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Bioanalytical Applications of Nanobiotechnology

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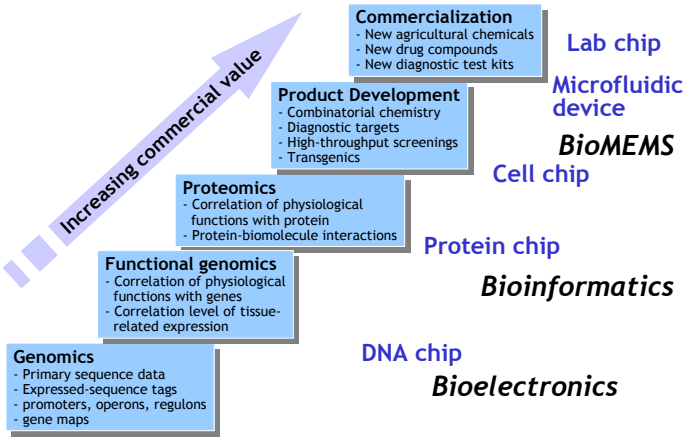
Outlines

- ✓ Introduction
- ✓ Applications Area: Technology Map & the Scope
- ✓ Trends in BioMEMS: Microfluidic Nanoscale Analysis
- ✓ Trends in Nanobiotechnology: Analytical Issues
- ✓ Future Perspectives

Introduction

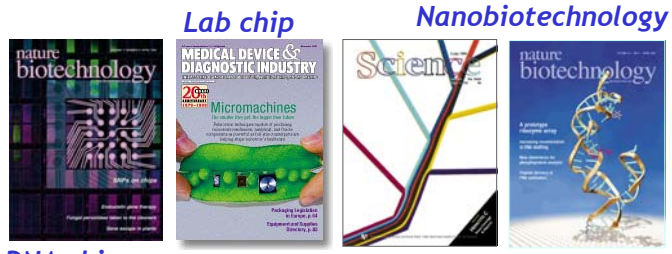
New Paradigm for Bio-Related Industry



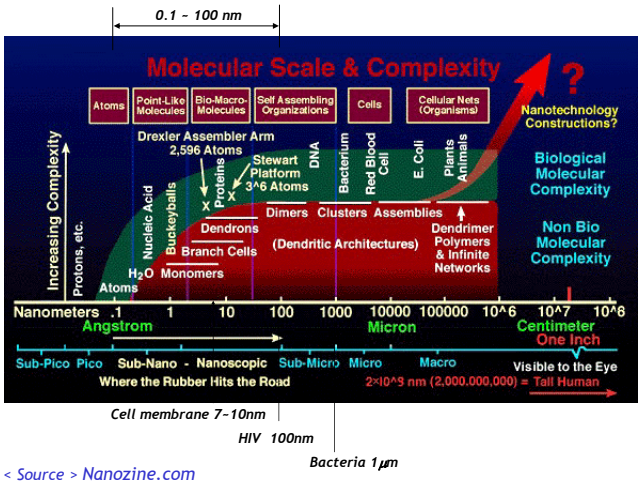
BioMEMS and Microfluidics

- *Implementation of MEMS (Micro Electro Mechanical Systems) to Bio-related areas*
- *Fluid delivery system at microliter scale*
- *Needs*
  - Lower chip cost *(Glass or plastic chips)*
  - Reduction of expensive reagents & test compound used
  - Integration of multiple functions onto a single chip *(Micro total analysis system (μ-TAS), Lab-on-a-chip)*
  - Point-of-care diagnostics *(Easy sample preparation)*
  - High throughput *(Microfluidic HTS disposables)*

Multidisciplinary Research



Nanobiotechnology Overview

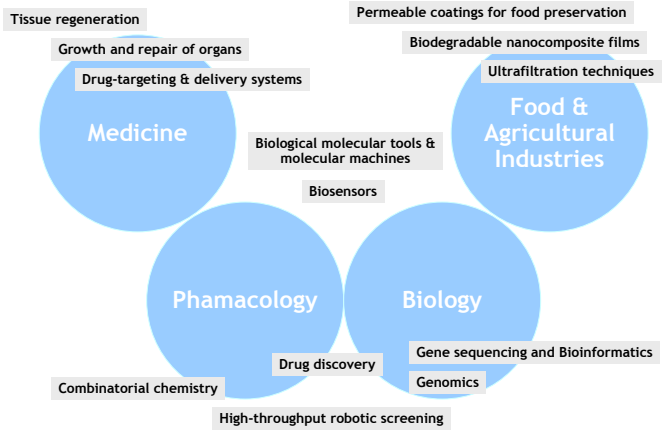


< Source > Nanozine.com

Why Nanobiotechnology?

