Nono-Sensors for Drug Monitoring in Biological Systems

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Why Measure Drug Concentration?

Same nominal dose does not guarantee the same drug exposure.

Pharmacokinetics varies with age, body composition, genetics, organ function, interactions and adherence.

For selected drugs, excessive exposure can cause toxicity while insufficient exposure can reduce efficacy.

TDM connects measured exposure with therapeutic decisions.

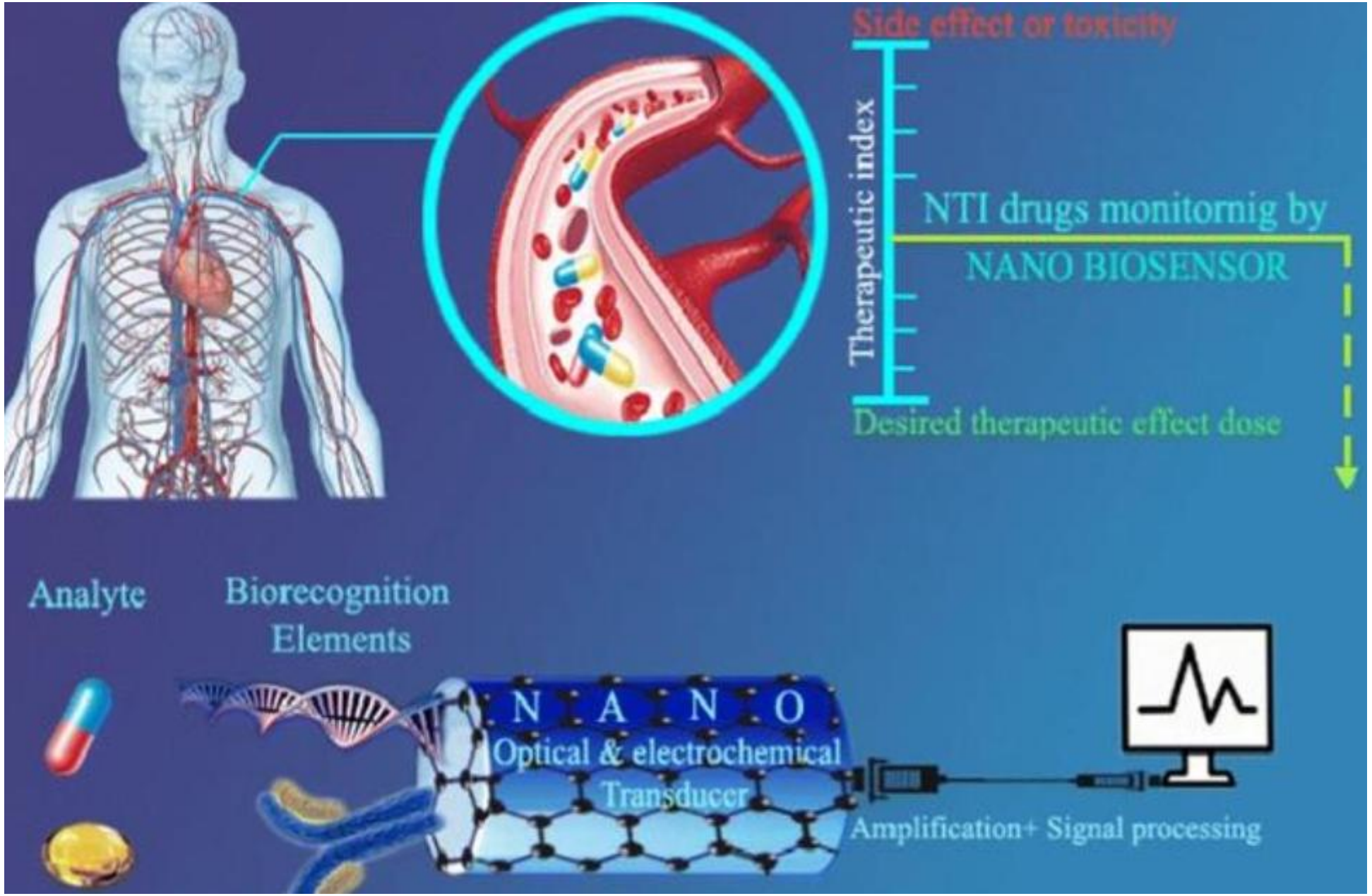
Dose → Exposure → Measurement → Decision

The concept of therapeutic drug monitoring (TDM) started in 1970 with the basic principle based on the fact that some drugs show a close relationship between the plasma level of the drug and its clinical effect

Medical doctors usually monitor the pharmacodynamics of medicines by directly measuring the physiological indices of therapeutic response, e.g., lipid concentrations, blood glucose, blood pressure, and coagulation tests. In other cases, it is difficult to distinguish between disease progression and the pharmacological effects of a drug.

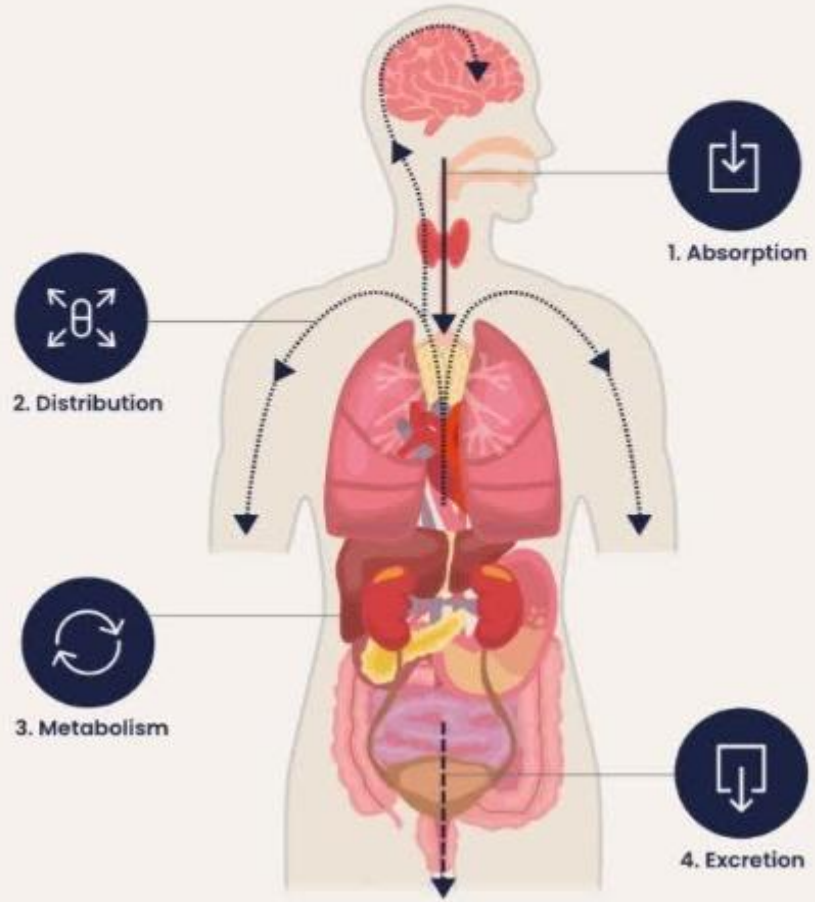
In these situations, TDM is an essential part of clinical management, which process is based on the assumption that there is a definable relationship between the dose and the concentration of the drug in plasma or blood and between the latter and the pharmacodynamic effect

