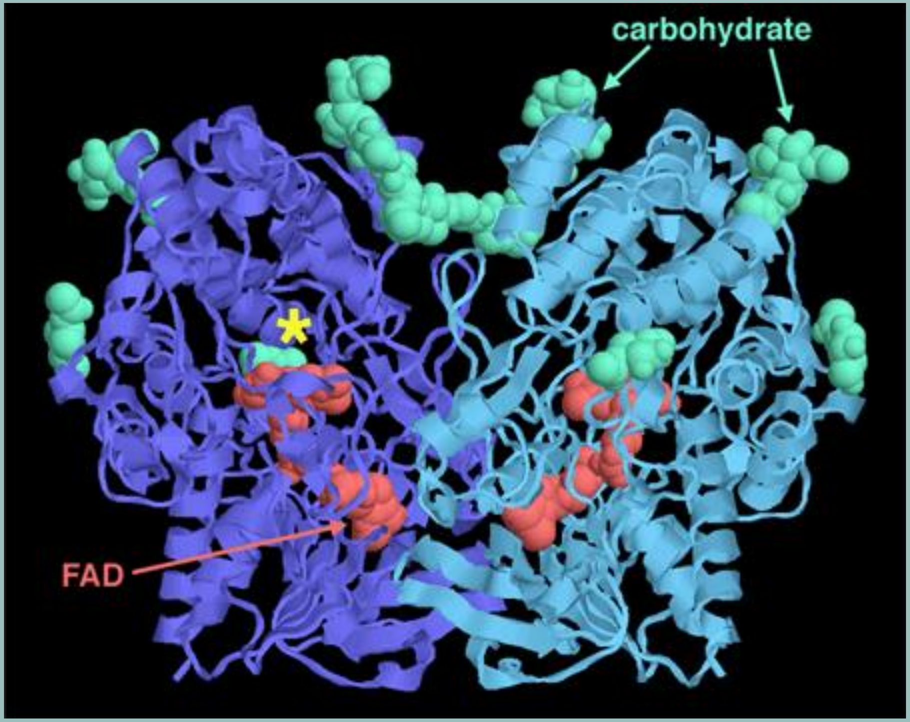

ELECTROCHEMICAL BIOMARKER SENSORS

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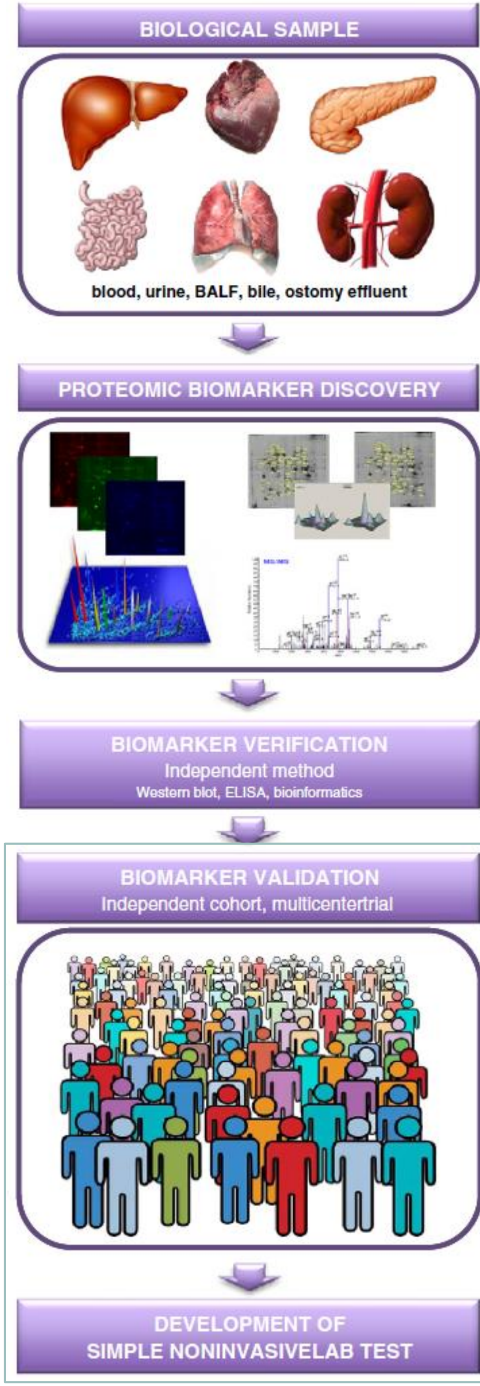
UCLA

BIO-MARKER DEFINITION & DEVELOPMENT

A biomarker is a measureable substance that uniquely indicates some phenomenon relating to health, disease, infection, bodily information, or environmental exposure.

Biomarker Development:

- Analyze biological sample
- Biomarker discovery
- Biomarker verification and validation
- Development of simple lab test



ELECTROCHEMICAL BIO-MARKER SENSORS

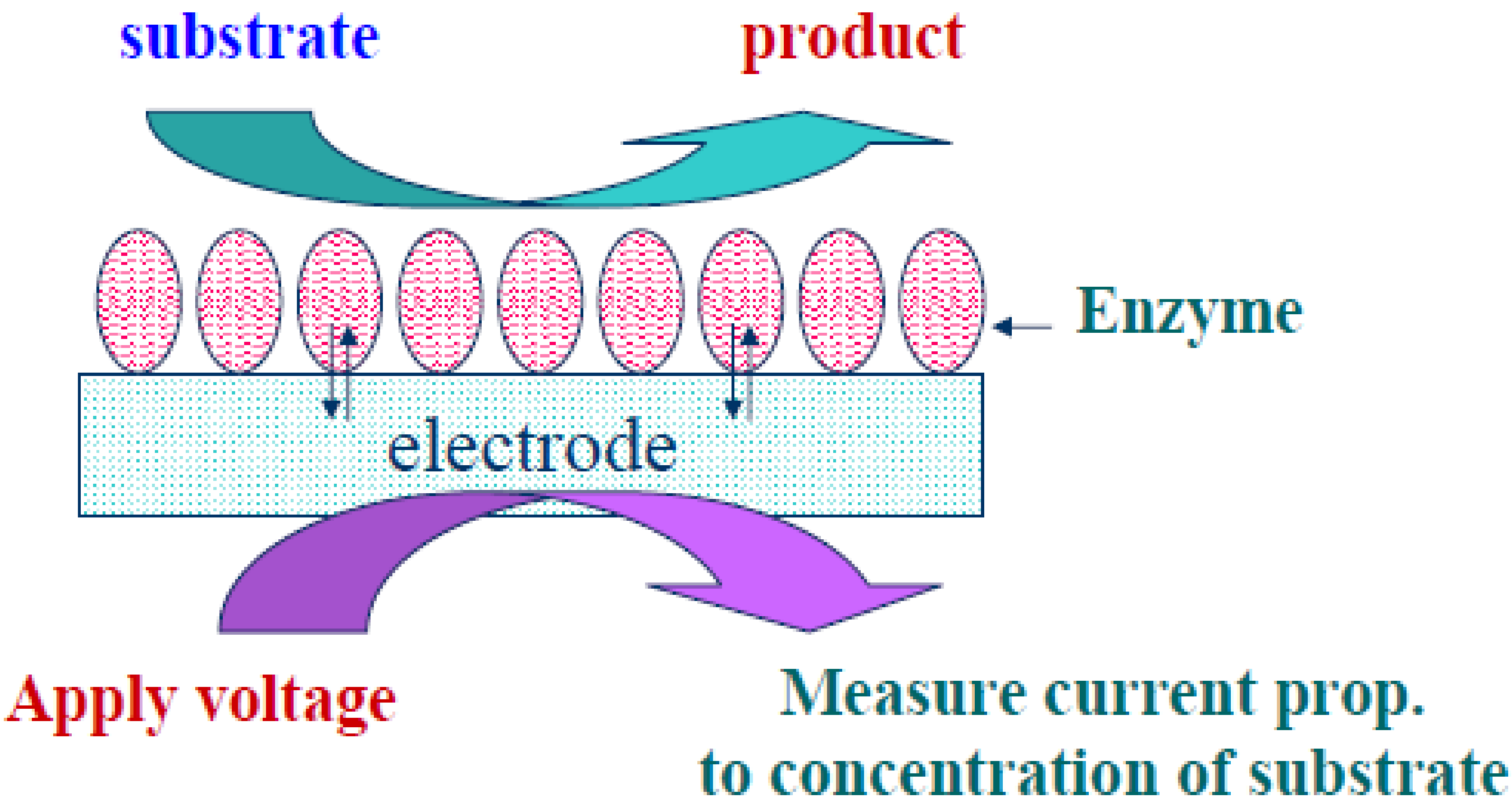
Conventional sensing such as a blood test is a multistep approach that requires the invasive drawing of a patient’s blood before it is analyzed.

