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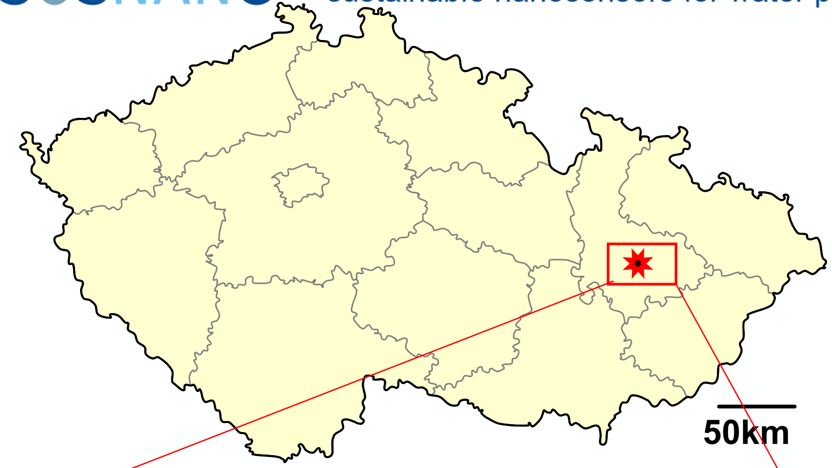
Antibiotic Sensing in the 21st Century: Innovations and Future Directions

Petr Jakubec

Antibiotic Sensing in the 21st Century: Innovations and Future Directions



CATRIN
Czech Advanced Technology and Research Institute

Regional Centre of Advanced Technologies and Materials (RCPTM)

Institute of Molecular and Translational Medicine (IMTM)

Centre of the Region Haná for Biotechnological and Agricultural Research (CR Haná)

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Antibiotic Sensing in the 21st Century: Innovations and Future Directions

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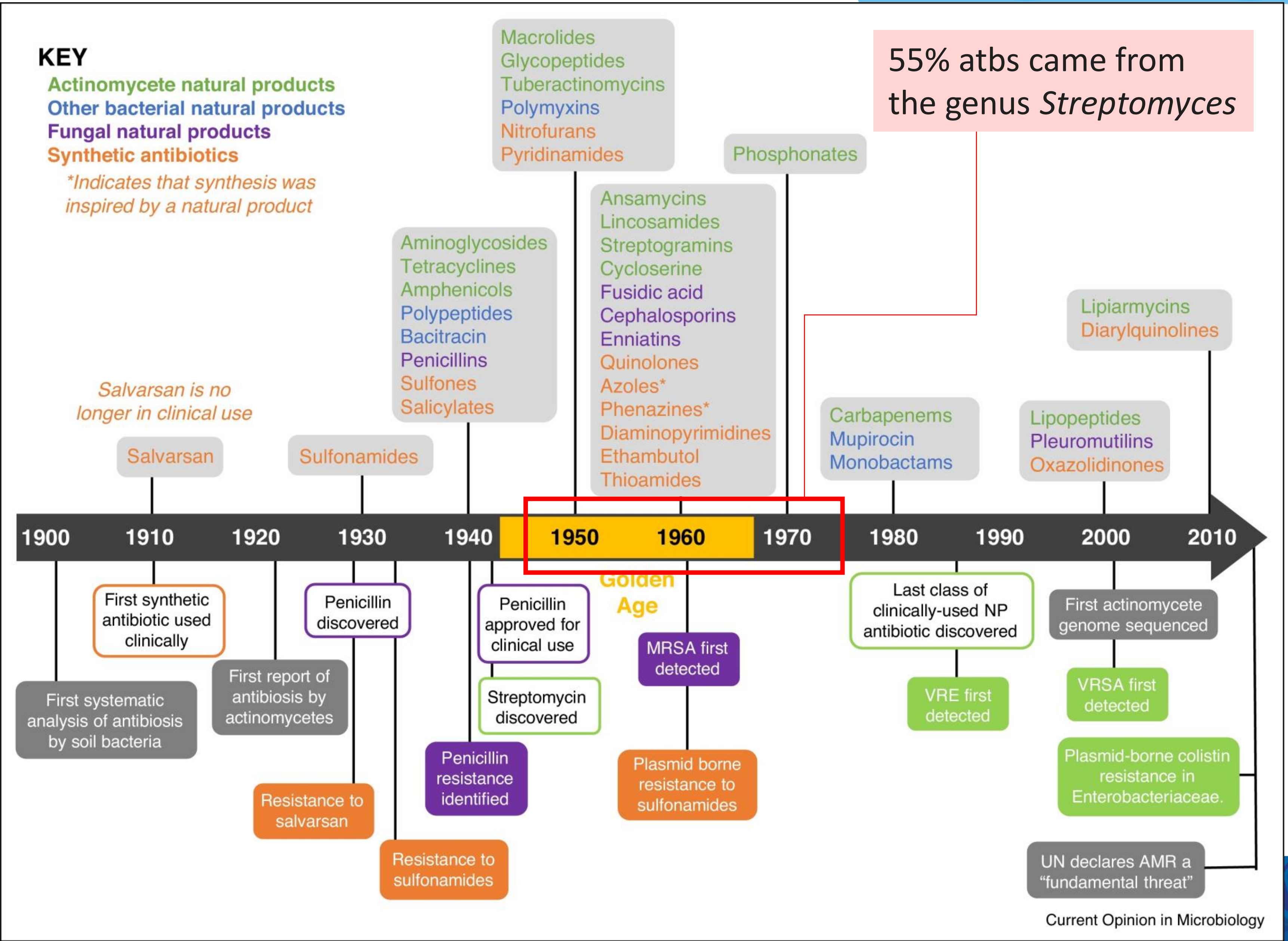
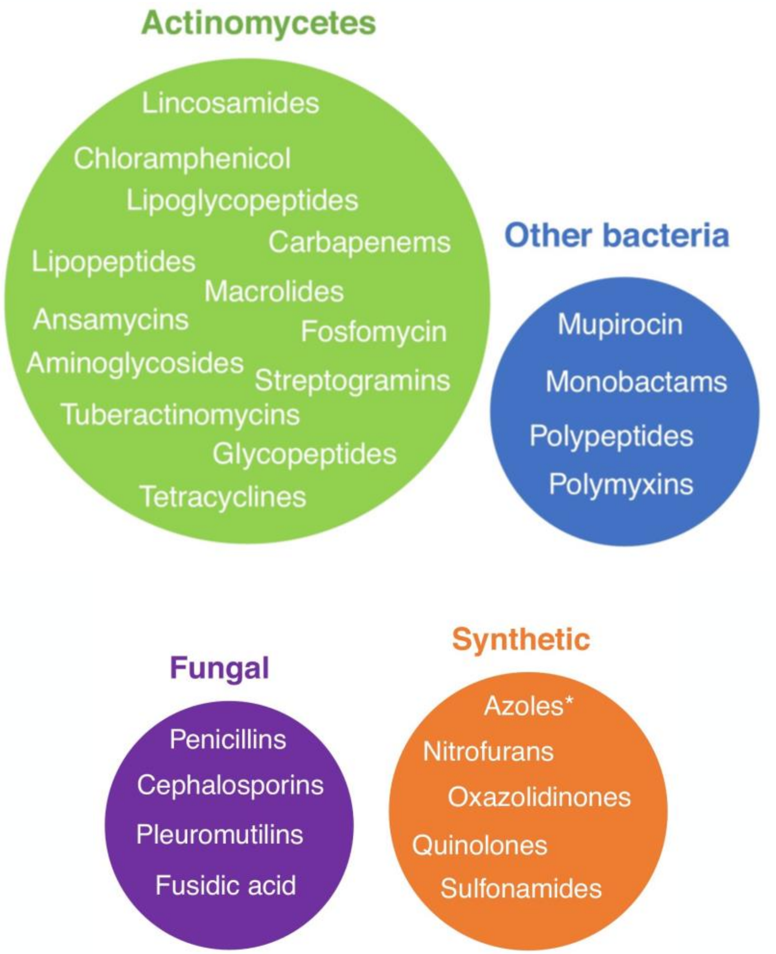