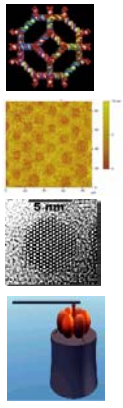
- Nature applies nanotechnology daily to grow the multifunctional cells and tissues of plants and animals from a single biological cell
- There exist biomolecular analogues of conventional functional devices
- Biology can teach the physical world of electronics, computing, materials science and manufacturing
- Nanomanufacturing of biomimetic devices is moving ahead strongly

The Scope of Nanobiotechnology



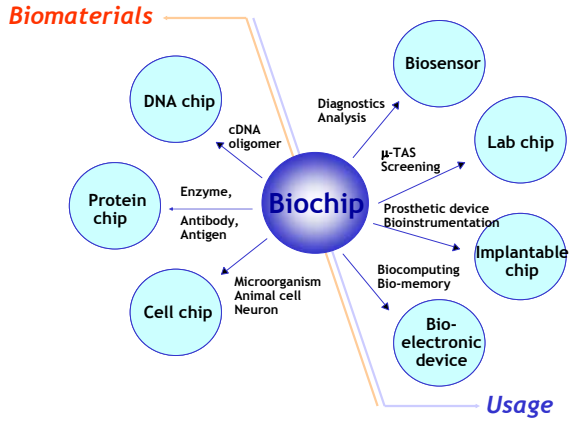
Nanobiotechnology Approaches

- Molecular self-assembly on surfaces
- Spatial micropositioning techniques
- Scanning probe microscopy
- Biological templates for microconstruction
- Bioaggregation, biomineralization and biocomposites
- Biological motors and nanomachines
- Nanofactories
- Biocomputation

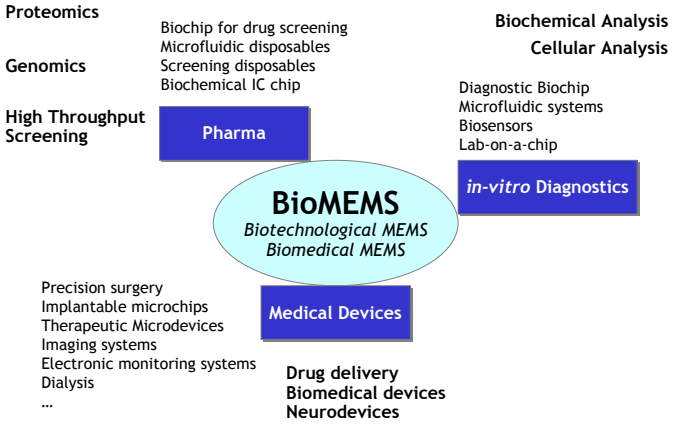


Applications Area:
Technology Map & the Scope

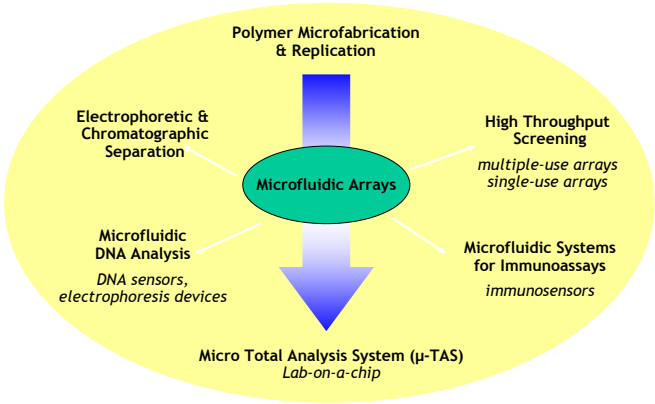
Classification of Biochip



The Scope of BioMEMS



Microfluidic Analytical Applications



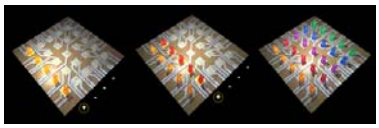
Trends in BioMEMS:
Microfluidic Nanoscale Analysis