Electrochemical bio-marker sensors represent an integrated non-invasive approach to sensing with advantages in its low cost, high sensitivity, and compatibility with microelectronics.

Compared to traditional bench processes, biosensors can be both faster and smaller while detecting a wide range of phenomena.

Advancements in the biosensor materials and portability are topics of active research.

ELECTROCHEMICAL BIOMARKER SENSOR (OVERVIEW)



TYPE OF BIOMARKER SENSORS

IUPAC definition of a biosensor is a chemical sensor device “that transforms chemical information, ranging from concentrations of specific sample component to total composition analysis, into analytically useful signal”

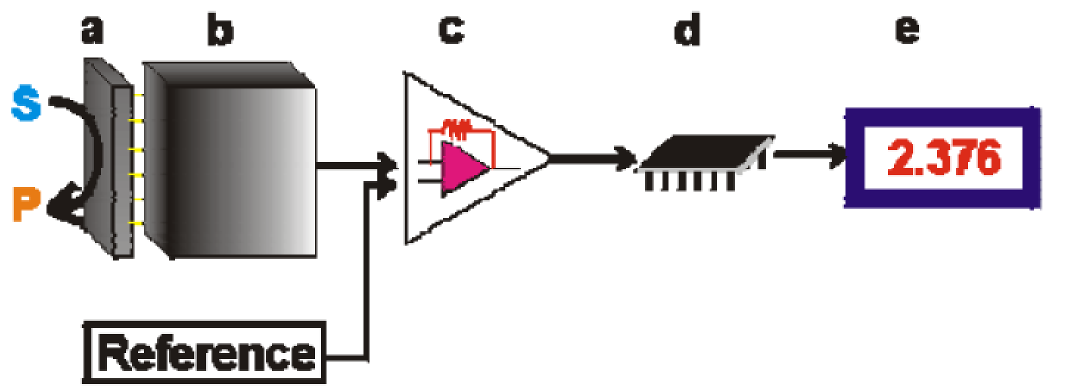
A – converts substrate to product

B – convert to electrical signal

C – signal amplified

D – Processed

E – Displayed



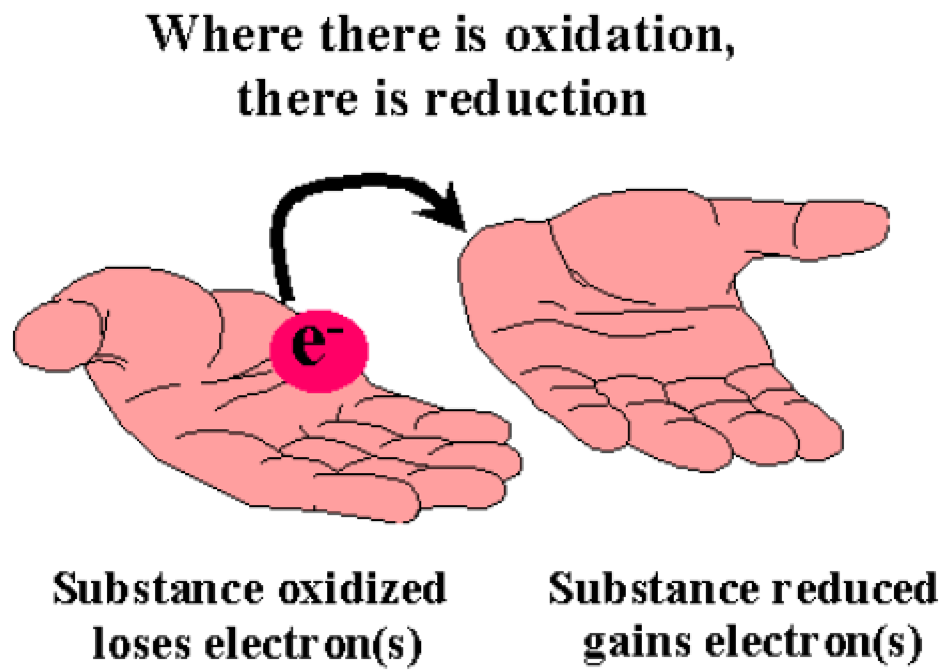
"ELECTROCHEMICAL" SENSORS

"Electrochemical" sensors use either current, electric potential, resistance, or impedance to help regulate changes and determine abnormal changes.

Electrochemistry (EC) –

The term electrochemical comes from EC defined as the study of charge transfer phenomena.

Electrochemistry includes wide range of different chemical and physical phenomena.