Hutchings M. I. et al. Current Opinion in Microbiology 51, 2019.

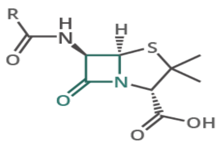
An overview of classes of antibiotics

COMPOUND INTEREST

Key: Commonly act as **bacteriostatic agents**, restricting growth and reproduction | Commonly act as **bactericidal agents**, causing bacterial cell death

B-lactams

Most widely used antibiotics in the NHS



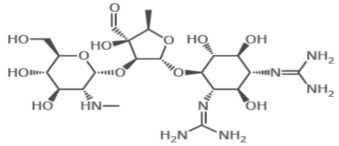
All contain a beta-lactam ring

Examples: Penicillins (shown) such as amoxicillin and flucloxacillin; Cephalosporins such as cefalexin.

Mode of action: Inhibit bacteria cell wall biosynthesis.

Aminoglycosides

Family of over 20 antibiotics



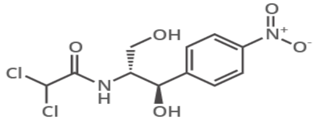
All contain aminosugar substructures

Examples: Streptomycin (shown), neomycin, kanamycin, paromomycin.

Mode of action: Inhibit bacteria protein synthesis, causing cell death.

Chloramphenicol

Commonly used in low-income countries



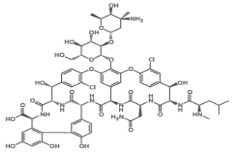
Distinct individual compound

Not a first line drug in developed nations (except for conjunctivitis) due to resistance and safety concerns.

Mode of action: Inhibits synthesis of bacteria proteins, preventing growth.

Glycopeptides

Common drugs of last resort



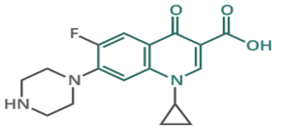
A carbohydrate linked to a peptide

Examples: Vancomycin (shown), teicoplanin.

Mode of action: Inhibit bacteria cell wall biosynthesis.

Quinolones

Resistance evolves rapidly



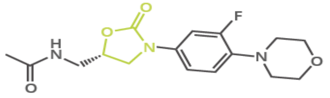
Contain fused aromatic rings with an attached carboxylic acid group

Examples: Ciprofloxacin (shown), levofloxacin, trovafloxacin.

Mode of action: Interfere with bacteria DNA replication and transcription.

Oxazolidinones

Resistance evolves rapidly



All contain 2-oxazolidone somewhere in their structure

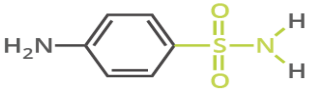
Examples: Linezolid (shown), posizolid, tedizolid, cycloserine.

Mode of action: Inhibit synthesis of bacteria proteins, preventing growth.

Discovery — 1930 — 1940 — 1950 — 1960 — 1970 — 1980

Sulfonamides

First commercial antibiotics



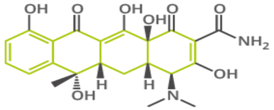
All contain the sulfonamide group

Examples: Prontosil, sulfanilamide (shown), sulfadiazine, sulfisoxazole.

Mode of action: Prevent bacterial growth and multiplication.

Tetracyclines

Less popular due to development of resistance



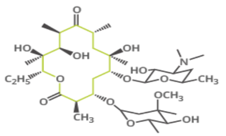
Contain four adjacent cyclic hydrocarbonrings

Examples: Tetracycline (shown), doxycycline, limecycline, oxytetracycline.

Mode of action: Inhibit synthesis of bacteria proteins, preventing growth.

Macrolides

Second most prescribed antibiotics in the NHS



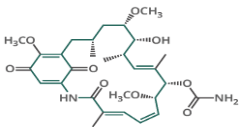
All contain a 14-, 15-, or 16-membered macrolide ring

Examples: Erythromycin (shown), clarithromycin, azithromycin.

Mode of action: Inhibit bacteria protein synthesis, causing cell death.

Ansamycins

Also show antiviral activity



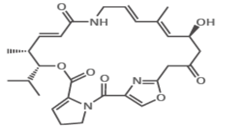
Contain aromatic ring with hydrocarbon bridge

Examples: Geldanamycin (shown), rifamycin, naphthomycin.

Mode of action: Inhibit bacterial RNA synthesis, leading to cell death.

Streptogramins

Two groups of antibiotics that act synergistically



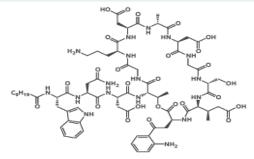
Combination of two structurally differing compounds, from groups denoted A & B

Examples: Pristinamycin IIA (shown), Pristinamycin IA.

Mode of action: Inhibit bacteria protein synthesis, causing cell death.

Lipopeptides

Instances of resistance are rare



All contain a lipid bonded to a peptide

Examples: Daptomycin (shown), surfactin.

