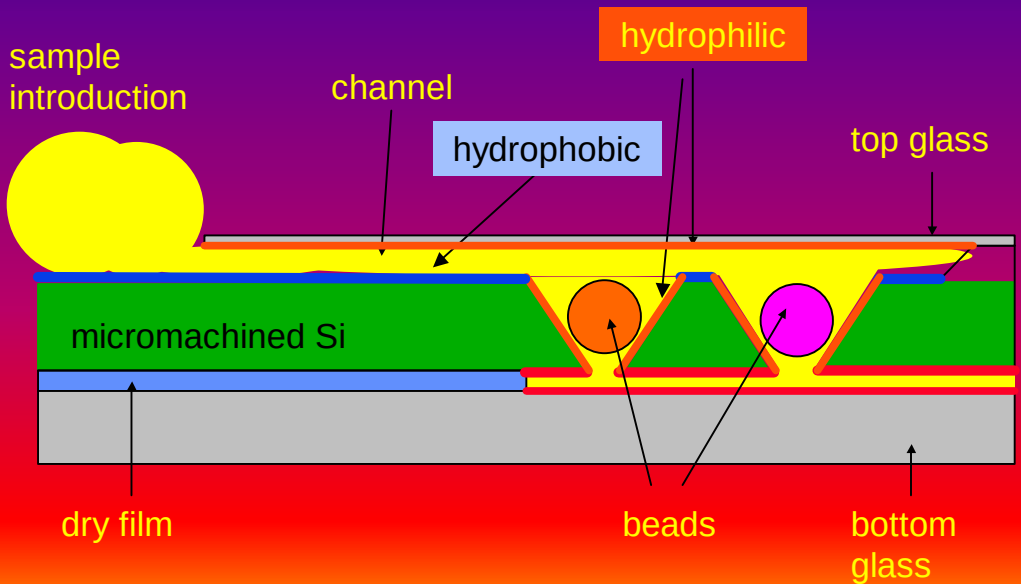


Passive design

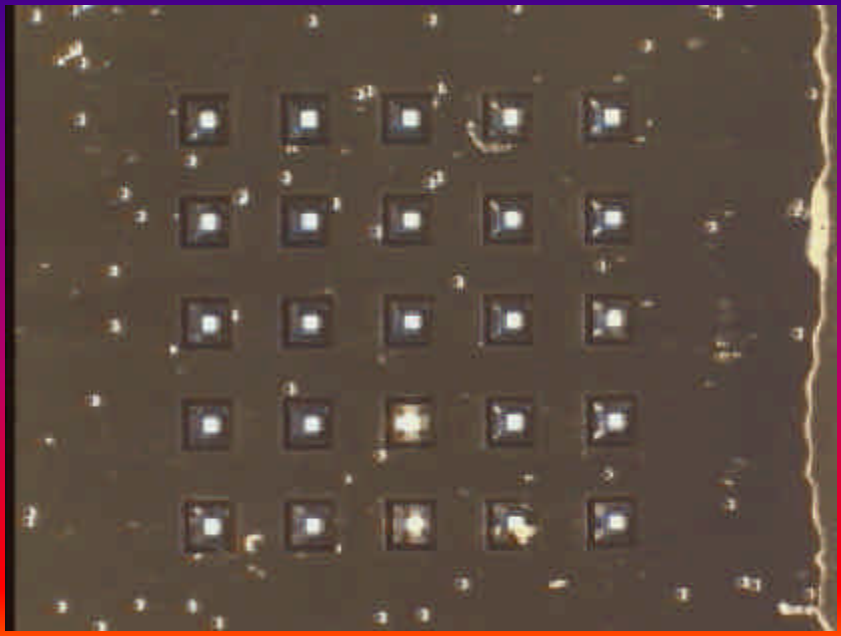
- Top and bottom view



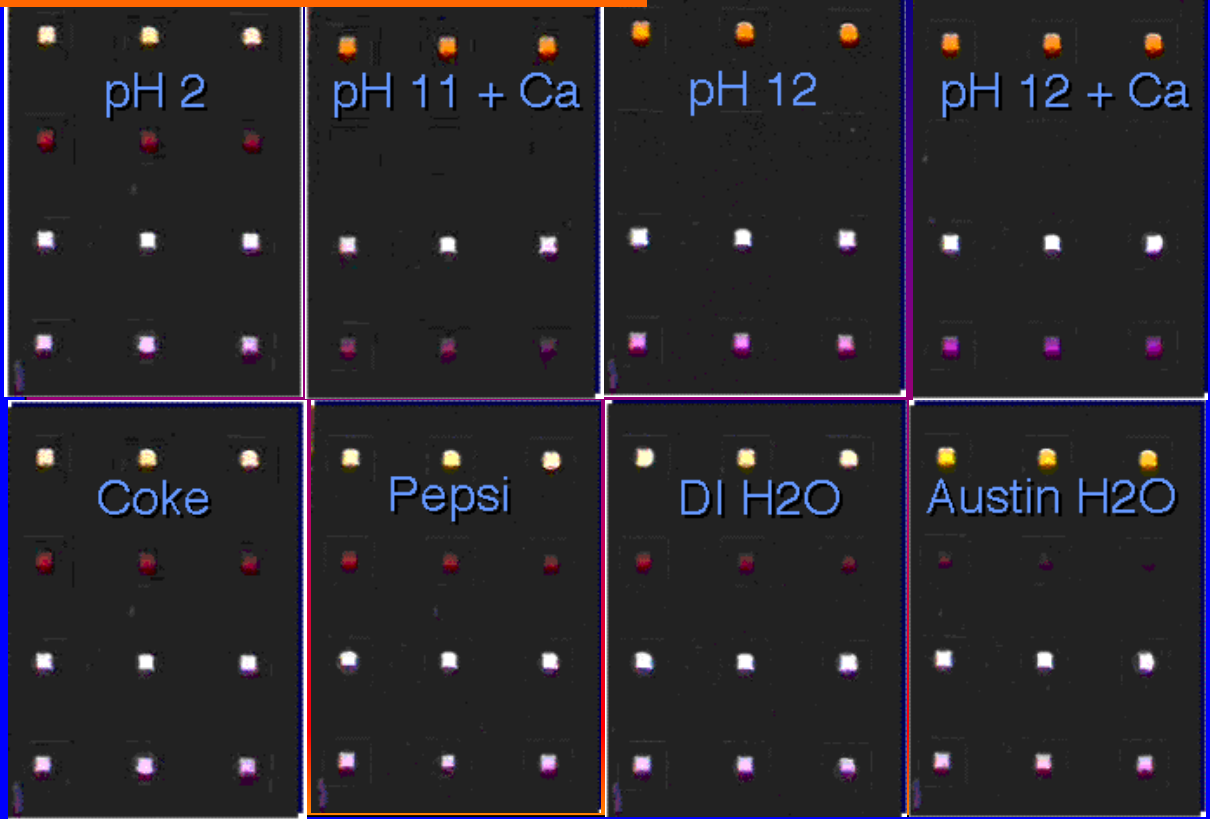
Function


sample introduction
channel
hydrophilic
hydrophobic
top glass
micromachined Si
dry film
beads
bottom glass

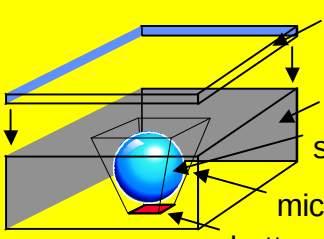
Surface tension-driven fluid introduction



Sample responses



Micromachines and chemistry: towards an "electronic tongue"



- wide range of potential applications
  - food, water monitoring
  - low cost, "real-time" medical testing
- initial demonstration of
  - small ion detection
  - sugars, enzyme based assays
  - antibody based assays
  - DNA recognition