SENSORS DETECTION MODE AND TYPES

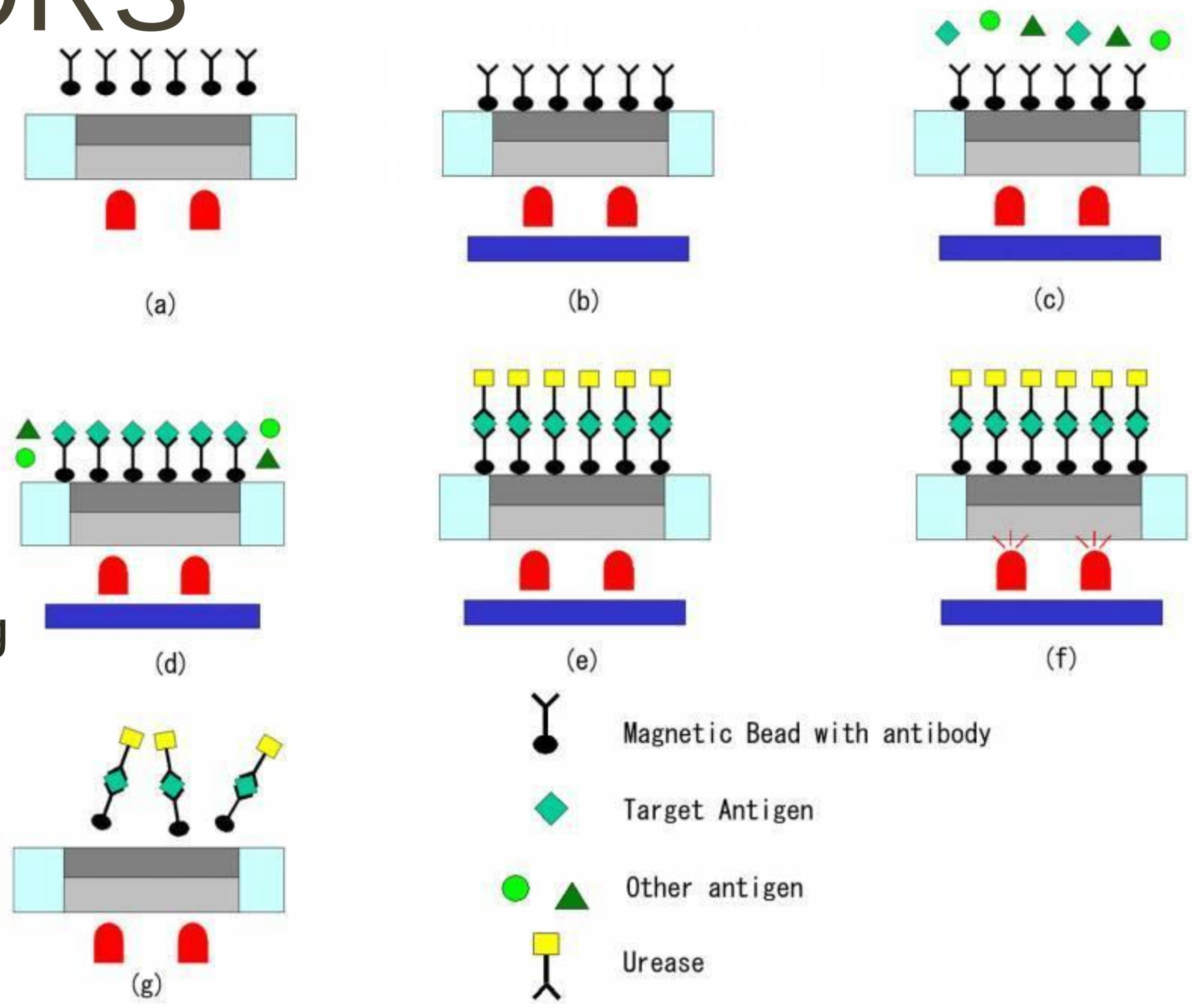
There are various types of electrochemical sensors:

- Potentiometric
- Amperometric
- Voltammetric
- Conductimetric
- Polarographic
- Impedimetric
- Capacitive
- Piezoelectric

The type of electrochemical sensors cover in this research include only a few of the list above.

POTENTIOMETRIC SENSORS

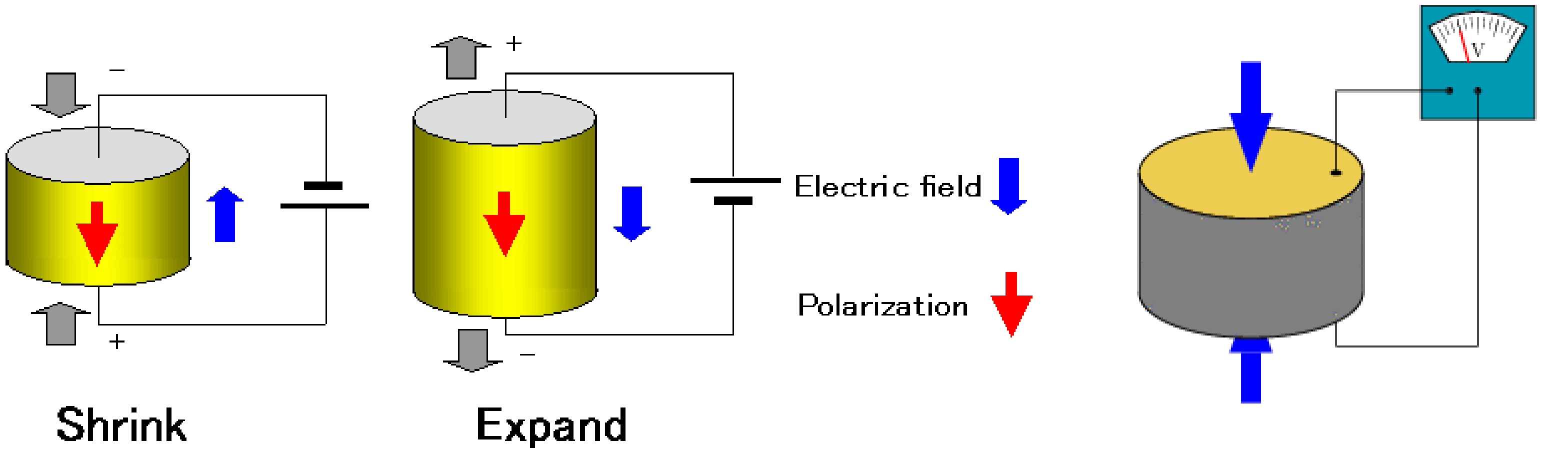
Potentiometric Sensors: passively measures the electric potential between two electrodes without affection the subject being measure.



LAPS(Light Addressable Potentiometric Sensor)

PIEZOELECTRIC SENSORS

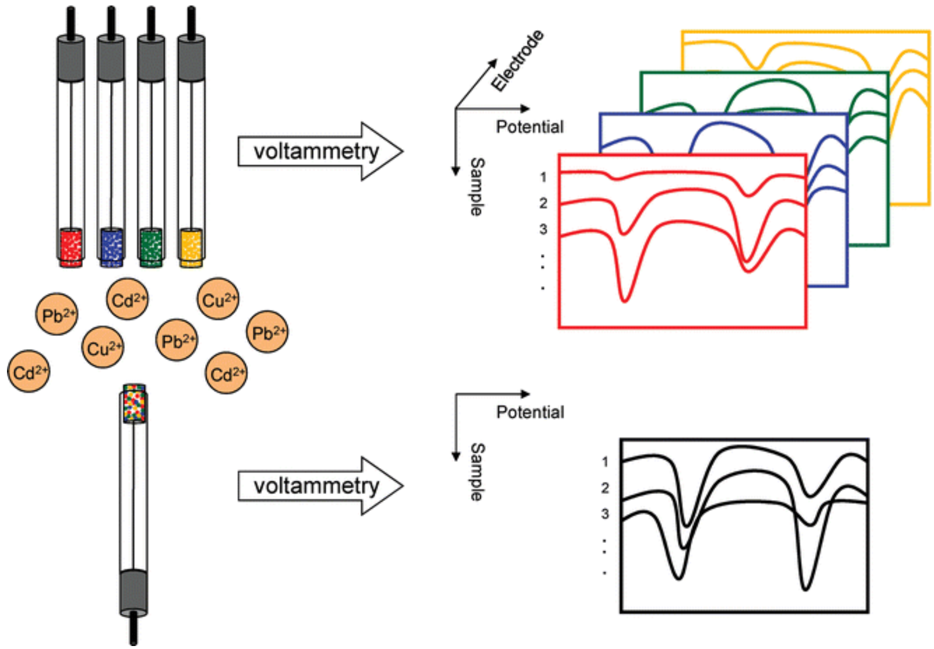
This type of sensors measures the change in pressure, acceleration, strain, and force by converting the physical signal information into an electrical charge.