Mode of action: Disrupt cell membrane functions, causing cell death.

www.compoundchem.com

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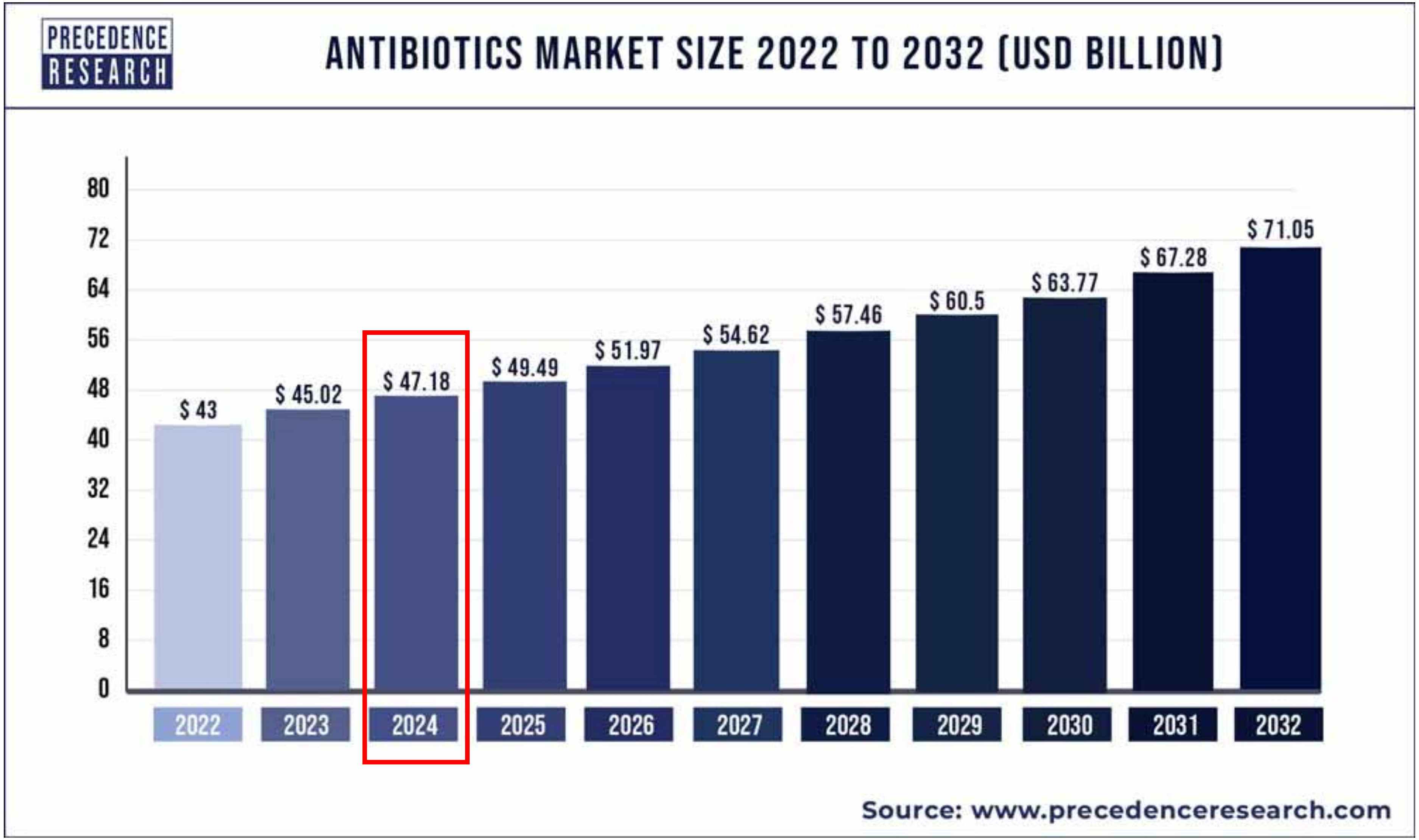

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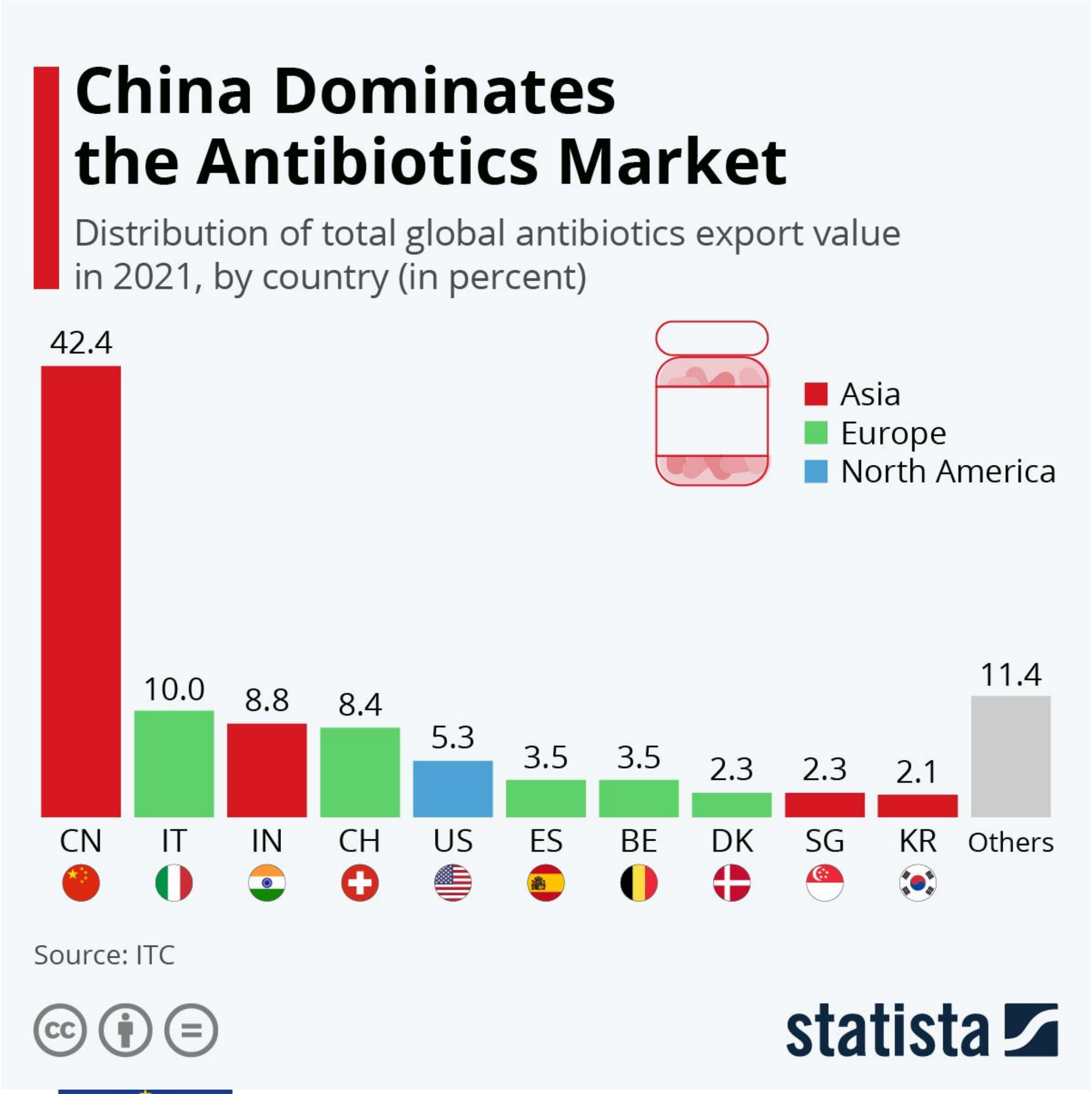