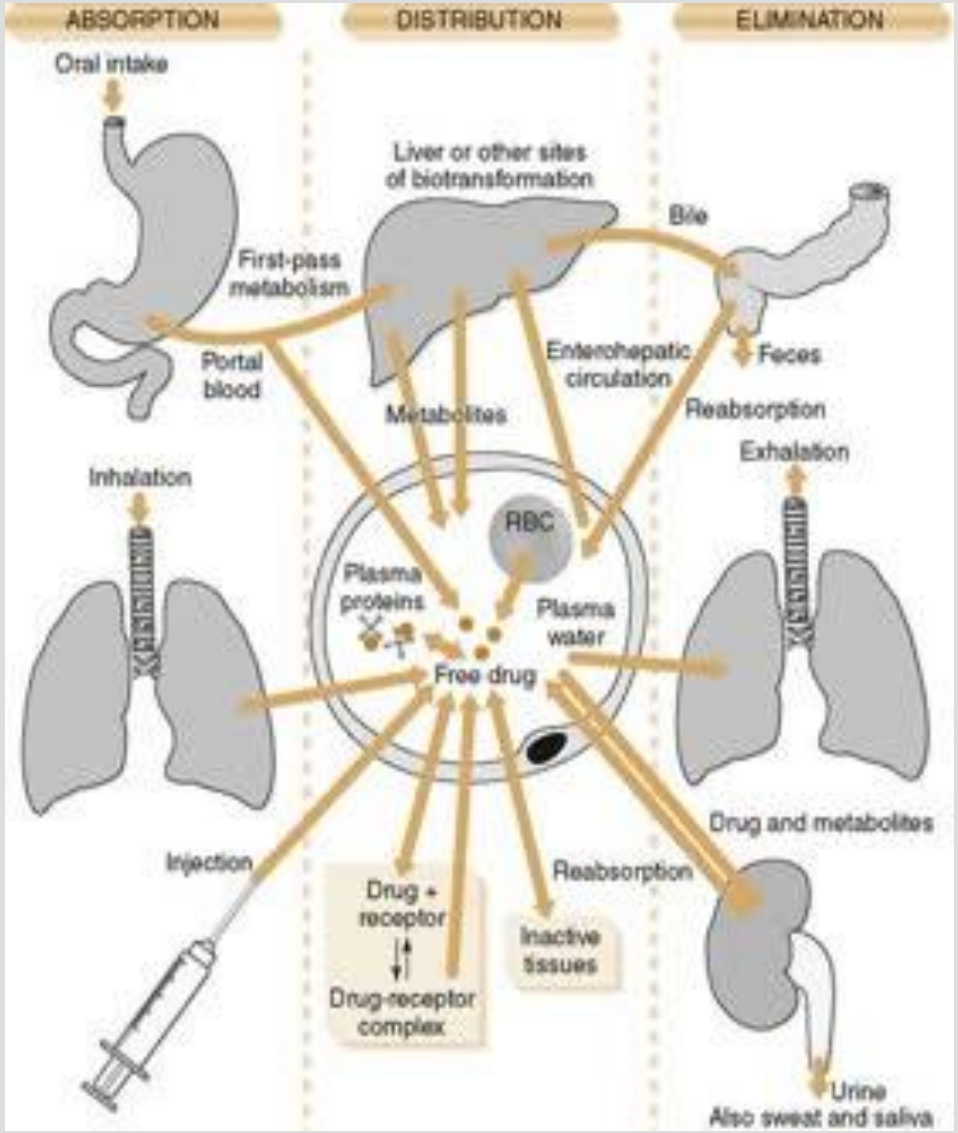



Side effect or toxicity
Therapeutic index
NTI drugs monitornig by
NANO BIOSENSOR
Desired therapeutic effect dose
Analyte
Biorecognition
Elements
N A N O
Optical & electrochemical
Transducer
Amplification+ Signal processing

Pharmacokinetics

"Pharmacokinetics is the study of kinetics of absorption, distribution, metabolism and excretion (ADME) of drugs and their corresponding pharmacologic, therapeutic, or toxic responses in man and animals." [1]





Conventional Drug Analysis

HPLC and LC–MS/MS offer strong selectivity and quantitative performance.

Immunoassays are established for selected drugs and clinical workflows.

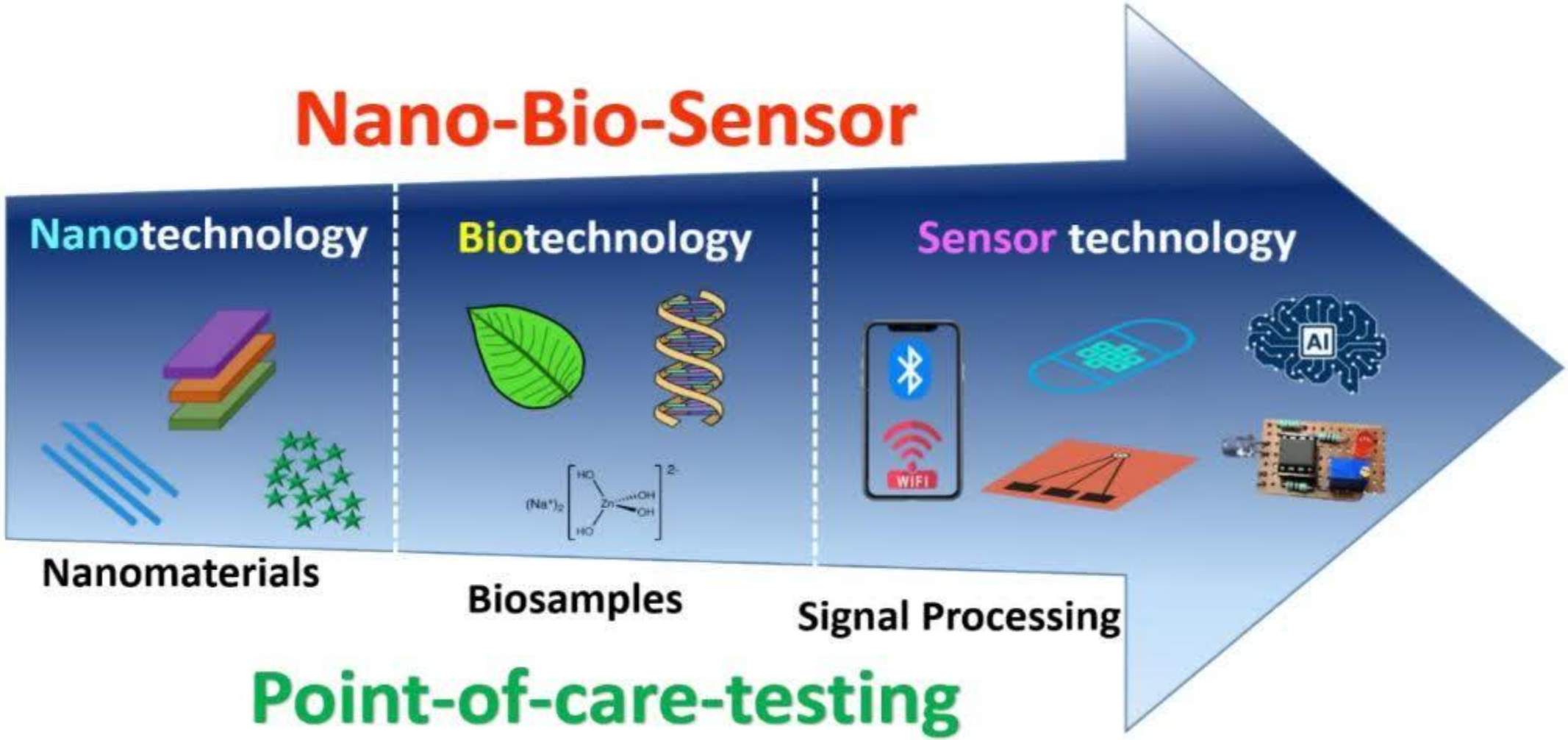
Typical barriers include centralized laboratories, sample preparation, instrument cost and turnaround time.

Nanobiosensors aim to complement reference methods with

rapid

miniaturized

potentially point-of-care analysis


Nano-Bio-Sensor
Nanotechnology
Biotechnology
Sensor technology
WIFI
AI
Nanomaterials
Biosamples
Signal Processing
Point-of-care-testing

Therapeutic Drug Monitoring

Clinical need and Therapeutic Drug Monitoring (TDM)

Nanobiosensor architecture and nanomaterial engineering

Electrochemical sensing: CV, DPV, SWV and EIS

Optical sensing: fluorescence, SPR, colorimetry and SERS

Applications: antibiotics, anticancer and antiepileptic drugs

Wearable, microneedle and smartphone-integrated systems

Challenges, clinical translation, AI, multiplexing and future directions

Why Nanomaterials?

High specific surface area can increase accessible functional sites.

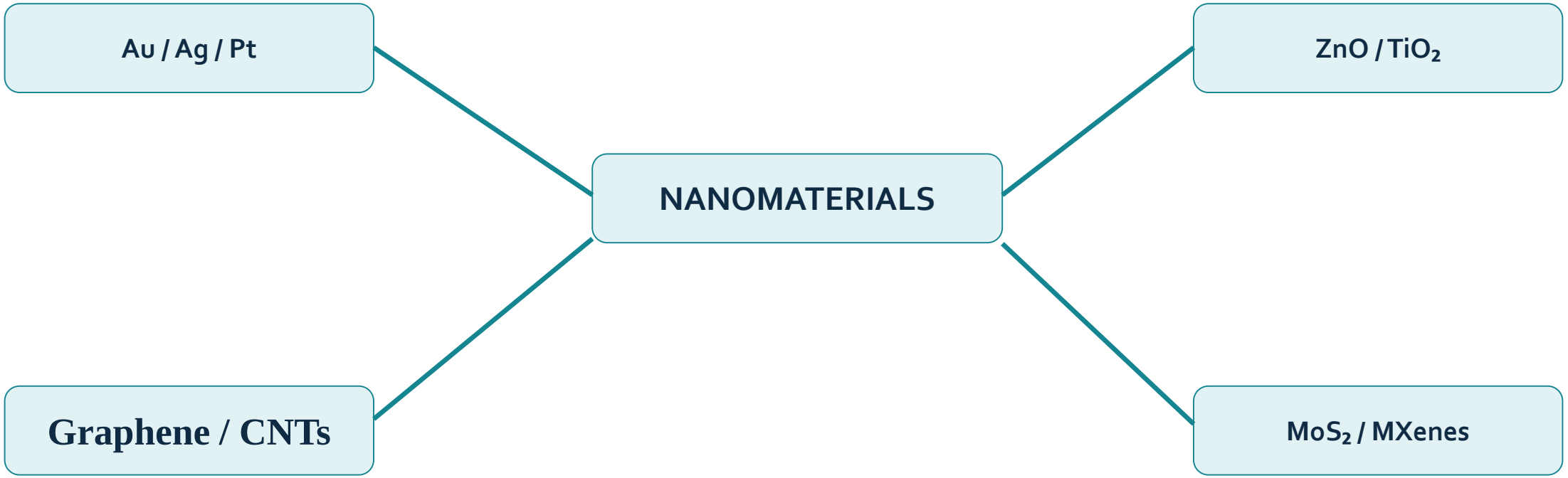
Conductive nanostructures can facilitate interfacial electron transfer.