VOLTAMMETRIC SENSORS

These sensors can be used in the analysis of various organic and inorganic analyte.

Voltammetric sensors function by measuring the current as the potential is varied.



GOLD NANO-BIOSENSOR TO DETECT GENOTOXINS IN WATER SAMPLES

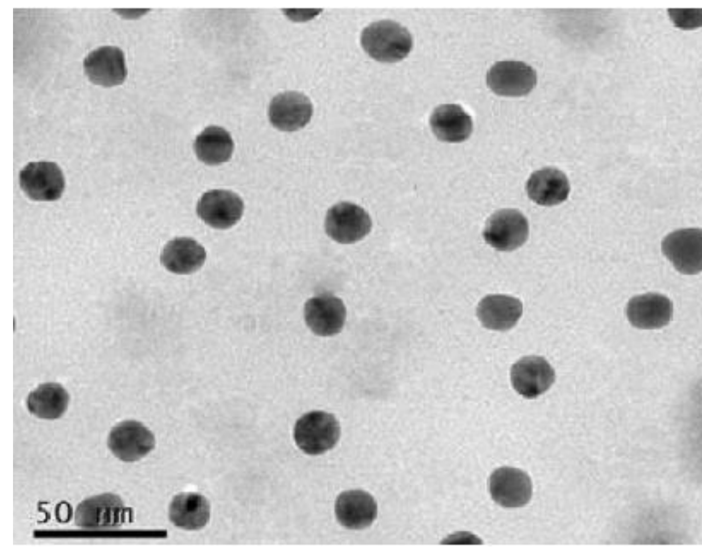
Genotoxicity describes the chemical agents that could damage the genetic information within a cell causing cell mutations and other defects.

Traditional Methods:

- Chromatography & Spectroscopy
- Bioassay

Gold Nano-Biosensor Methods:

- Build-in detection
- DNA for Bioassay (quicker)



TEM image of gold (Au) nanoparticles

GOLD NANO-BIOSENSOR (CONT')

Benefit these gold nanoparticle electrochemical sensors bring over classical methods comes from the ability to accumulate genotoxicity information with small amount of sample and uses biological interaction.

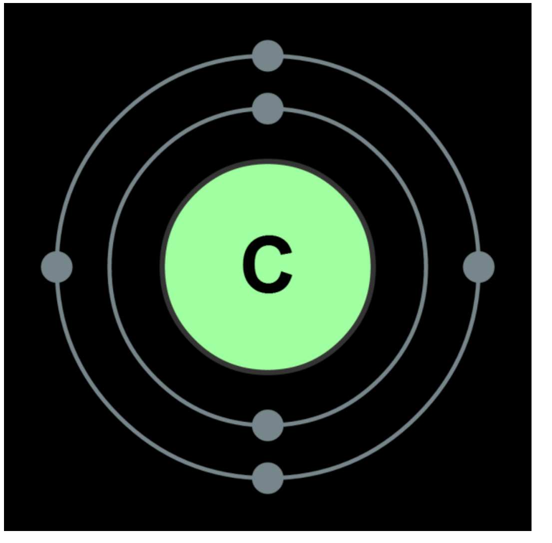
This genotoxicity sensor is a type of voltammetric sensor.

Electrochemical DNA nano-biosensor for quicker detection of genotoxic compounds in water pollution.

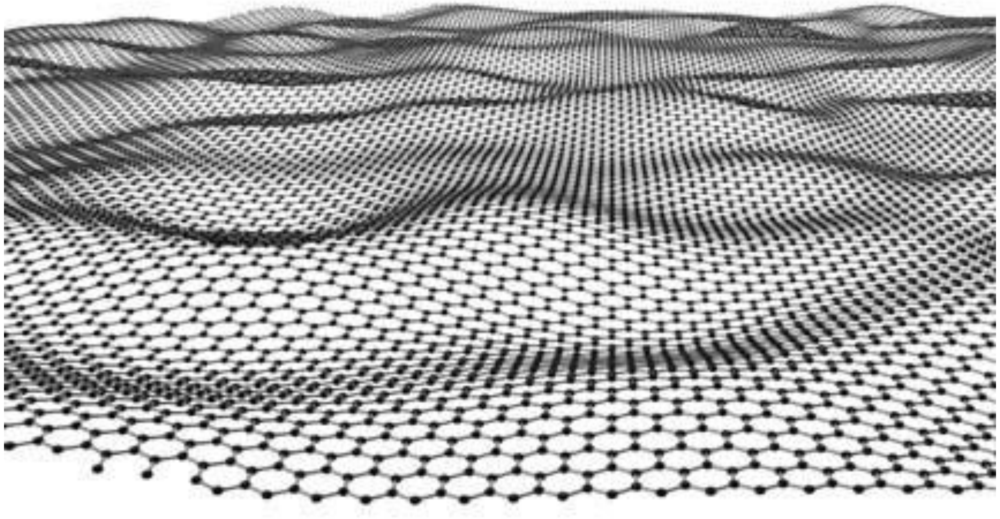
EMERGENCE OF CARBON NANOMATERIALS

Favorable characteristics as biosensor transducer elements:

1. High electrical conductivity (higher than metals)
2. High mechanical strength (proportionally higher than steel)
3. Ability to form unique geometrical structures (1D, 2D, or 3D)
4. Good biocompatibility



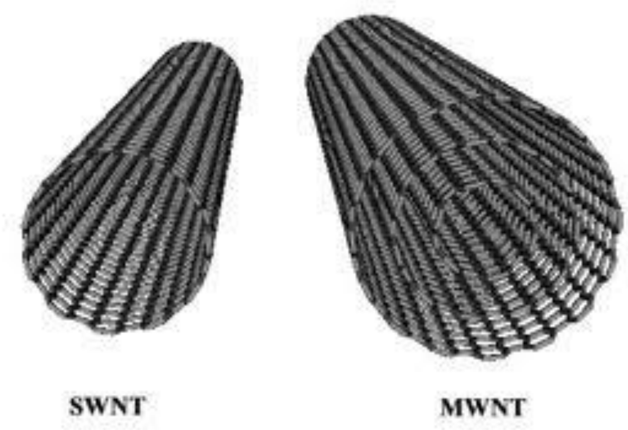
GRAPHENE



Definition: Graphene sheets are monolayers of carbon atoms

1. Large surface areas
2. Considered 2-D carbon structures
3. Originally created by delamination of bulk graphite

CARBON NANOTUBES



Definition:

As the name suggests, carbon nanotubes are nothing more than rolled up sheets of carbon into tubes