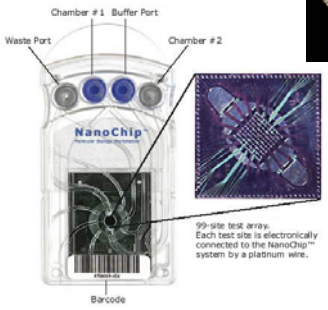
Nanoscale Chemical Analysis

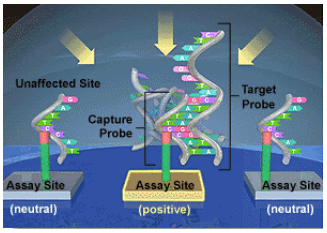
- Liquid-based chemical microsystems
- Done in sub-microliter volumes of liquid
- The use of microtechnologies (BioMEMS)
- Microfluidic devices
- Miniaturized total chemical analysis system (μ-TAS)
- Lab-on-a-Chip.com Miniaturized technology for lab applications

An Active Microelectronic Device for Multiplex DNA Analysis

NanoChip™

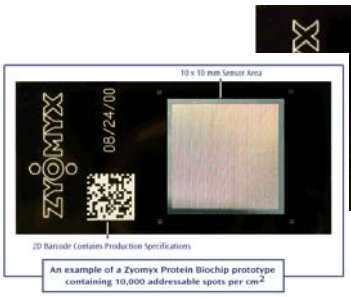


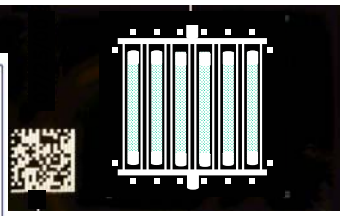




Nanogen Inc.(San Diego)

Zyomyx: Proteomics Biochip



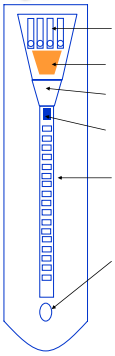


Zyomyx Multi-Cell Chip

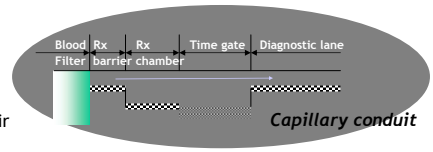
→ Sub-picomolar sensitivity achievable

www.Zyomyx.com

Microfluidics Protein Chip



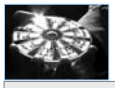
- Sample addition zone by capillary conduit
- Blood filter or lysis chamber
- Reaction chamber (5 min incubation)
- Time gate
- Protein array (6~ 100 zones)
- Waste reservoir



- *Sample flow in microcapillaries*
- *Detection: Fluorescence energy transfer in particles Laser diode 670nm -> silicon photodiode 760nm*

Biosite Diagnostics

Microfluidic Strategies



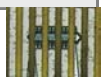
Fluid in motion strategy

Centrifugal
Tecan, Gyros

Capillary forces
Steag MicroParts
Biosite Diagnostics

External actuation
bioMerieux, Micronics

Magnetism/ Acoustic
Aviva BioSciences

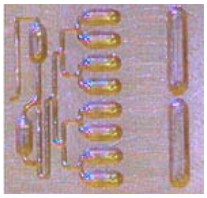


Electrophoresis/ Capillarity/ Osmosis
Caliper Technologies, Nanogen, Philips Research Center Agilent Technologies

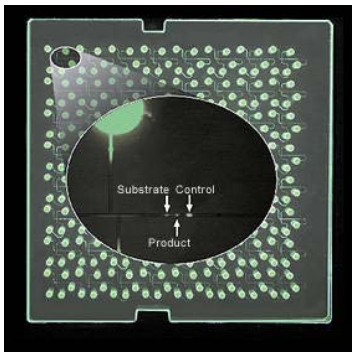
Piezoelectric
IMM, Tronic's Microsystem, IEMN

Microfluidic-based Lab-on-a-chip

DiagnoSwiss, Switzerland



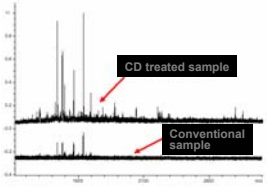
BioMicro Systems



ACLARA BioSciences

CD Laboratory

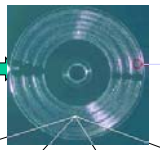
Mass spectrum of BSA showing higher peak intensity and a greater number of peptides detected after preparation on the CD microlaboratory



Co-crystallized peptides And matrix on the MALDI target in the CD

Single microstructure

Protein digests to CD microlaboratory



Digests are applied and concentrated onto reverse phase chromatographic columns within the CD