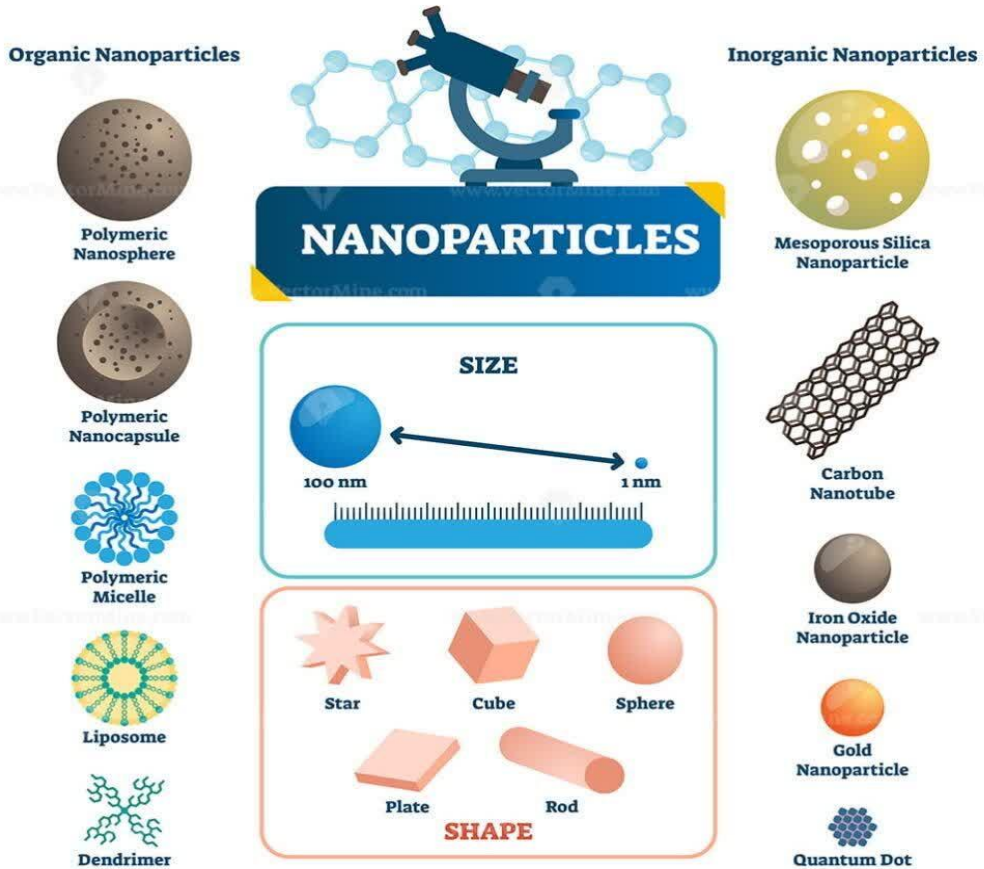
Catalytic nanoparticles can amplify electrochemical reactions.

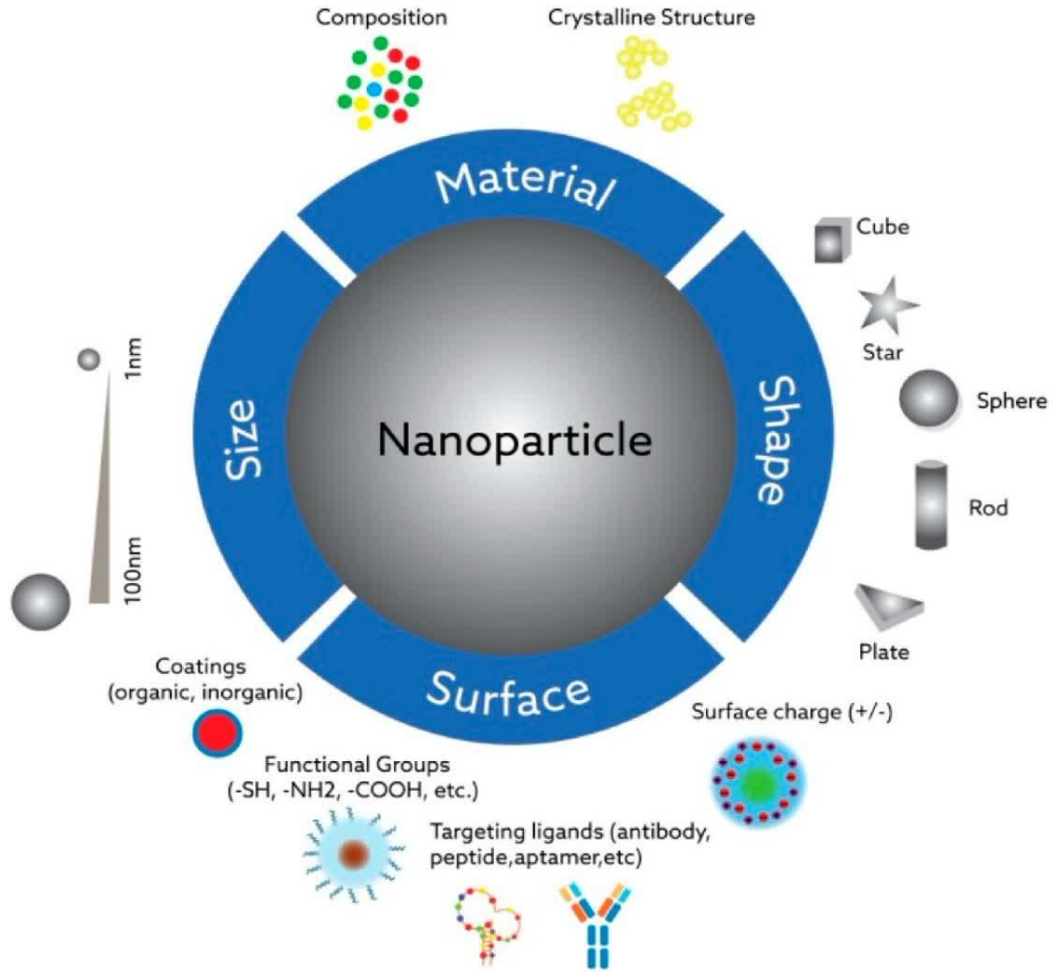
Plasmonic effects can enhance optical readouts.