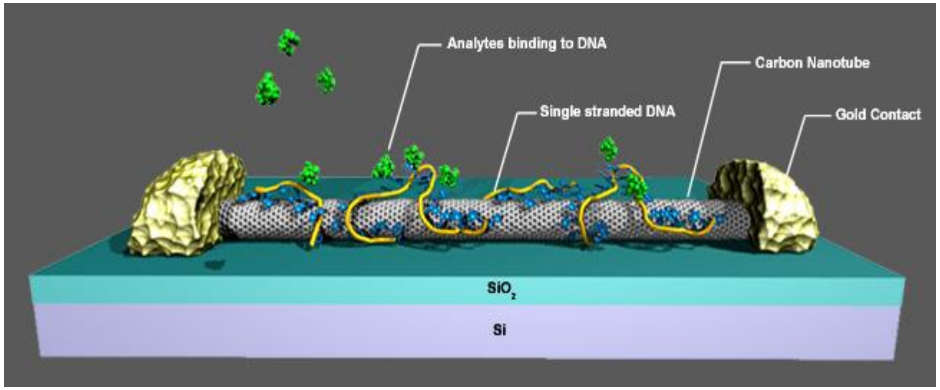
Significant dimensional properties:

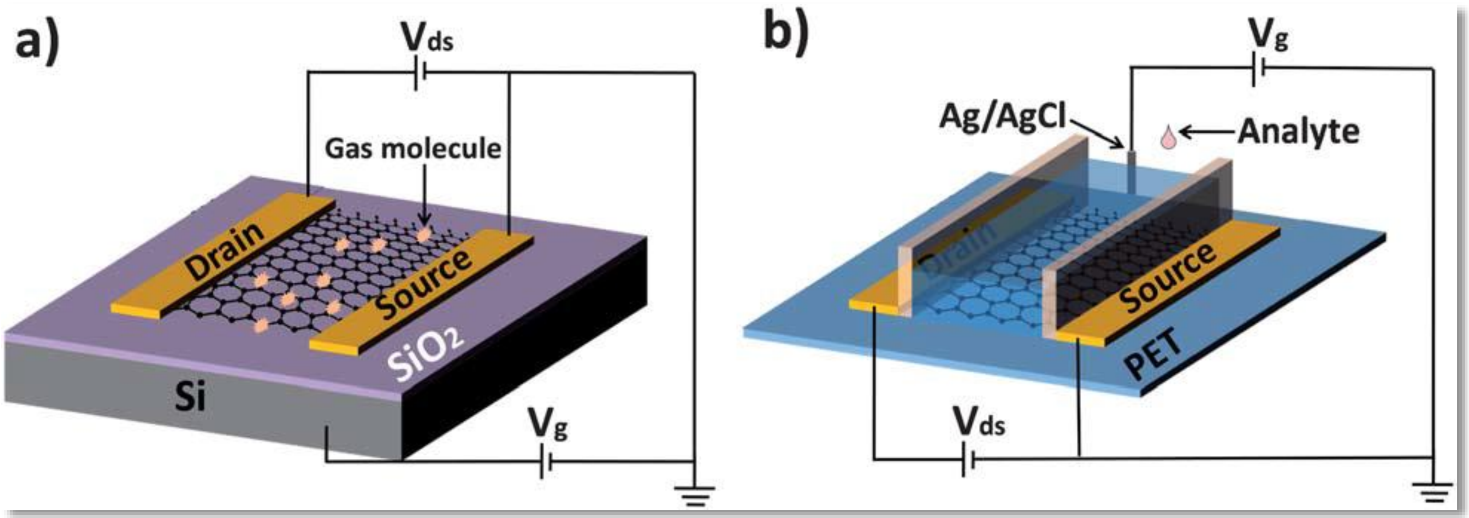
1. Can be singled-walled (SWNT) or multi-walled (MWNT)
2. Diameters range from 2-100 nm
3. Variations in diameter and length can result in aspect ratios as high as 100 million to 1
4. Often referred to as 1D "electron nanowires" because of their high aspect ratios and high electrical conductivities

APPLICATION TO BIOSENSORS

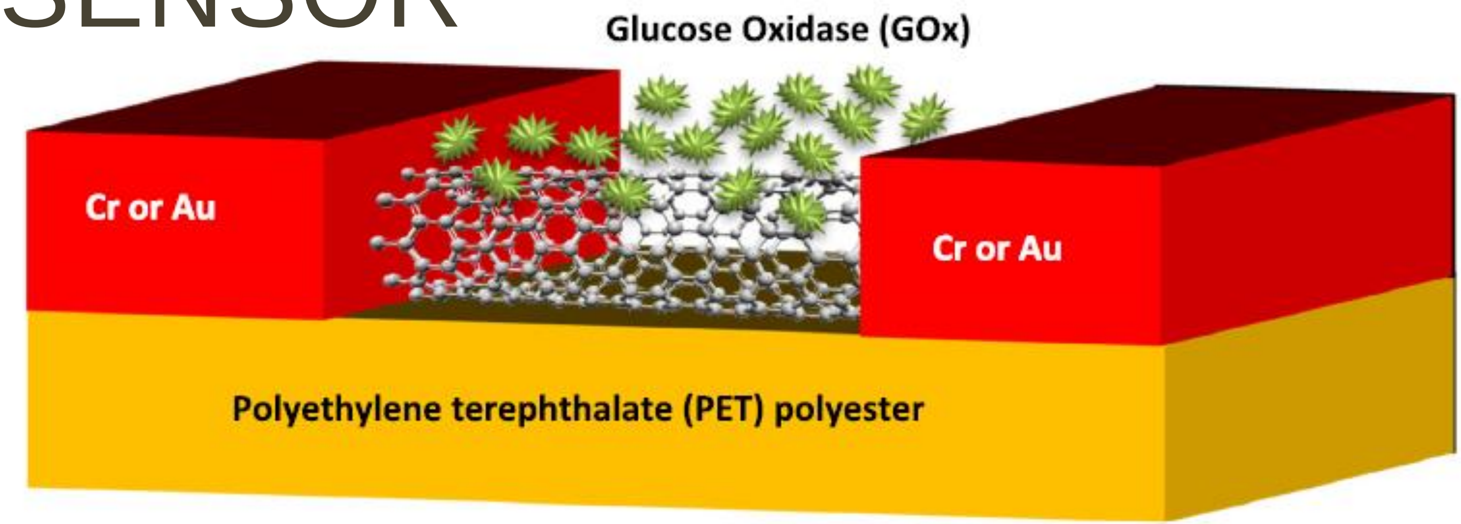
Graphene and carbon nanotubes are effective as sensor transducer elements because:

1. High electrical conduction = faster sensing
2. Strong mechanical strength = better device durability
3. High surface areas and length-to-diameter ratios = more efficient sensing geometries