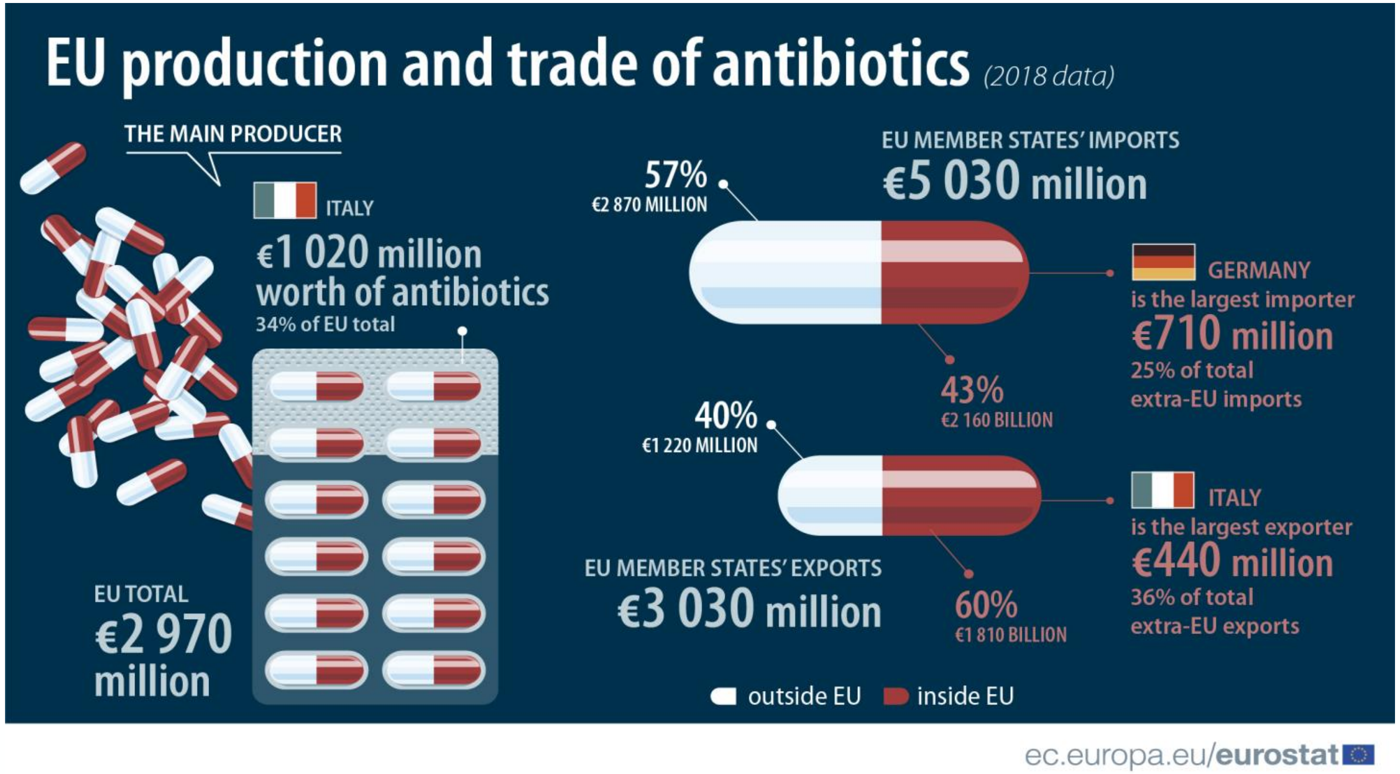

https://www.statista.com/chart/27709/distribution-of-global-antibiotics-export-value-by-country/

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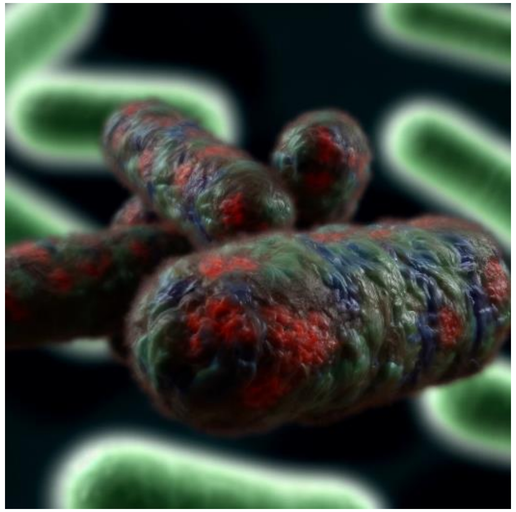
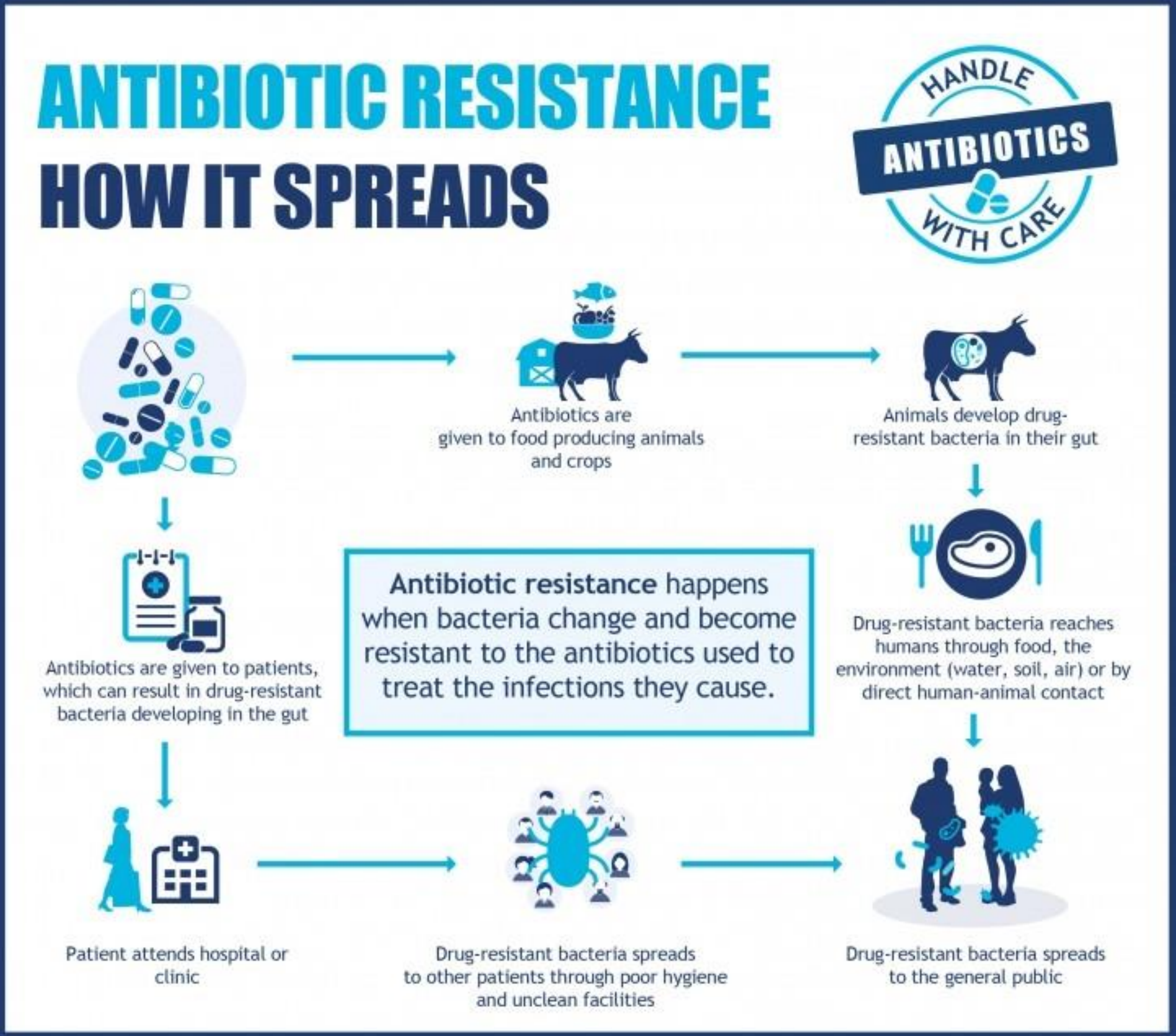
https://amr-review.org/