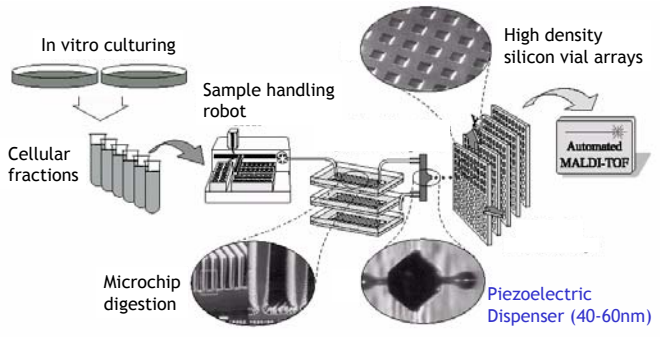
Peptides are desalted and purified during elution with organic solvent containing the MALDI matrix

Peptides and matrix co-crystallize within the MALDI target areas (d=300-500 μm) on the CD

The CD is transferred directly to a MALDI-ToF instrument for analysis

Gyros AB, Sweden

Microfabricated Toolbox Concept

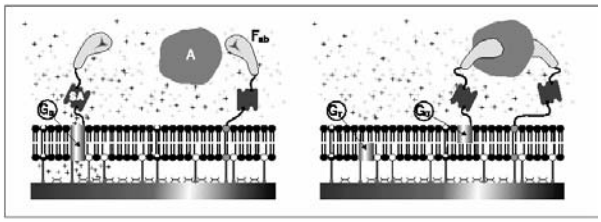


AstraZeneca, Sweden

Trends in Nanobiotechnology:
Analytical Issues

Ion-channel Switch Biosensor

Two-site sandwich assay → Membrane conductivity decreased

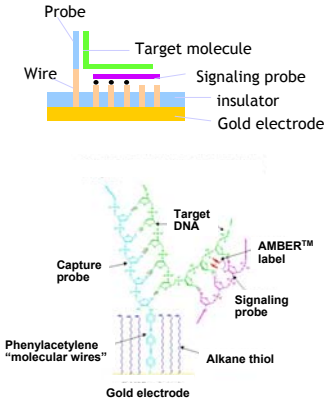


Immobilized ion channels (G_T), Conducting dimers(G_D)
Synthetic archaebacterial membrane-spanning lipids (MSL)
Half-membrane-spanning tethered lipids(DLP)
Polar spacer molecules (MAAD)
Mobile half-membrane-spanning lipids (DPEPC/GDPE)
Mobile ion channels (G_α), Streptavidin (SA), Biotinylated-antibody fragments(Fab)
Analyte (A)
Membrane spanning lipids(MSL_α)

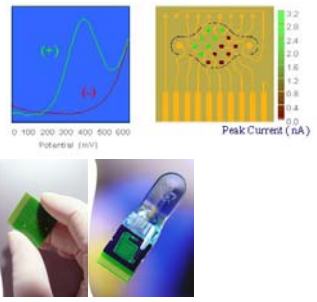
Nature 387: 580-583 (1997)

www.ambri.com.au

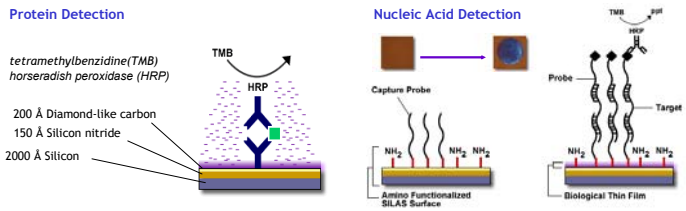
eSensor™ for DNA Diagnostics



www.microsensor.com



SILAS™, Silicon Assay Surface Technology



Protein and nucleic acid detection in a sensitive, rapid format

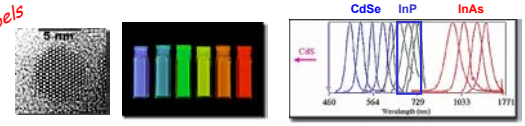
- Rapid detection: 5-30 minutes total assay time
- Simple assay tests: capture, amplify and read result
- Easy to prepare: simple coating protocols
- High Sensitivity: picogram/mL detection levels
- Permanent results: convenient documentation
- Flexible applications: multiple capture and target molecule combinations

www.biostar.com

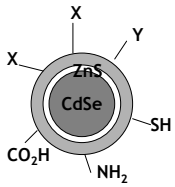
Laboratory-On-A-Bead (Qbeads™) Technology

Qdot™ nanocrystals are water-soluble, highly fluorescent, molecular-sized semiconductor crystals such as cadmium selenide