EXAMPLE: CARBON NANOTUBE GLUCOSE SENSOR

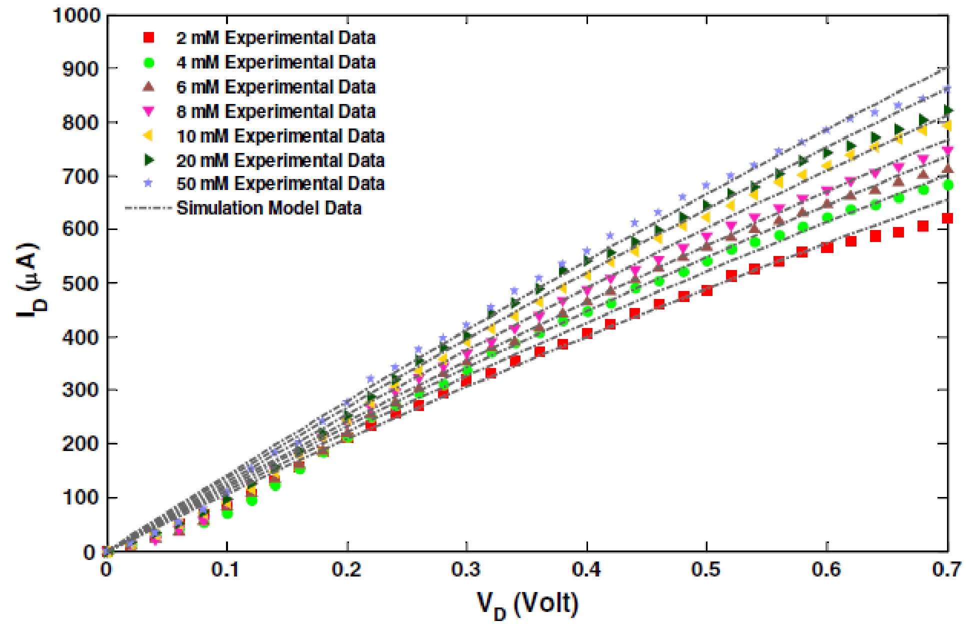


The carbon nanotube glucose sensor above is composed of the following elements:

1. Two chromium or gold electrodes, one source and one drain
2. A PET substrate layer
3. An interconnecting carbon nanotube as the transducing element
4. Immobilized glucose oxidase enzymes to facilitate redox reactions with glucose

CARBON NANOTUBE GLUCOSE SENSOR CONT'D

The sensing capability of the previous carbon nanotube glucose sensor was experimentally tested and compared with a mathematical model.

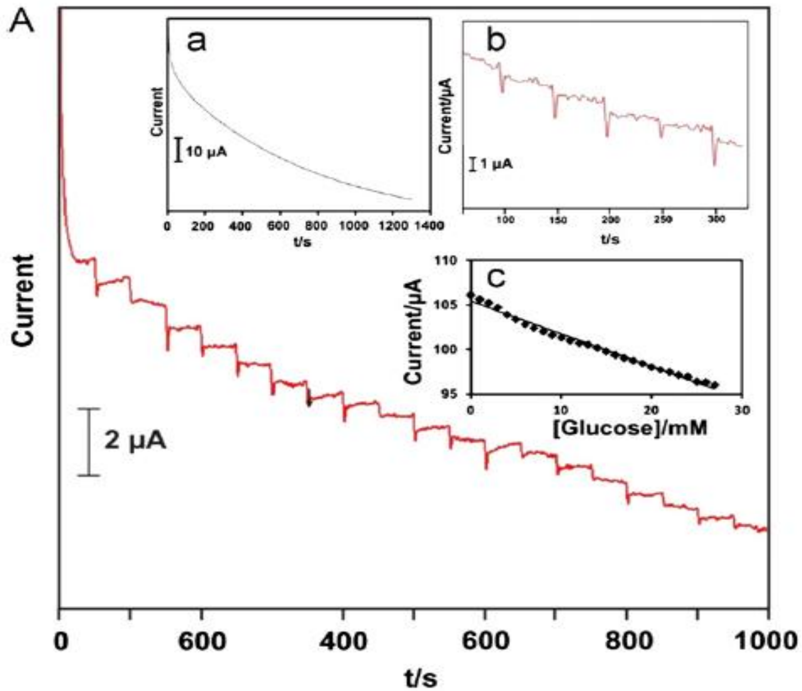


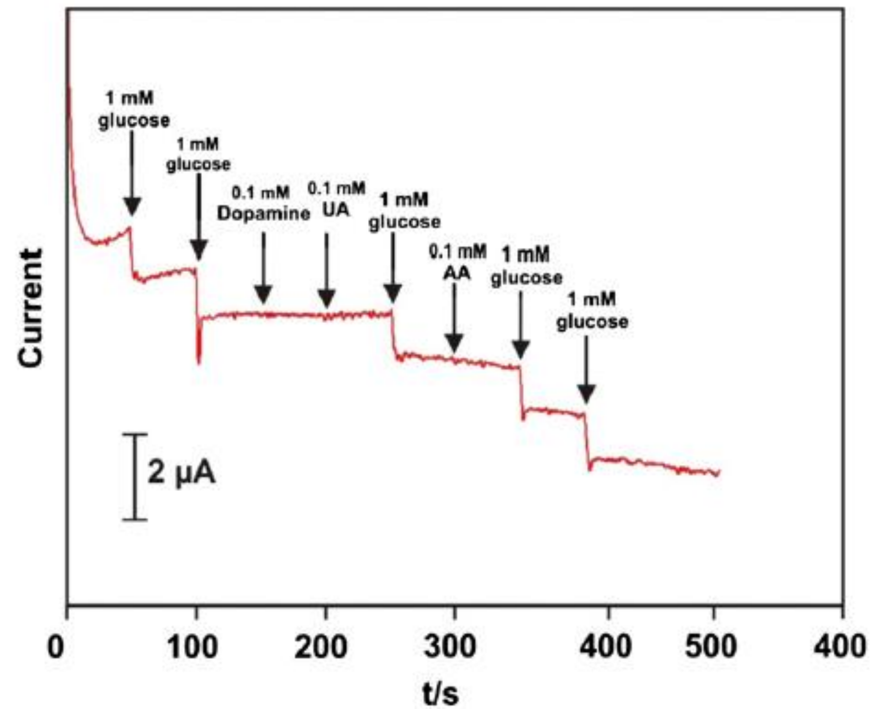
The data showed that the current and voltage values of the drain electrode for different glucose concentrations varied little between experimental and modeled results.

Glucose (mM)	Absolute RMS errors	Normalized RMS errors (%)
0 (with PBS)	19.24	5.66
2	57.55	12.22
4	49.05	9.75
6	59.47	11.23
8	53.99	9.80
10	55.60	9.53
20	69.18	11.17
50	75.07	11.60

Normalized RMS error never exceeded 13% at any glucose concentration level

EXAMPLE: GRAPHENE GLUCOSE BIOSENSOR





Results of a sensor featuring a reduced-graphene transduction film:

- The left data plot shows how the measured current across the electrodes decreased
  proportionally with added glucose
- The right plot demonstrates that the current did not change when dopamine, uric acid or ascorbic acid were added. This demonstrates good selectivity.