TACKLING DRUG-RESISTANT INFECTIONS GLOBALLY:
FINAL REPORT AND RECOMMENDATIONS

THE REVIEW ON ANTIMICROBIAL RESISTANCE
CHAIRED BY JIM O'NEILL

O'Neill report: without urgent action 10 million people a year will die from drug resistant infections by 2050





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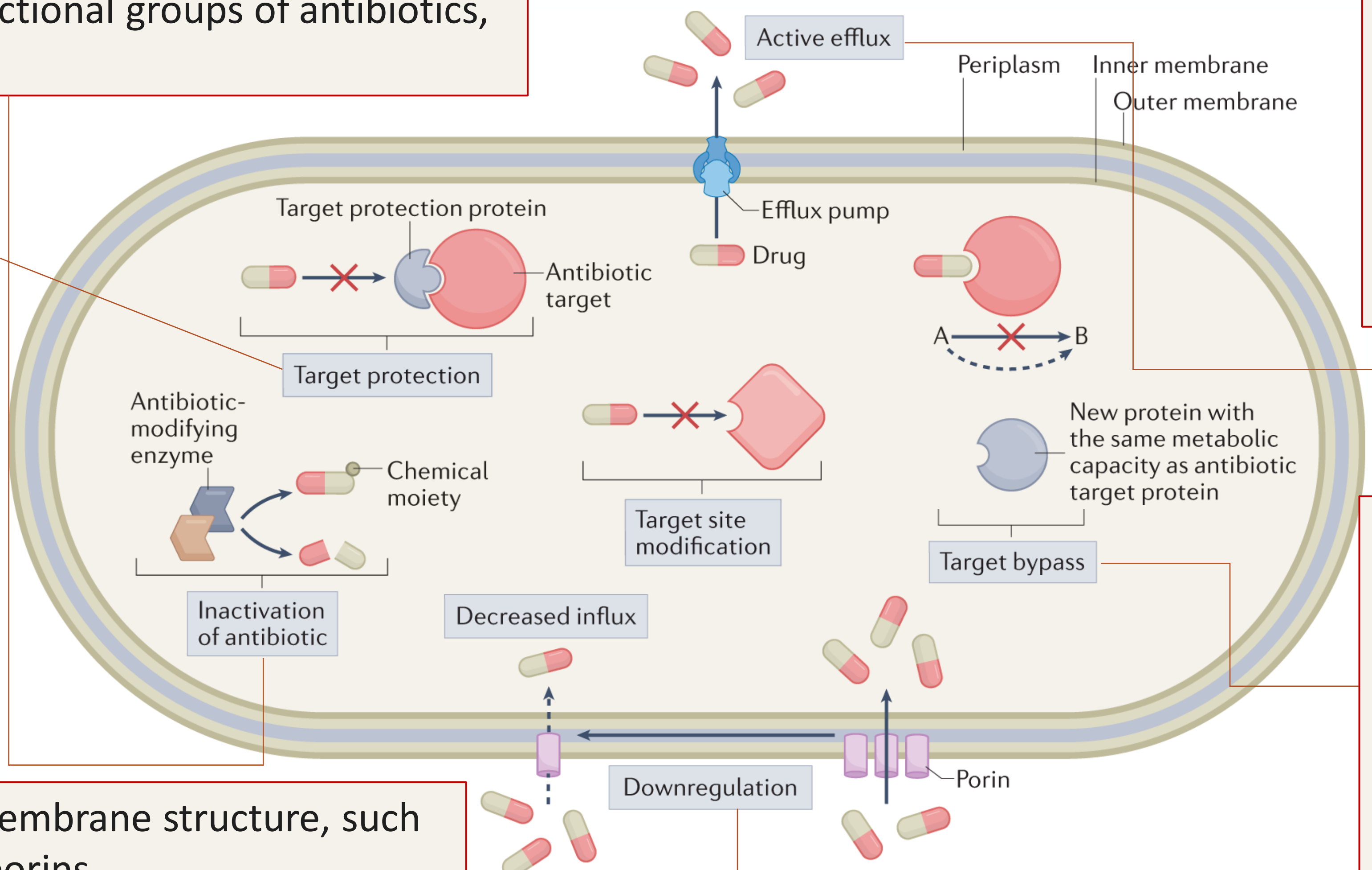
Enzymes hydrolyze the functional groups of antibiotics, rendering them ineffective

Involves changing the antibiotic's target site to reduce or prevent binding of the antibiotic (via mutations, enzymatic alterations).

Involves transmembrane efflux pumps that actively transport antibiotics out of the bacterial cell



A target protection protein physically associates with the antibiotic's target site, protecting it from being inhibited by the antibiotic.