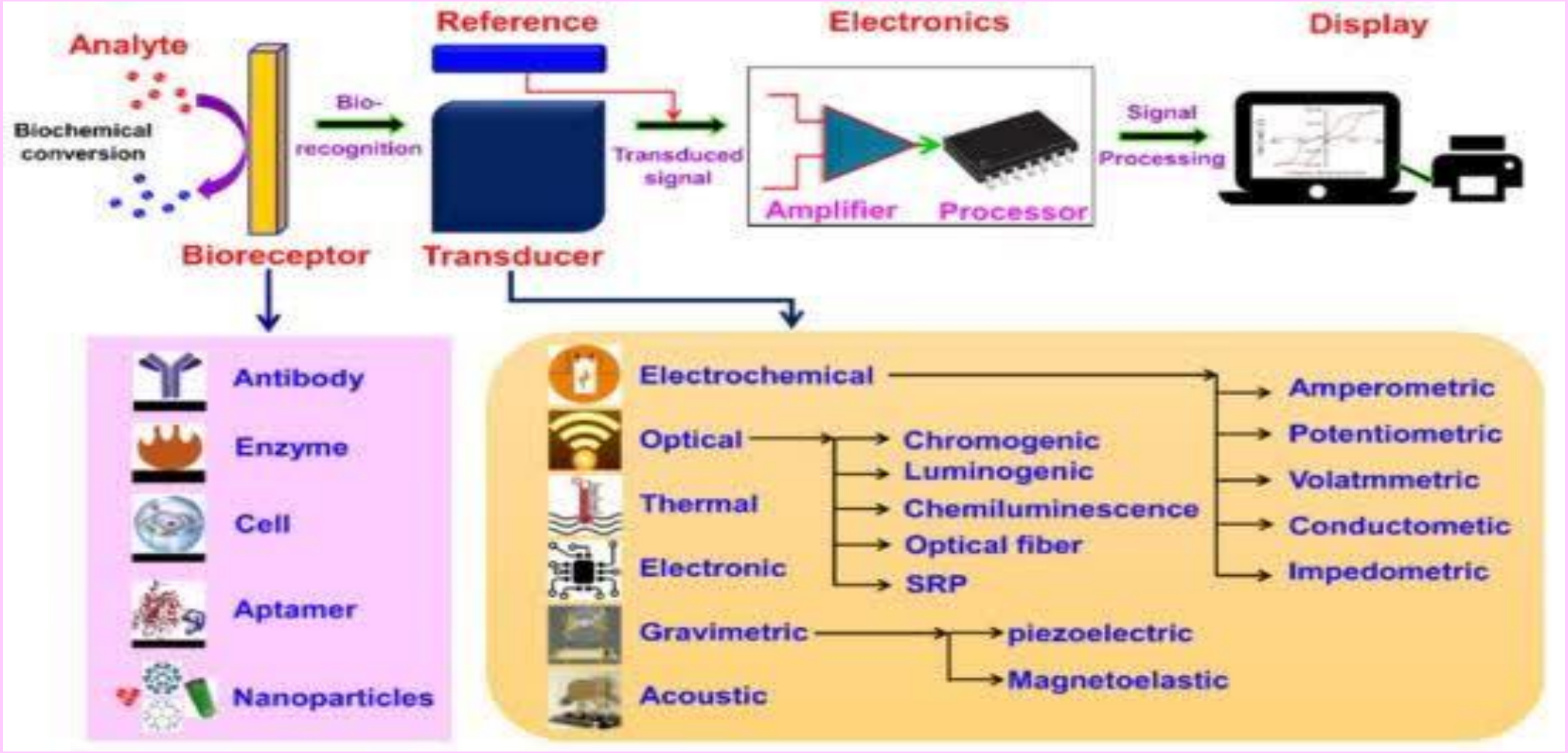
Hybrid nanocomposites combine conductivity, catalytic activity and biorecognition support.

Nanomaterial




Organic Nanoparticles
Polymeric Nanosphere
Polymeric Nanocapsule
Polymeric Micelle
Liposome
Dendrimer
NANOPARTICLES
SIZE
100 nm
1 nm
Star
Cube
Sphere
Plate
Rod
SHAPE
Inorganic Nanoparticles
Mesoporous Silica Nanoparticle
Carbon Nanotube
Iron Oxide Nanoparticle
Gold Nanoparticle
Quantum Dot

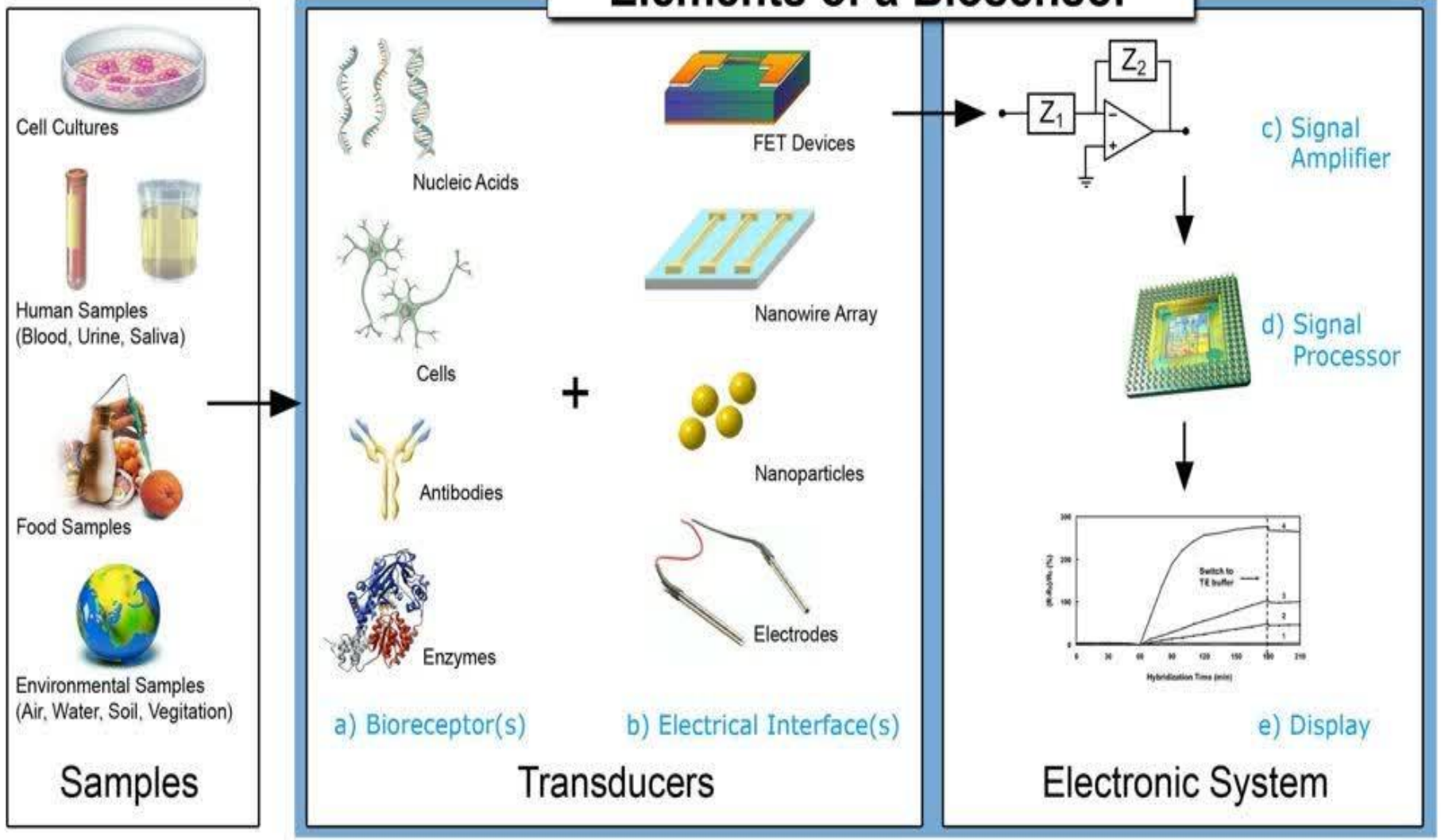

Composition
Crystalline Structure
Material
Size
Shape
Surface
Nanoparticle
1nm
100nm
Cube
Star
Sphere
Rod
Plate
Coatings (organic, inorganic)
Surface charge (+/-)
Functional Groups (-SH, -NH2, -COOH, etc.)
Targeting ligands (antibody, peptide,aptamer,etc)


Analyte
Biochemical conversion
Bio-recognition
Bioreceptor
Reference
Transducer
Transduced signal
Electronics
Amplifier
Processor
Signal Processing
Display
Antibody
Enzyme
Cell
Aptamer
Nanoparticles
Electrochemical
Optical
Thermal
Electronic
Gravimetric
Acoustic
Chromogenic
Luminogenic
Chemiluminescence
Optical fiber
SRP
piezoelectric
Magnetoelastic
Amperometric
Potentiometric
Volatmmetric
Conductometic
Impedometric