EXAMPLE: GRAPHENE-BASED BIOSENSOR TO DETECT BACTERIA OR MICROORGANISMS

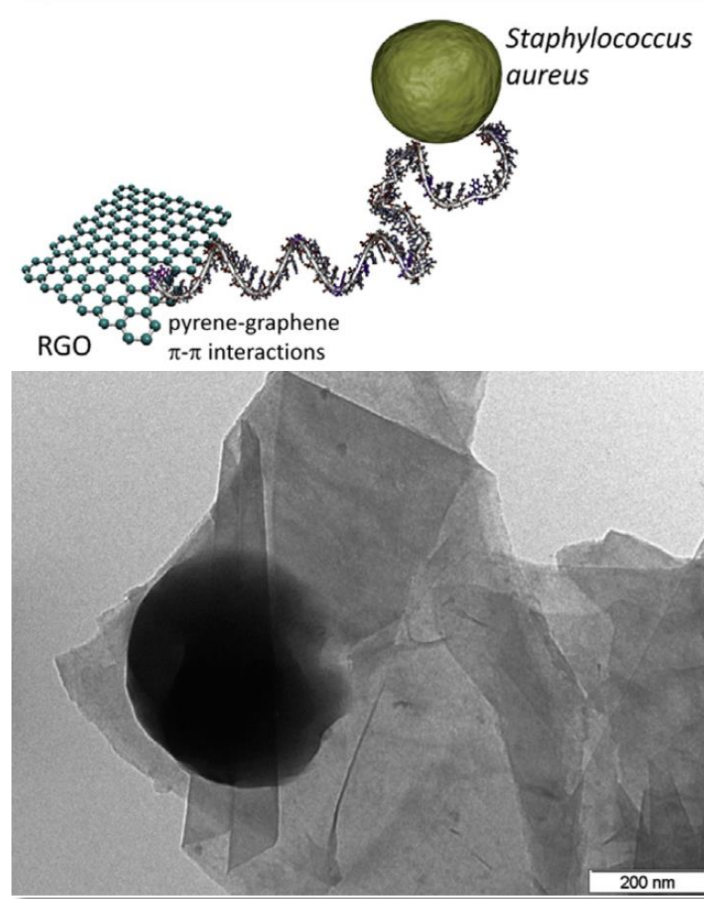
Aptasensors to detect bacteria

Chemically modified graphene and aptamers to detect S. aureus

A type of potentiometric sensor

Advantage: high selectivity, technique simplicity, ultra-low detection limit, and very short time responses to detection of microorganisms.

Biomarkers and biosensors using electrochemical techniques which are usually much simpler and non-expensive.



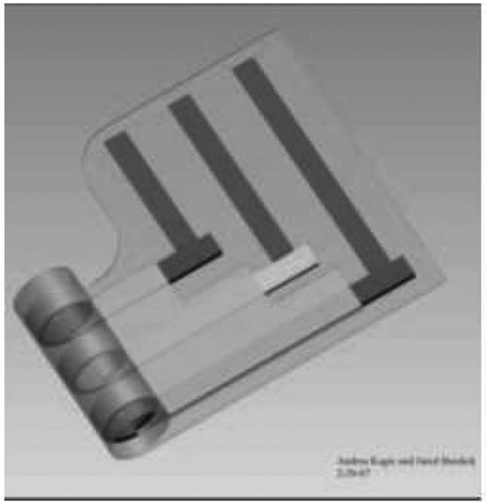
FUTURE AND LIMITATIONS OF CARBON NANOMATERIAL SENSORS

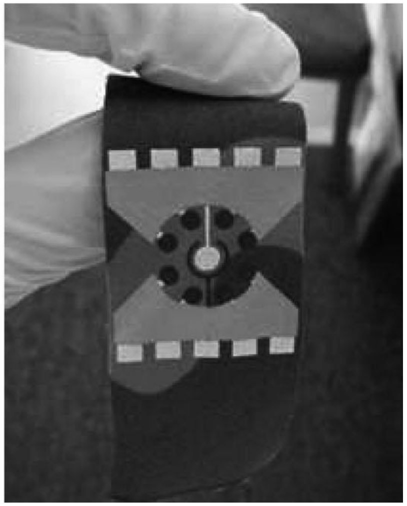
- Scientifically, electrochemical sensors using carbon nanomaterial transducing elements are plausible and have been demonstrated over the past decade.
- However, manufacturing high quality and high purity graphene and carbon nanotubes in mass quantities is difficult and expensive.
- The scientific application is promising and exciting, but is currently limited by high cost of fabrication.
- Carbon nanomaterial biosensors will probably enter the market one day, but not until the cost to benefit ratio is improved.

WEARABLE BIOSENSORS

Wearable biosensors that are integrated to clothing or directly on the skin can provide real time measurements to enable a more comprehensive understanding of health in a discrete manner.

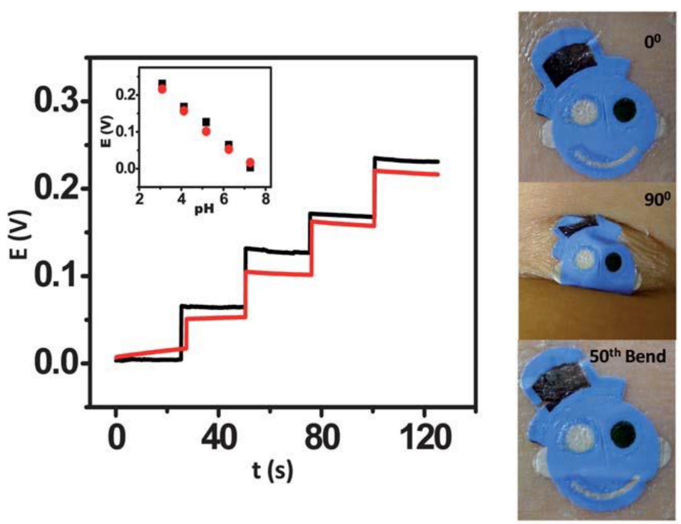
Can measure physical parameters such as heart rate, respiration, blood oxygenation, blood pressure, temperature, motion, brain activity, and more. Can measure external environments such as air quality and contaminants (hazards, detection).



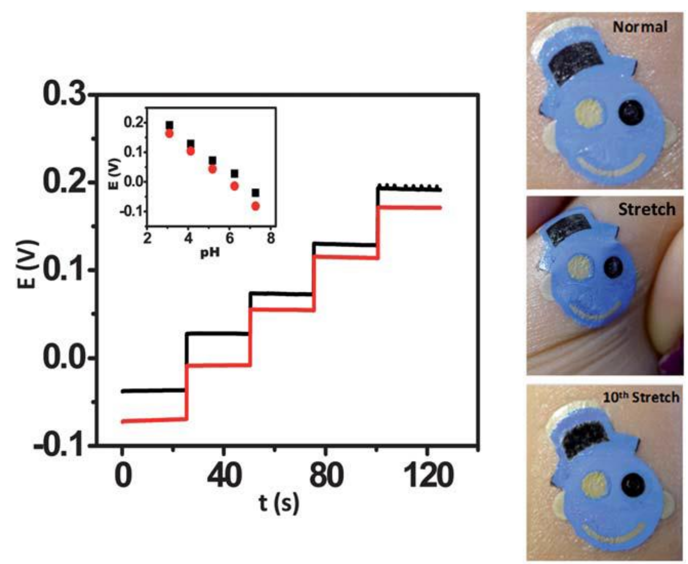


MECHANICAL STRESS

Must maintain consistently accurate measurements while withstanding continuous mechanical wear. The effect of bending (left) and stretching (right) mechanical stress on the pH-tattoo response signal.