As fluorescent labels To encode beads



Size- and material-dependent optical properties



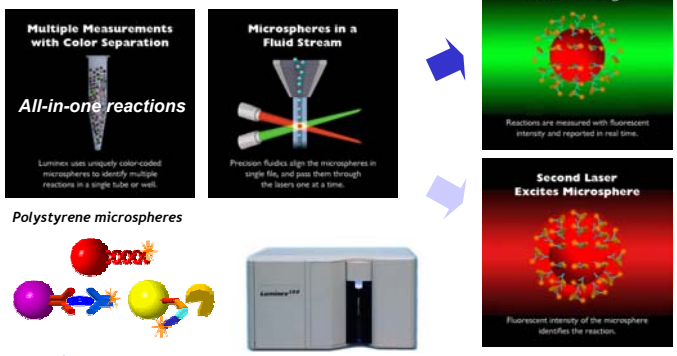
www.qdots.com

Advantages

- The ability to multiplex (biological barcoding)
- Simple excitation (lasers are not required)
- The availability of red/infrared colors (whole blood assays)
- Simultaneous multicolor, multi-component assays
- Higher sensitivity (photo-stability and large Stokes shift)
- Simpler instrumentation

High Throughput Applications with Suspension Arrays

LabMAP: Laboratory Multiple Analyte Profiling

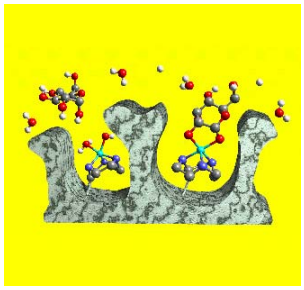


Polystyrene microspheres

www.luminexcorp.com

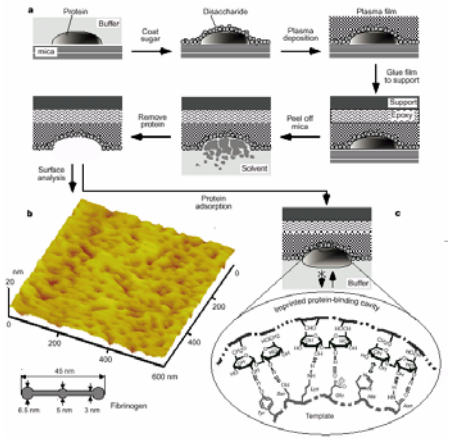
Molecular Imprinting Technology

Design and characterization of metal-complexing materials for high resolution separations and chemical sensing
A way of making artificial "locks" for "molecular keys"



- ✓ Recognition studies
- ✓ Separations, isolations
  - Chiral separations
  - Substrate-selective separations
- ✓ Antibody/receptor binding mimics
  - Competitive ligand binding assays
  - Diagnostic applications
- ✓ Enzyme mimics/Catalysis
- ✓ Biosensor-like devices
- ✓ Site-mediated synthesis

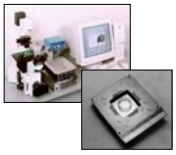
Nanostructured Surfaces for Protein Recognition



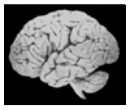
Nature 398: 593-597 (1999)

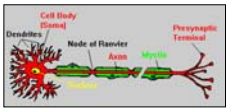
Neuron Chip using NeuroMEMS

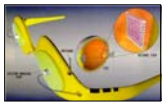
Applications & Impact

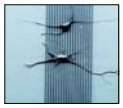


- ✓ Multi-channel Extracellular Recording System
- ✓ Drug Screener (Handheld Drug Testers)
- ✓ Toxin Tester (Microchemical Processor)
- ✓ Tools for Cognitive Neuroscience (Electrophysiology Tools, Brain Research)
- ✓ In vitro Study on Neurotransmission
- ✓ Digital Spine (?)
- ✓ Telecommunications Development in the Future Neural Network









Future Perspectives

Future Applications & Impact

- Cost-effective tools enabling more efficient genomics, proteomics, drug discovery research
  - ✓ *Improvements in health care, therapeutics, and diagnostics*
- Miniaturization in high throughput screening
  - ✓ *Miniaturized total chemical analysis system (μ-TAS), Lab-on-a-chip*
- *In vitro* diagnostics disposable for genetic testing or protein detection
  - ✓ *Development of novel point-of-care diagnostics and home tests*
- Synergistic technologies for BT, IT, and NT
  - ✓ *Biotechnology as a route to nanotechnology*