Nanobiosensor Fundamentals

Recognition + nanomaterials + signal transduction

Elements of a Biosensor



General Nanobiosensor Architecture

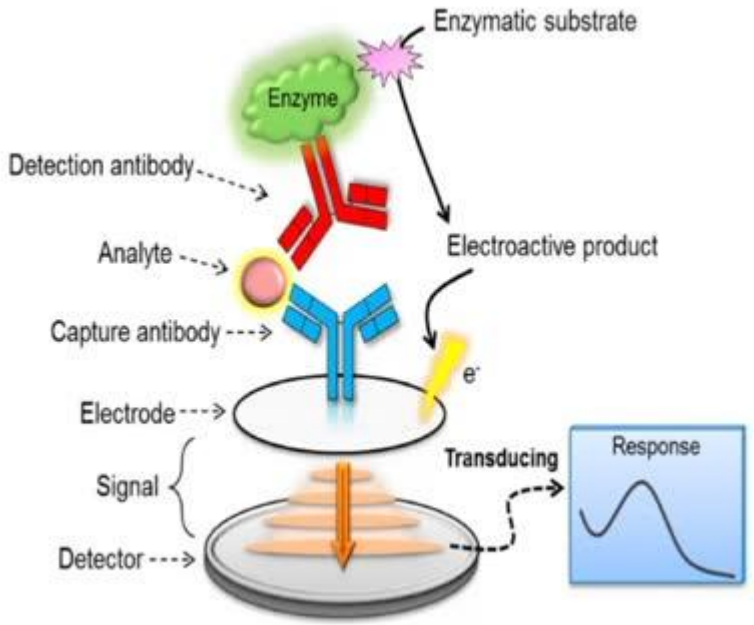


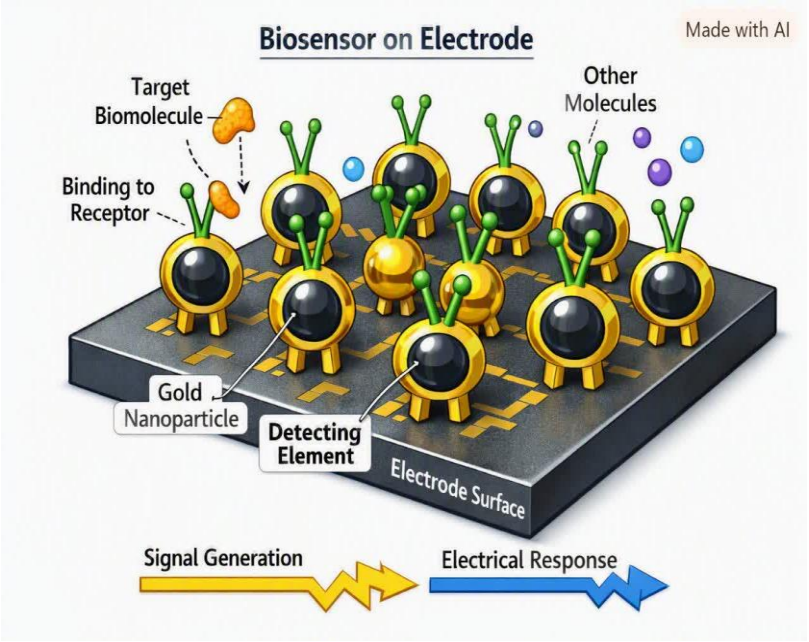
Electrochemical Nanobiosensors

A central platform for rapid and portable drug analysis

From Drug Molecule to Electrochemical Signal

Drug — Nanoelectrode — Electron Transfer — Current / Impedance — Concentration

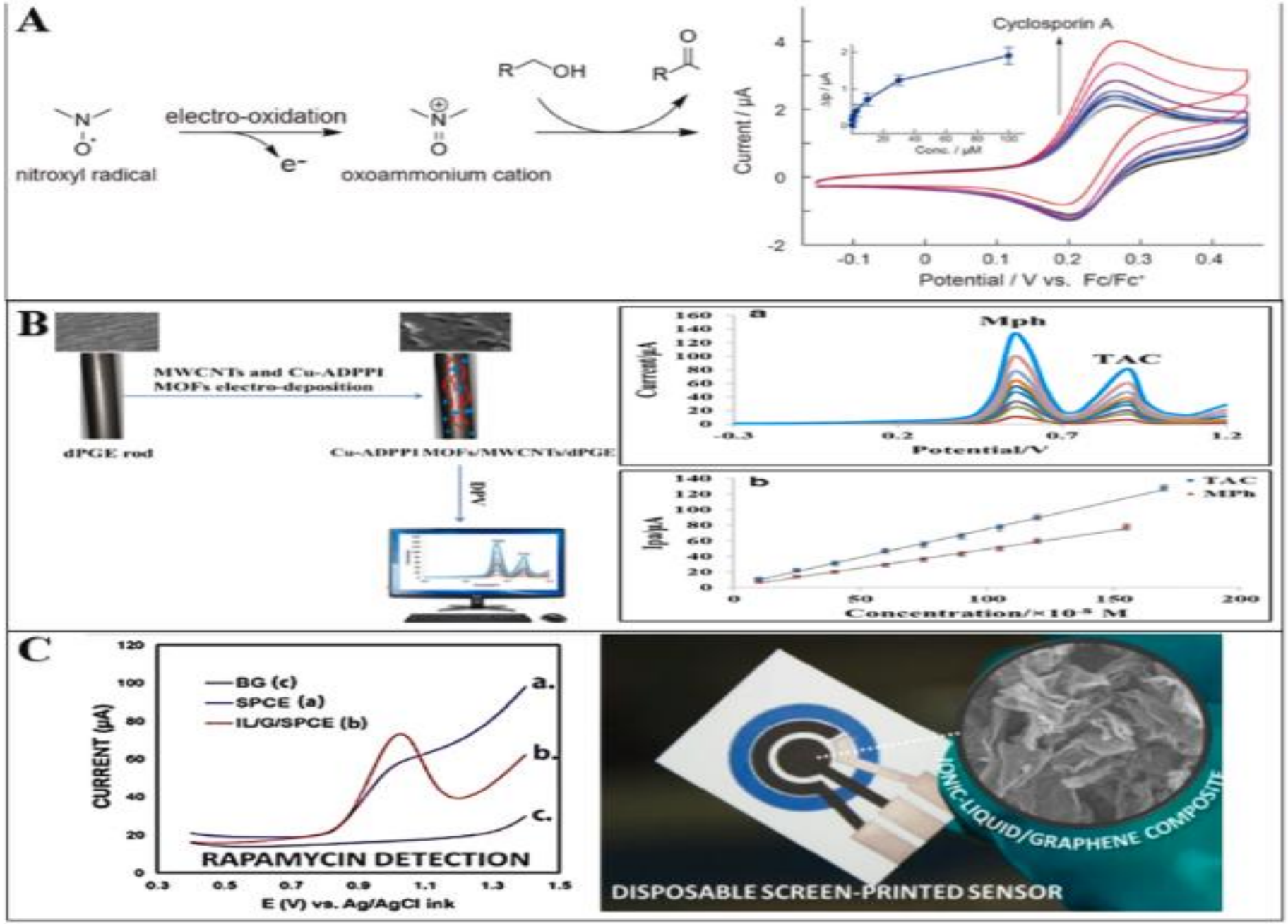


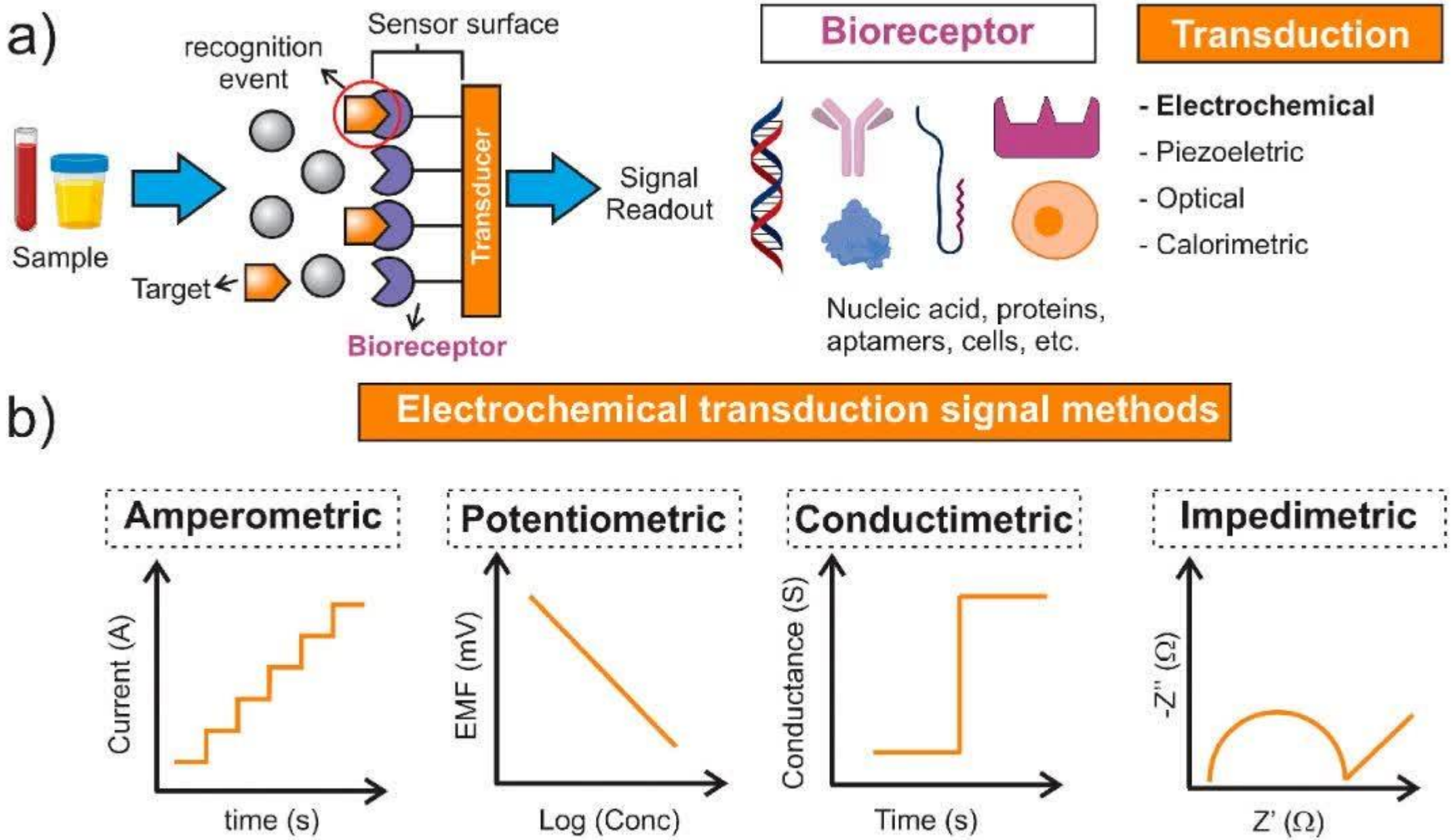


cyclosporin

Tacrolimus

Rapamycin




a)
Sensor surface
recognition event
Sample
Target
Transducer
Signal Readout
Bioreceptor
Bioreceptor
Transduction
- Electrochemical
- Piezoeletric
- Optical
- Calorimetric
Nucleic acid, proteins, aptamers, cells, etc.
b)
Electrochemical transduction signal methods
Amperometric
Current (A)
time (s)
Potentiometric
EMF (mV)
Log (Conc)
Conductimetric
Conductance (S)
Time (s)
Impedimetric
-Z'' (Ω)
Z' (Ω)

The Three-Electrode System

Working electrode: site of the analytical reaction.

Reference electrode: provides a stable reference potential.

Counter electrode: completes the electrical circuit.

Nanomaterial modification is commonly applied to the working electrode.

Differential Pulse Voltammetry (DPV)

Small potential pulses are superimposed on a potential ramp.

Current is sampled at defined points to reduce capacitive/background contributions.

DPV provides high sensitivity and is widely used for trace electrochemical analysis.

It is particularly attractive for portable drug-sensing platforms.

Square-Wave Voltammetry (SWV)

Square-wave pulses are superimposed on a staircase potential.

Forward and reverse currents are combined into a net response.

SWV can provide rapid measurements with good sensitivity.

It is useful when fast electrochemical screening is desired.

Electrochemical Impedance Spectroscopy (EIS)

EIS probes the frequency-dependent response of the electrode interface.

Target binding can change charge-transfer resistance and interfacial capacitance.

EIS is especially useful for label-free affinity-based sensing.

Equivalent-circuit fitting should be supported by controls and physical interpretation.

Calibration & Analytical Performance

Build a calibration curve using standards with known concentrations.

Evaluate sensitivity, linear range, LOD/LOQ and signal-to-noise behavior.

Validate selectivity, accuracy, precision, recovery, repeatability and reproducibility.

Test stability and real biological samples—not only buffer solutions.

Molecular Recognition & Biological Matrices

The sensor must work in the sample—not only in buffer

Selectivity in Blood and Plasma