(i) (ii)

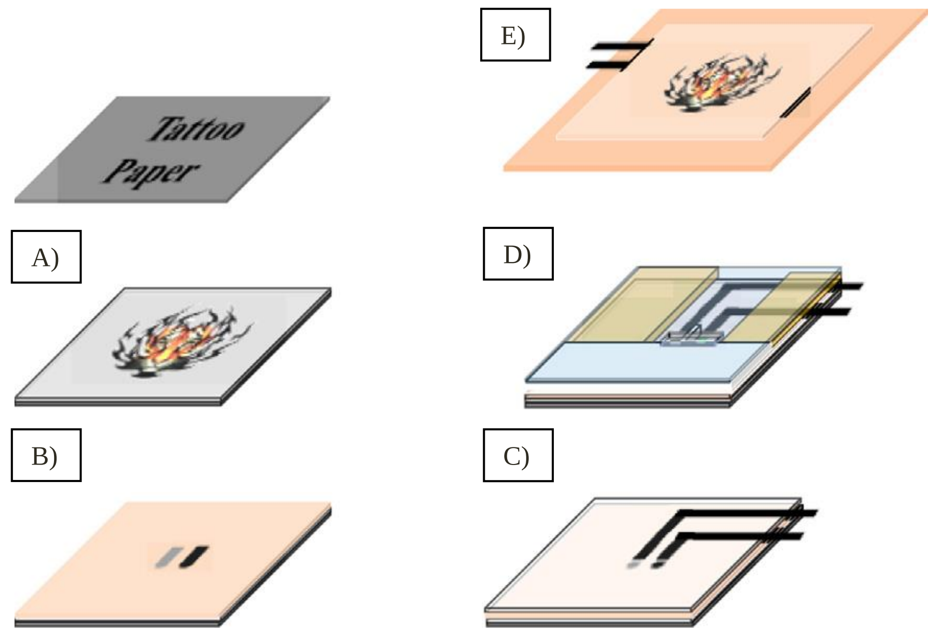


(i) (ii)

FABRICATING WEARABLE BIOSENSORS

Fabricated on clothing with screen printing (patterned mesh-screen stencils, various layers of conductivity, bio catalytic functionality, insulation, processed) or stamp transfer electrodes (transferred via reliefs) which is used for its conformal ability.

Fabrication for epidermal integration with screen printing and transfer tattoo hybrids with carbon fiber reinforcement.

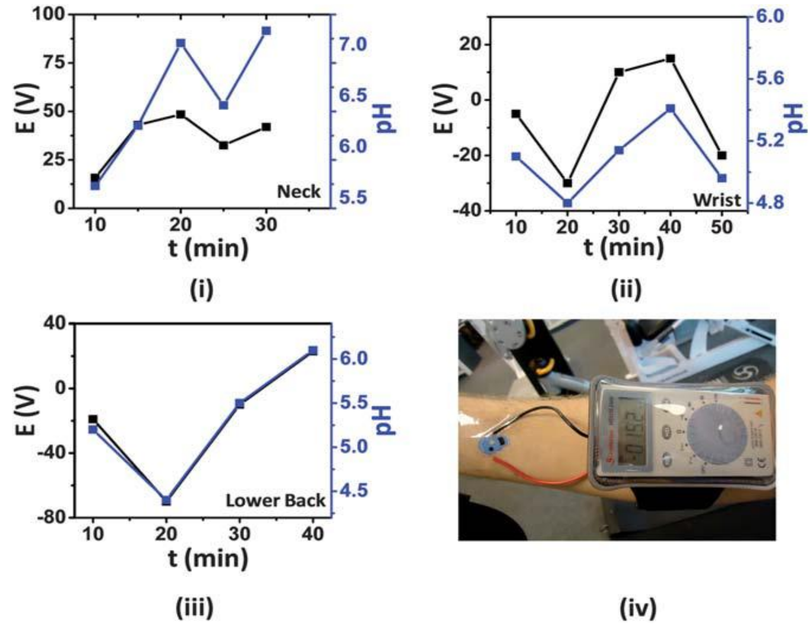


Steps for the fabrication of the Na-tattoo sensors. A) Screen-printing an insulator layer on tattoo paper with design B) Skin colored ink is coated and two electrodes are printed C) Another insulator layer is coated defining electrode area and contact points D) Electrodes modified with membrane bio-marker solutions E) Na-tattoo sensor is ready for application

WEARABLE BIOSENSORS

Potentiometric ion selective electrode measures (pH, Sodium, Ammonium, Lactate) optimal electrolyte levels, metabolic state, and tissue oxygenation to monitor health and performance.

The comparison between the tattoo sensors (black) and conventional pH meters (blue) on the neck (i), wrist (ii), and lower back (iii). The setup (iv).



INTEGRATING WEARABLE BIOSENSORS

The level of coverage not only reduces the amount of time it takes to respond to health conditions, but also facilitates preventative healthcare by being able to recognize and address complications at an early stage where more options are available and effective.

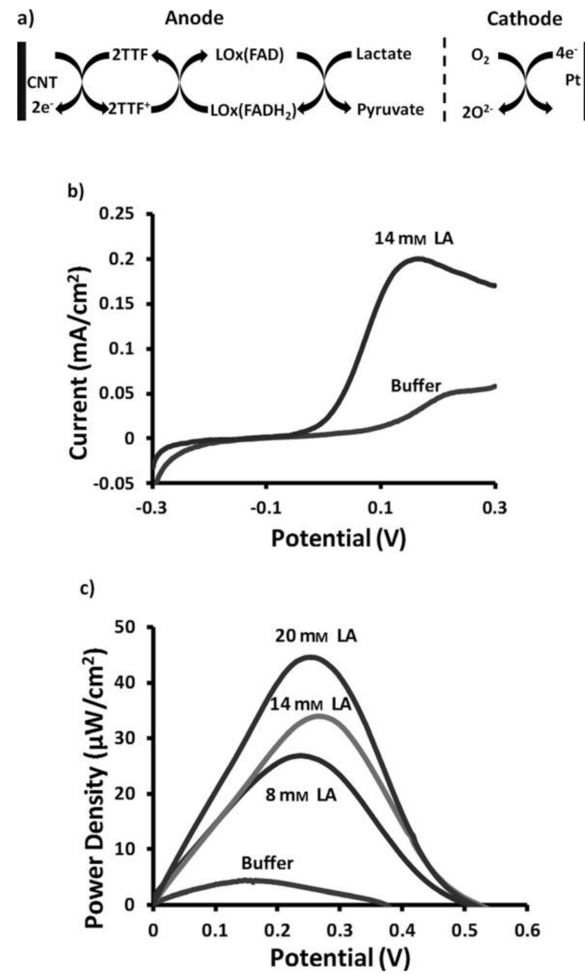
Breaks the inefficient cycle of regular checkups where its too late (after symptoms arise) or too early (waste of resources).

EPIDERMAL BIOFUEL CELL

To power biosensors, a novel approach using its own biomarkers to extract biochemical energy is possible.

Lactate dehydrogenase enzyme catalyzes the selective oxidation of lactate to pyruvate which converts NAD+ to NADH with the mediator TTF carbon nanotube composite creating a potential.

This is just one possible integrated solution among many. Batteries and piezoelectric based power could limit placement, size, and time.



CONCLUSIONS

With promising research in carbon nanomaterials and wearables, electrochemical bio-marker sensors are a powerful integrative device whose applications and impact has yet to be fully realized.

Made less invasive, more sensitive, smaller, and more connected than conventional sensing, electrochemical bio-marker sensors are poised to improve our health, fitness, performance, and safety.

ACKNOWLEDGEMENTS

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