Changes in the bacterial membrane structure, such as the downregulation of porins

Darby E. M. et al. Nature Reviews Microbiology 21, 2023

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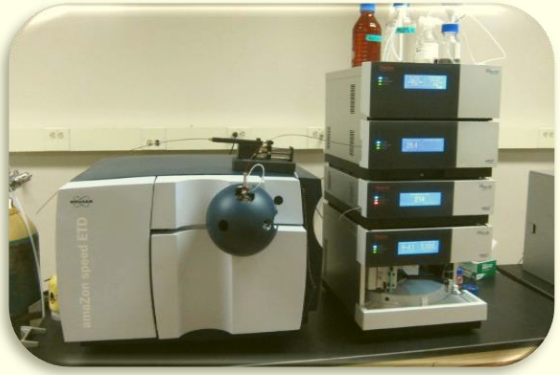
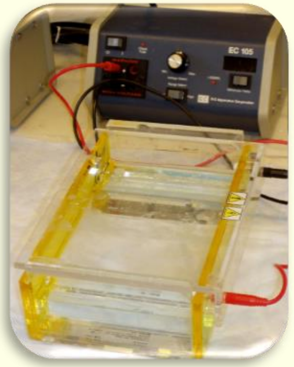
GC

HPLC/MS

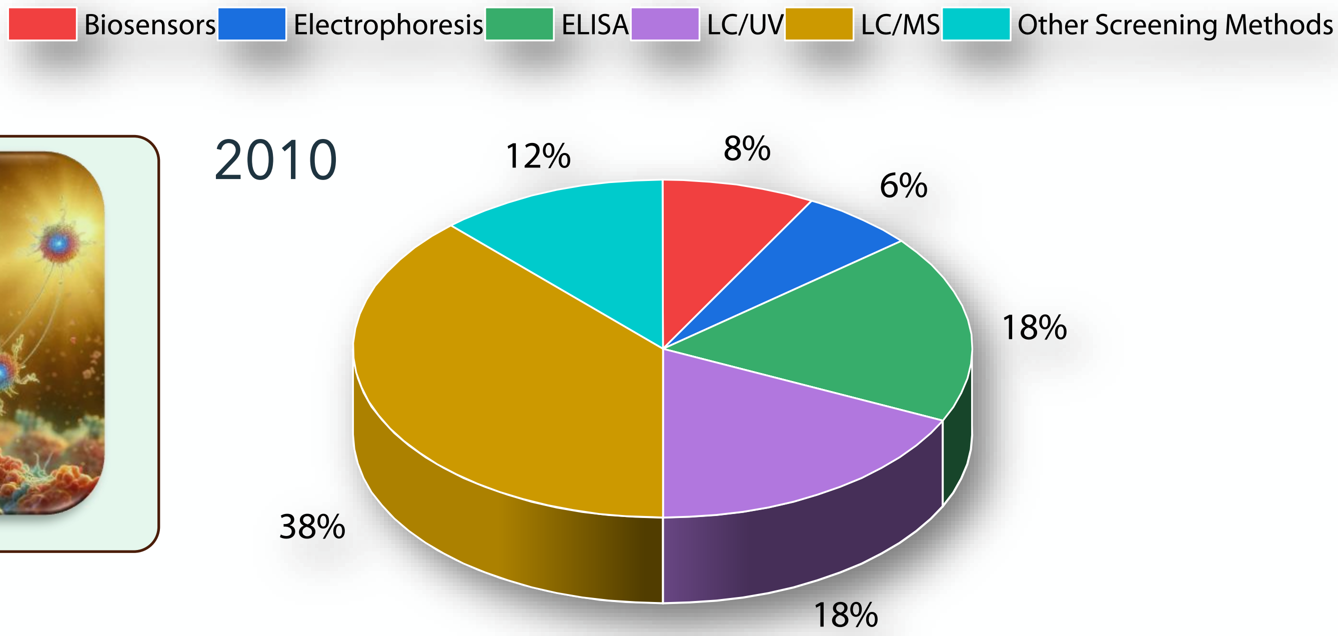


CE



TLC

Immunoassay



Pauter K. et al. Molecules 25, 2020

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TLC and Immunoassay images were generated by OpenAI's DALL·E, GPT-4, accessed on [10/04/2024], rest is available from wikipedia under common CC licences