Blood and plasma contain proteins, salts, metabolites, lipids and many potential interferents.

A large signal is not useful if another molecule produces a similar response.

Recognition chemistry must be designed together with nanomaterial and transducer selection.

Matrix effects can change baseline, sensitivity and recovery.

Aptamer-Based Recognition

Aptamers are selected nucleic-acid ligands with target-binding capability.

Binding can produce conformational or interfacial changes that modulate the signal.

They can be chemically synthesized and integrated with nanostructured interfaces.

Key variables include affinity, immobilization, orientation, regeneration and matrix stability.

Antibody-Based Recognition

Antibodies provide highly specific molecular recognition.

Nanoparticles can function as labels, catalytic amplifiers or high-area supports.

Immobilization chemistry and orientation influence binding accessibility.

Stability, cost and matrix compatibility must be considered.

Drug Applications

Connecting analytical chemistry to clinically relevant examples

Case Study: Vancomycin

Vancomycin is a classic therapeutic drug-monitoring example.

Rapid measurement could shorten the feedback loop between sampling and dose optimization.

Recent reviews describe electrochemical approaches using aptamers, graphene, gold nanoparticles and molecularly imprinted polymers.

Clinical translation requires accurate quantification in real blood samples.

Case Study: Anticancer Drugs

Methotrexate and doxorubicin are examples explored with advanced sensing platforms.

Challenges include low concentrations, complex matrices, metabolites and toxicity-related decisions.

Nanostructured surfaces can improve sensitivity while affinity elements improve selectivity.

Microfluidics, multimodal sensing and AI are emerging directions.

Case Study: Antiepileptic Drugs

Phenytoin and carbamazepine are established TDM examples.

Pharmacokinetic variability can make concentration information clinically useful.

Portable sensing could potentially reduce turnaround time.

Clinical interpretation still depends on dose history, sampling time, symptoms and patient context.

Optical Nanobiosensors

A complementary route to molecular detection

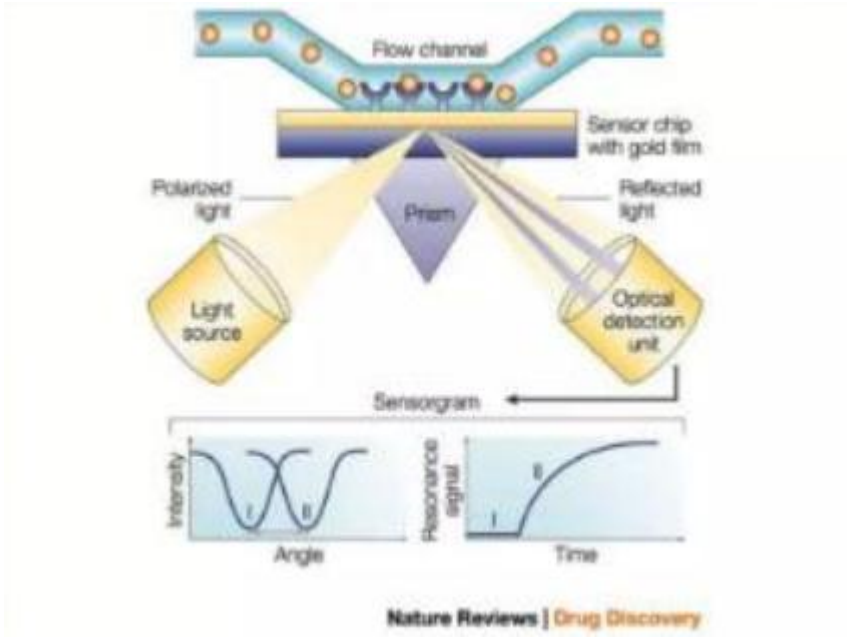
Optical Detection Strategies

Fluorescence: changes in intensity, lifetime or spectral behavior.

Colorimetry: visible color changes potentially readable by smartphones.

Surface plasmon resonance (SPR): refractive-index changes near a functionalized surface.

SERS: plasmonic nanostructures enhance Raman signals near the sensing surface.



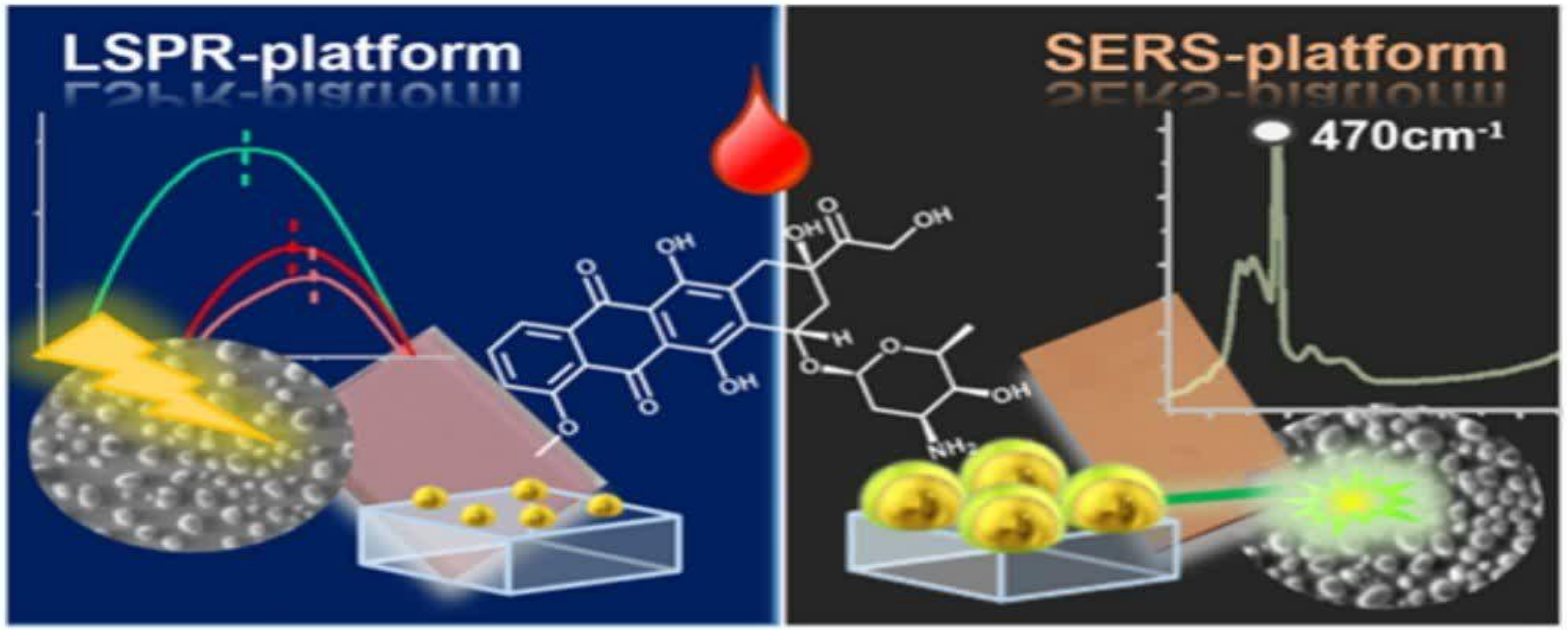
Why Optical Nanomaterials?

Gold and silver nanostructures exhibit strong plasmonic responses.

Quantum dots provide tunable optical properties.

Nanostructures can enhance fluorescence or Raman signals.

Optical platforms are attractive for miniaturized and potentially multiplexed devices.



SERS for Molecular Fingerprinting

Surface-enhanced Raman spectroscopy can amplify Raman scattering near plasmonic nanostructures.

The spectrum provides a chemically rich molecular fingerprint.

Gold and silver nanostructures are common SERS substrates.

Quantitative sensing requires reproducible substrates, controlled sampling and robust calibration.

Wearable & Microneedle Sensors

Moving from occasional sampling toward repeated or continuous monitoring

Wearable Drug Monitoring

Potential biofluids include sweat and other epidermally retrievable fluids.

Voltammetry can directly quantify some electroactive drug molecules.

Key challenges include endogenous electroactive interferents, baseline variation and wireless signal acquisition.

Wearable systems are being developed toward personalized dosing and digital-health applications.

Microneedle-Based Sensing

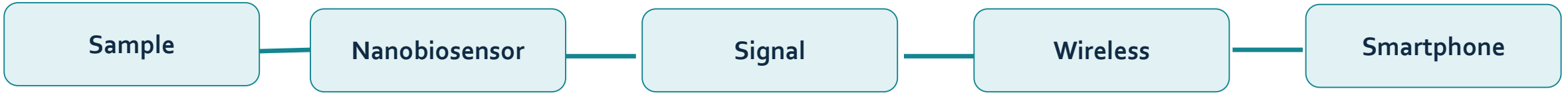
Microneedles can access interstitial fluid with minimal invasiveness.

They can combine sampling and sensing in a compact platform.

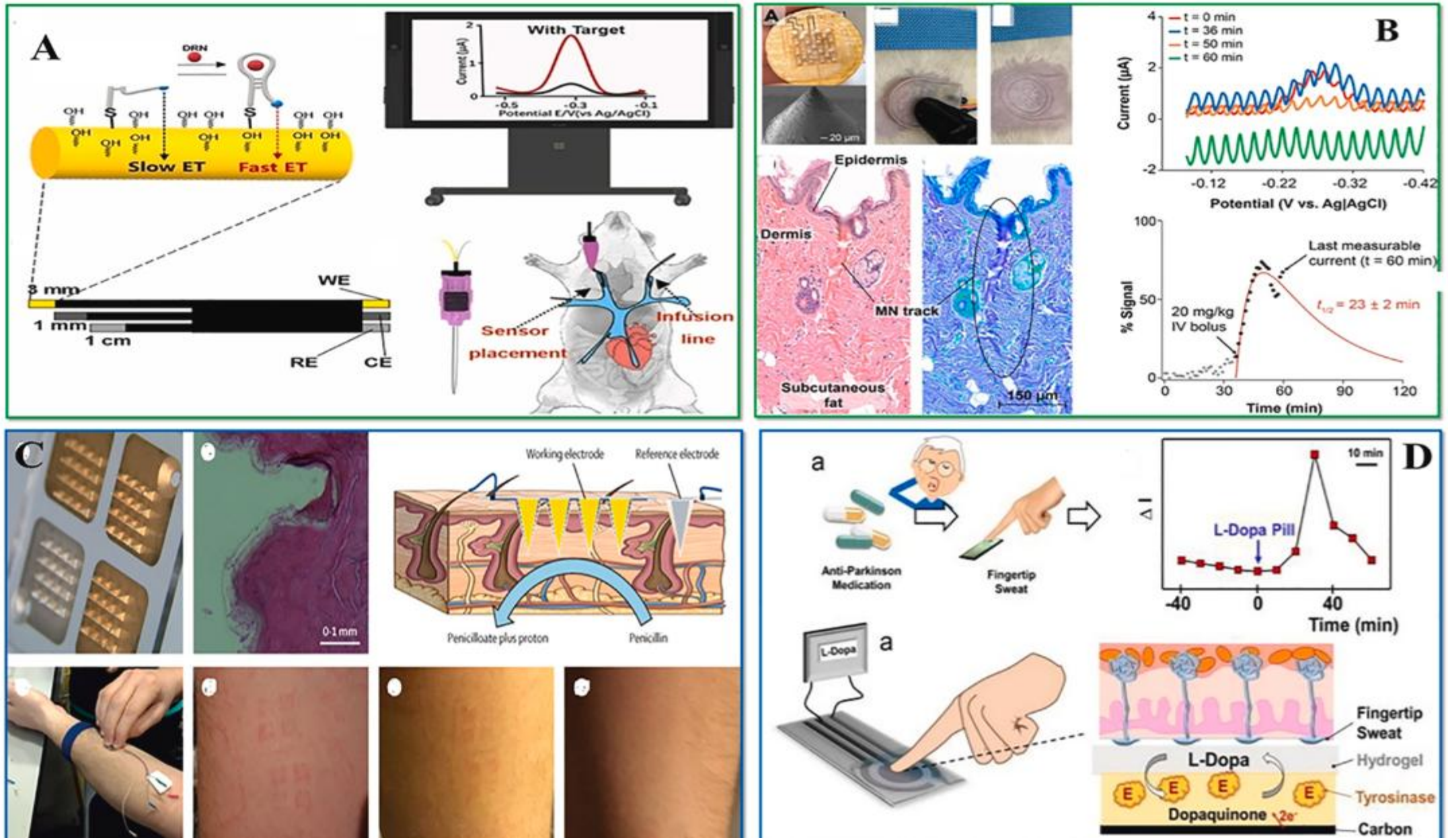
Advantages include small sample volumes and compatibility with wearable electronics.

Challenges include biofouling, mechanical reliability and correlation between interstitial-fluid and blood concentrations.

Sensor → Wireless Link → Smartphone → Clinical View



Continuous data → trends → personalized therapeutic insight


A
DRN
Slow ET
Fast ET
3 mm
1 mm
1 cm
WE
RE
CE
With Target
Current (µA)
Potential E/V(vs Ag/AgCl)
Sensor placement
Infusion line
A
20 µm
Epidermis
Dermis
MN track
Subcutaneous fat
150 µm
B
t = 0 min
t = 36 min
t = 50 min
t = 60 min
Current (µA)
Potential (V vs. Ag|AgCl)
% Signal
Last measurable current (t = 60 min)
20 mg/kg IV bolus
t1/2 = 23 ± 2 min
Time (min)
C
0·1 mm
Working electrode
Reference electrode
Penicilloate plus proton
Penicillin
D
a
Anti-Parkinson Medication
Fingertip Sweat
10 min
ΔI
L-Dopa Pill
Time (min)
L-Dopa
Fingertip Sweat
Hydrogel
Tyrosinase
Dopaquinone
Carbon

Challenges & Clinical Translation

Why a high-performance prototype is not yet a clinical device

Biological systems complexity

- Blood
- Interstitial fluid
- Cellular environments
- Enzymatic degradation
- Protein binding

Biofouling & Matrix Effects

Proteins and biomolecules can adsorb onto sensing surfaces.

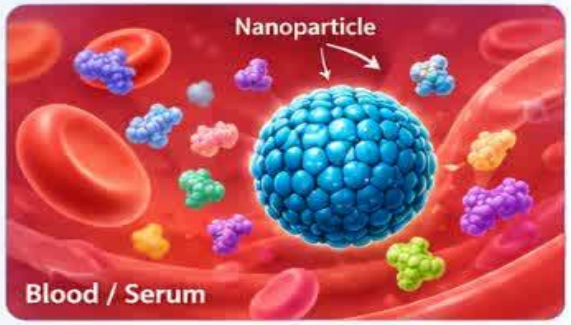
Biofouling can block active sites and alter electron transfer.