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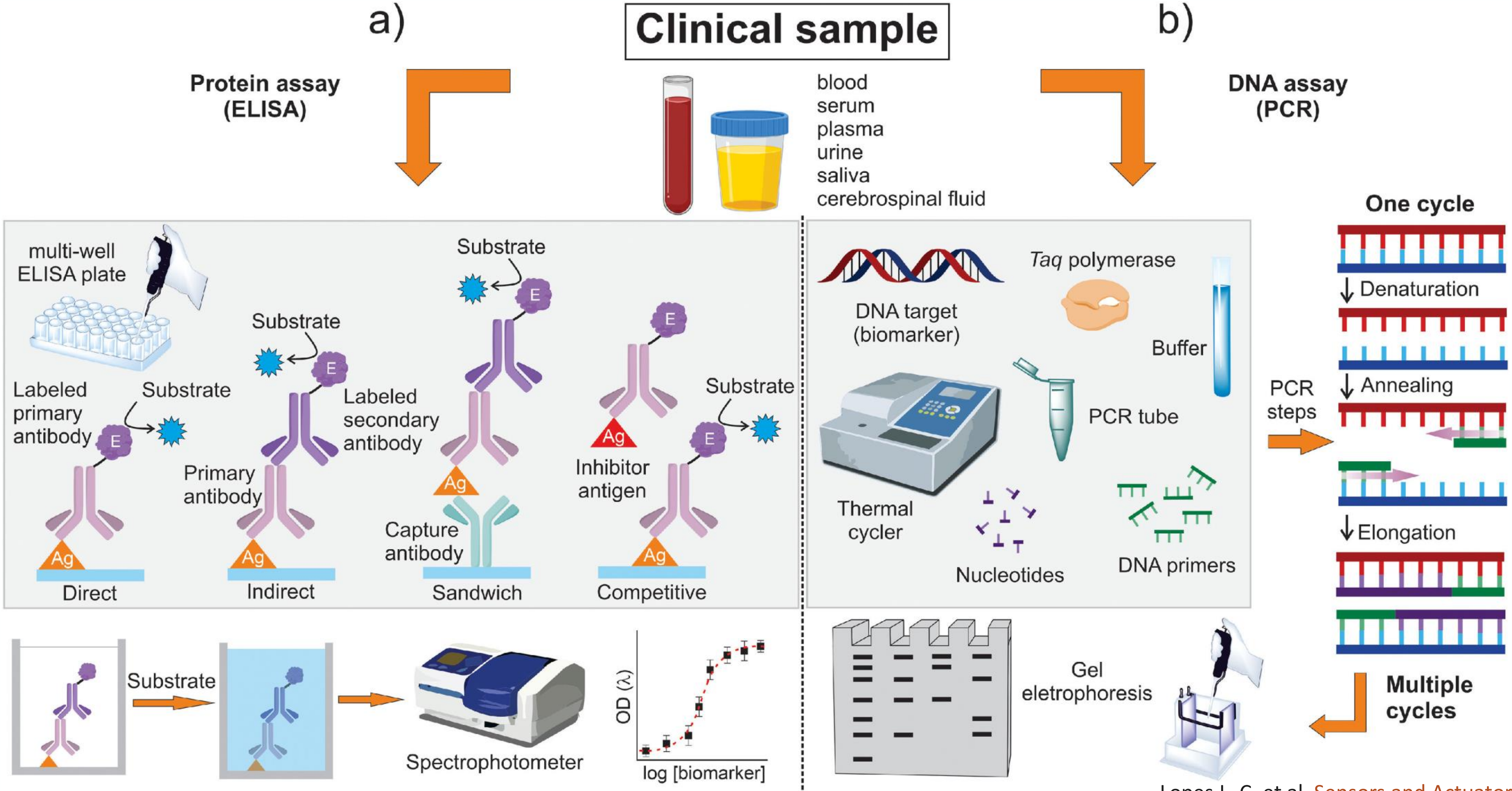
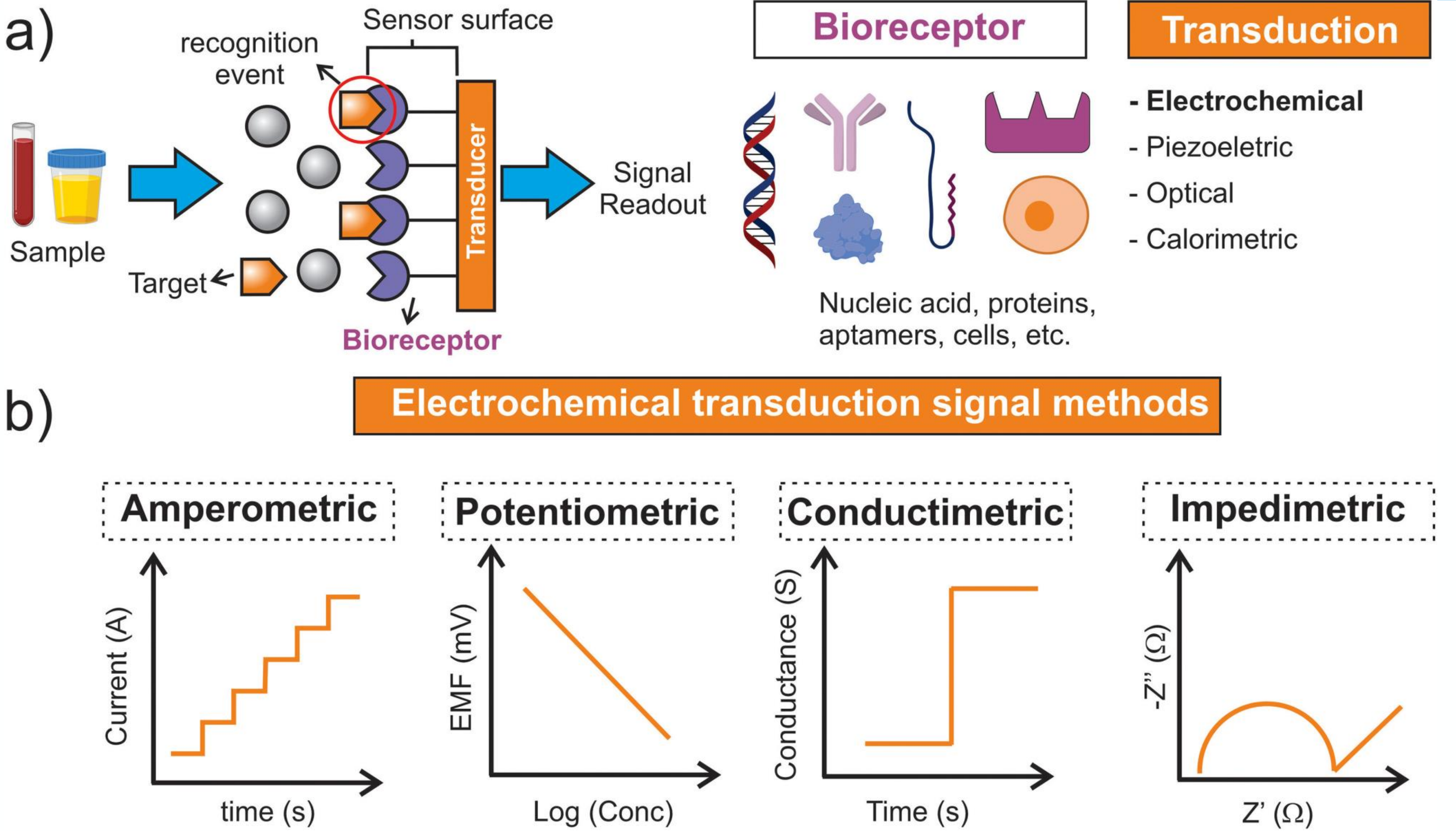


Lopes L. C. et al. Sensors and Actuators Reports 4, 2022



Lopes L. C. et al. Sensors and Actuators Reports 4, 2022

Table 2
Representative examples of recent developed electrochemical biosensors for the detection of antibiotic residues.

Detection method	Strategy	Bioreceptor	Nanomaterial	Target antibiotic	LOD (ng ml^{-1})	Linear range (ng ml^{-1})	Assay time	sample
DPV	Exonuclease III-powered DNA walking machine	Aptamer DNAzyme	–	Ampicillin	2.6×10^{-4}	3.5×10^{-4}-3.5	nr[a]	Milk
DPV	Electrode modification with MIP-coated AuNPs	MIP	AuNPs	Tetracycline	288.9	444.4–8888.7	nr	Shrimp
Amperometry	Antibody coupled on AuNPs/Dendrimer/CdS nanoparticles modified conducting polymer	Antibody	AuNPs CdS QDs	Chloramphenicol	0.045	0.05–0.95	nr	Beef, pork and chicken
Amperometry	Graphene sheet-nafion/thionine/Pt nanoparticles modified electrode	Antibody	PtNPs	Kanamycin	0.006	0.01–12.0	nr	Chicken tissues
Amperometry	Genetically modified whole-cell based amperometric biosensor	Whole-cell	–	Tetracycline	2.6 110	0.0–4.4 44.4–444.4	nr	Milk
Amperometry	A graphite-rod electrode modified with protein G for the immobilization of antibody	Antibody	–	Sulfapyridine	2.4	5–55	10 min	Milk
DPV	Aptasensor 1 was fabricated based on ferrocene (Fc) and AuNPs nanocomposite, the aptasensor 2 was prepared based on CNFs and AuNPs nanocomposite	Aptamer	AuNPs CNFs	Tetracycline	0.33	0.01–1000	60 min	Milk
DPV	Aptamer immobilization on the surface of SPCE modified with an alginate film containing rGO and MNPs	Aptamer	MNPs rGO	Tetracycline	0.27	0.44–2222.2	nr	Food sample
DPV	Sandwich-type electrochemical aptasensor based on GR-3D Au and aptamer-AuNPs-HRP	Aptamer	AuNPs Gr	Oxytetracycline	4.98×10^{-4}	5×10^{-4}-2000	110 min	Honey
DPV	Target-aptamer binding trigged quadratic recycling amplification	Aptamer	–	Ampicillin	3.8×10^{-4}	1.7×10^{-3}-3.49	nr	Milk
Electrochemical impedance spectroscopy (EIS)	Electrostriction of an antibody-terminated thiol layer self-assembled on a gold electrode surface	Antibody	–	Tetracycline	12.44	422.2–4444.3 4444.3–6.2×10^{4}	nr	Water
Square wave voltammetry (SWV)	Aptamer cocktail immobilization on gold screen-printed electrode for direct capture of tetracycline	Aptamer	–	Tetracycline	0.0073	0.01–1000	nr	Honey
DPV	Target-triggered ssDNA adsorption on molybdenum sulfide (MoS_2) nanosheet and enzymatic signal amplification	Aptamer	MoS_2 nanosheets	Kanamycin	0.014	0.048–48	nr	Eye drop