Serum, plasma or sweat can shift baseline and apparent sensitivity.

Anti-fouling chemistry, selective membranes, microfluidics or pretreatment may be required.

Protein Corona Formation
on Nanoparticles in Biological Environments

Nanoparticle enters a biological environment



Biomolecules in the environment
(proteins, lipids, etc.)

Electrostatic interactions
(charge–charge)

Hydrophobic interactions
(non-polar regions)

Van der Waals forces
(weak interactions)

Specific binding
(e.g., receptors, antibodies)

Protein Corona Formation

Soft Corona → **Hard Corona**



- Loosely bound proteins
- More dynamic and reversible
- Lower binding affinity

- Tightly bound proteins
- More stable and persistent
- Higher binding affinity

Soft Corona
Weaker interaction with the nanoparticle surface

Hard Corona
Stronger interaction with the nanoparticle surface

Consequences / Effects



Changes in cellular uptake
(e.g., receptor recognition)



Altered biodistribution
(e.g., opsonization, clearance)



Immune response
(e.g., complement activation)



Effect on sensor performance
(e.g., sensitivity, selectivity)

Biocompatibility & Safety

Material composition, size and surface chemistry matter for biological contact.

Potential nanoparticle release and long-term exposure require assessment.

Inflammatory and immune responses matter for prolonged-contact or implanted systems.

Analytical performance and biological safety must be evaluated together.

From Proof-of-Concept to Clinical Validation

Excellent LOD in buffer does not establish clinical utility.

Validate in clinically relevant matrices and compare with a reference method.

Assess accuracy, precision, recovery, stability, reproducibility and failure modes.

Manufacturing consistency, usability, cost and regulatory requirements become essential.

Future Directions

Multiplex sensing, AI and adaptive therapy

Multiplex & Multimodal Sensing

One platform can quantify multiple drugs and biomarkers.

Parallel sensing channels provide complementary information.

Microfluidics can automate sampling, routing and reagent handling.

Multiplexing is attractive for polypharmacy and complex clinical cases.

AI & Sensor Data Analytics

Machine learning can support denoising, drift correction and multivariate calibration.

Large wearable datasets can reveal trends rather than isolated measurements.

AI should support—not replace—analytical validation and clinical judgment.

Reliable data pipelines and transparent validation are essential.

Closed-Loop Therapy: Long-Term Vision

Sensing → data analysis → therapeutic decision → controlled drug delivery.

Continuous monitoring could, in principle, enable adaptive therapy.

Such systems require reliable sensing, fail-safe controls and validated algorithms.

Fully integrated closed-loop drug monitoring remains an active research direction.

Key Take-Home Messages

Drug exposure varies between individuals; TDM can support individualized therapy.

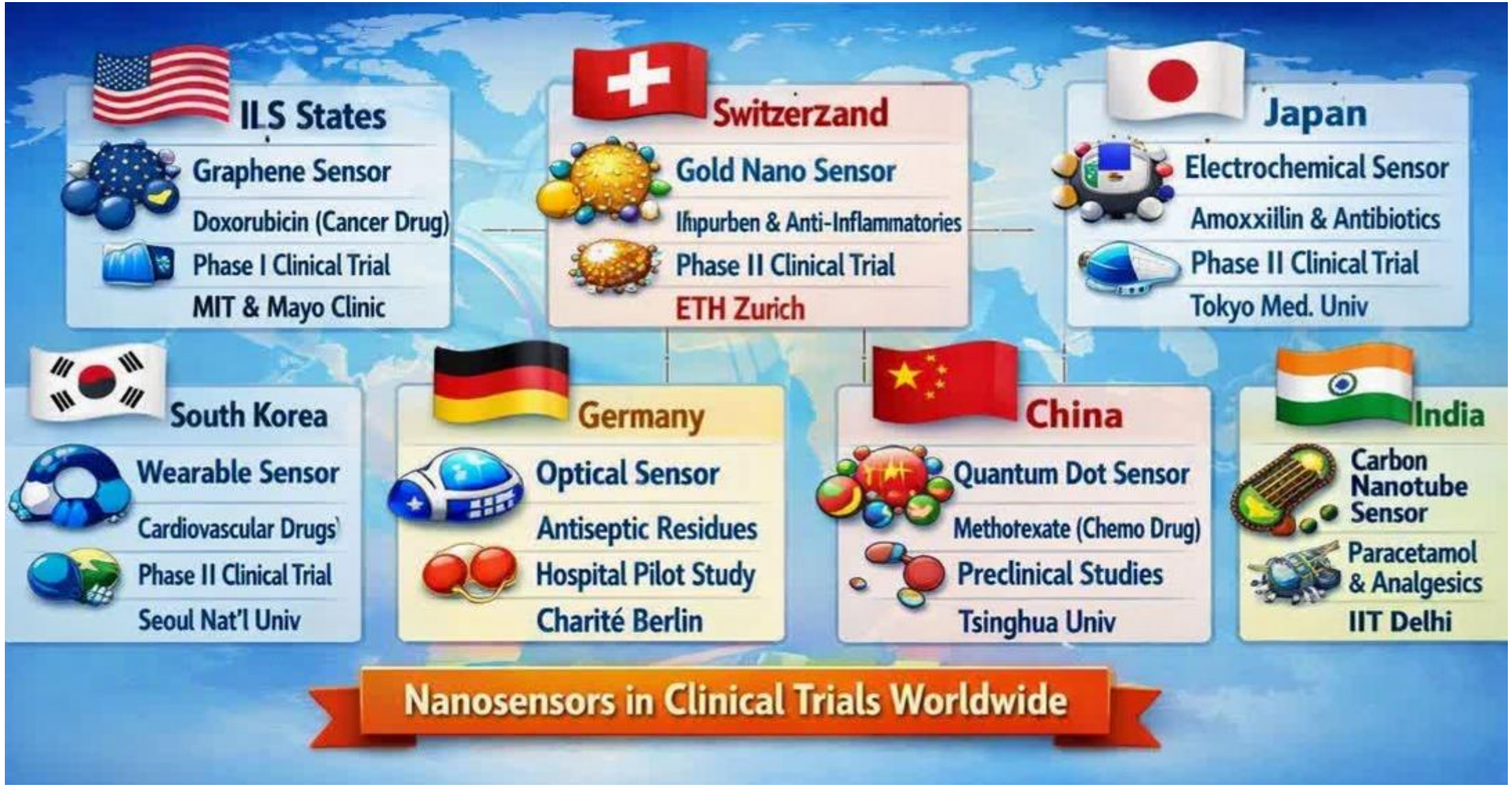
Nanomaterials enhance sensing through surface, electronic, catalytic and optical effects.

Electrochemical nanobiosensors are especially attractive for portable and point-of-care applications.

Wearable and microneedle platforms may enable repeated or continuous monitoring.

The major challenge is translation from laboratory performance to reliable clinical measurement.

Country	Type of Nanosensor	Target Drug / Biomarker	Application Area	Clinical Stage	Institution / Hospital
United States	Graphene-based electrochemical sensor	Doxorubicin (anticancer drug)	, Real-time blood monitoring	Phase I Clinical Trial	MIT & Mayo Clinic
Switzerland	Plasmonic gold nanoparticle sensor	Ibuprofen & anti-inflammatory drugs	Rapid plasma detection	Phase II Clinical Trial	ETH Zurich
Japan	Electrochemical nanosensor	Amoxicillin & antibiotics	Therapeutic drug monitoring	Phase I Clinical Trial	Tokyo Medical University
Germany	Optical nanosensor	Antiseptic drug residues	Blood sample analysis	Pilot Hospital Testing	"Charité Hospital, Berlin"
China	Quantum dot nanosensor	Methotrexate (chemotherapy drug)	Cellular uptake studies	Preclinical (in vitro)	Tsinghua University


ILS States
Graphene Sensor
Doxorubicin (Cancer Drug)
Phase I Clinical Trial
MIT & Mayo Clinic
Switzerzand
Gold Nano Sensor
Ifнpurben & Anti-Inflammatories
Phase II Clinical Trial
ETH Zurich
Japan
Electrochemical Sensor
Amoxxiilin & Antibiotics
Phase II Clinical Trial
Tokyo Med. Univ
South Korea
Wearable Sensor
Cardiovascular Drugs
Phase II Clinical Trial
Seoul Nat'l Univ
Germany
Optical Sensor
Antiseptic Residues
Hospital Pilot Study
Charité Berlin
China
Quantum Dot Sensor
Methotexate (Chemo Drug)
Preclinical Studies
Tsinghua Univ
India
Carbon Nanotube Sensor
Paracetamol & Analgesics
IIT Delhi
Nanosensors in Clinical Trials Worldwide

Selected References

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Thank You

Questions & Discussion