Majdinasab M. et al. TrAC Trends in Analytical Chemistry 127, 2020

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Key Factors for State-of-the-Art Biosensors

1. Bioreceptor Sensitivity and Specificity

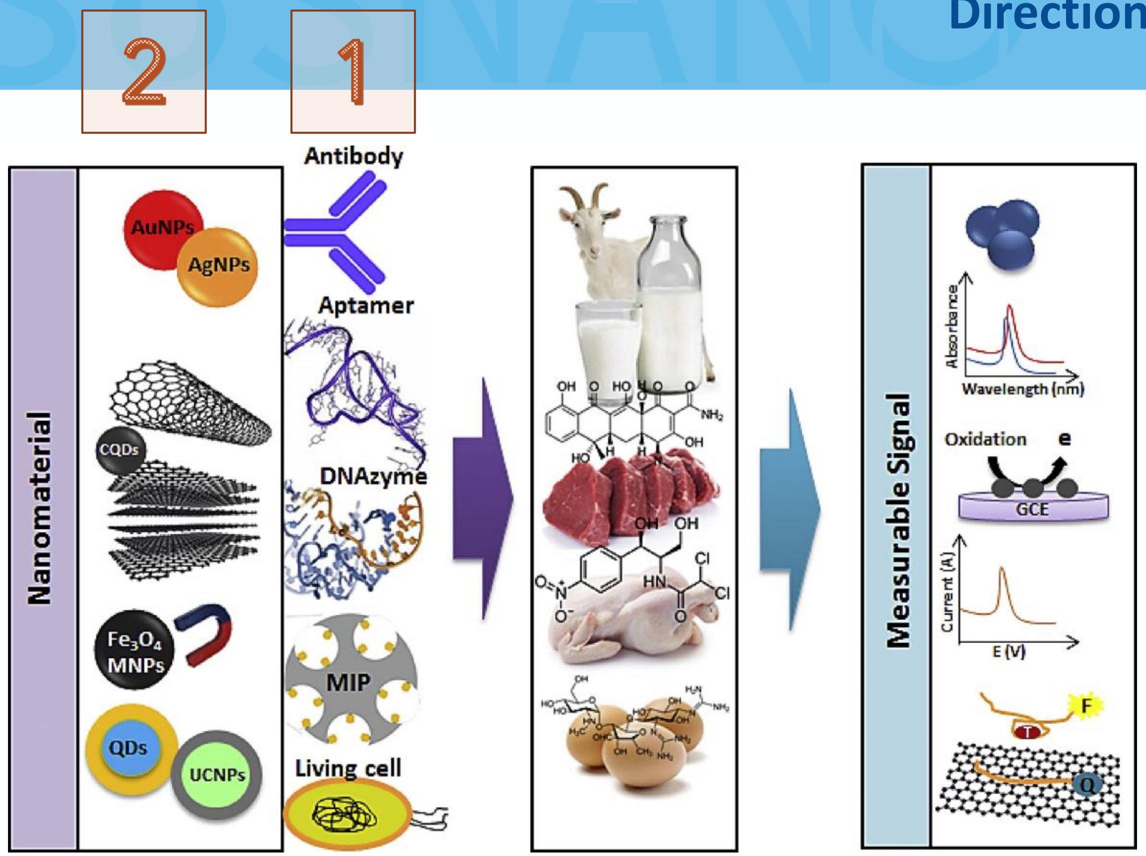
- Bioreceptor Engineering: Enhancing the selectivity and affinity of bioreceptors via genetic engineering.
- Surface Chemistry: Optimizing the surface to which bioreceptors are attached can enhance the interaction with the target analyte, improving sensitivity and specificity.

2. Materials Science

- Nanomaterials: Utilizing nanomaterials like graphene, carbon nanotubes, and quantum dots
- Hydrogels and Biocompatible Materials: These can improve the interface between the biosensor and biological systems, enhancing the stability and longevity of the sensor in vivo.

3. Transducer Technology

- Signal Transduction Enhancement: Innovations in optical, electrochemical, and piezoelectric transducers.



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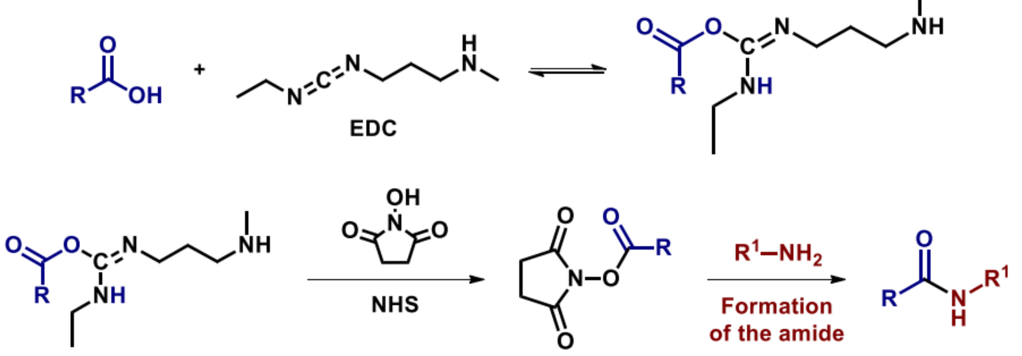
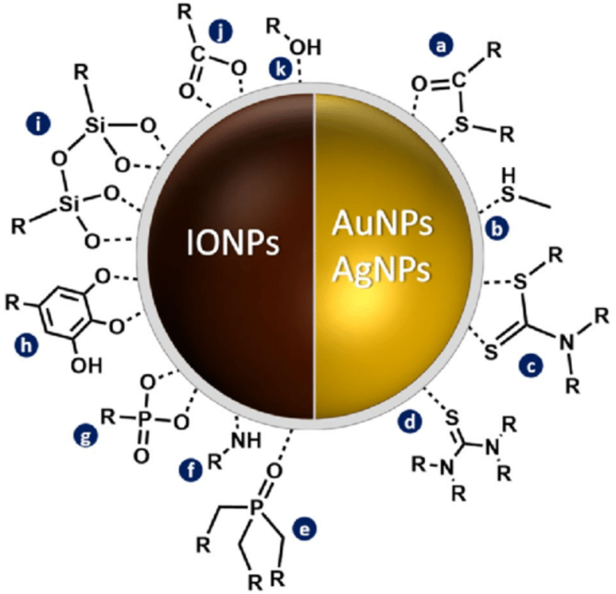
Iriarte-Mesa C. et al. Topic in Current Chemistry 378, 2020

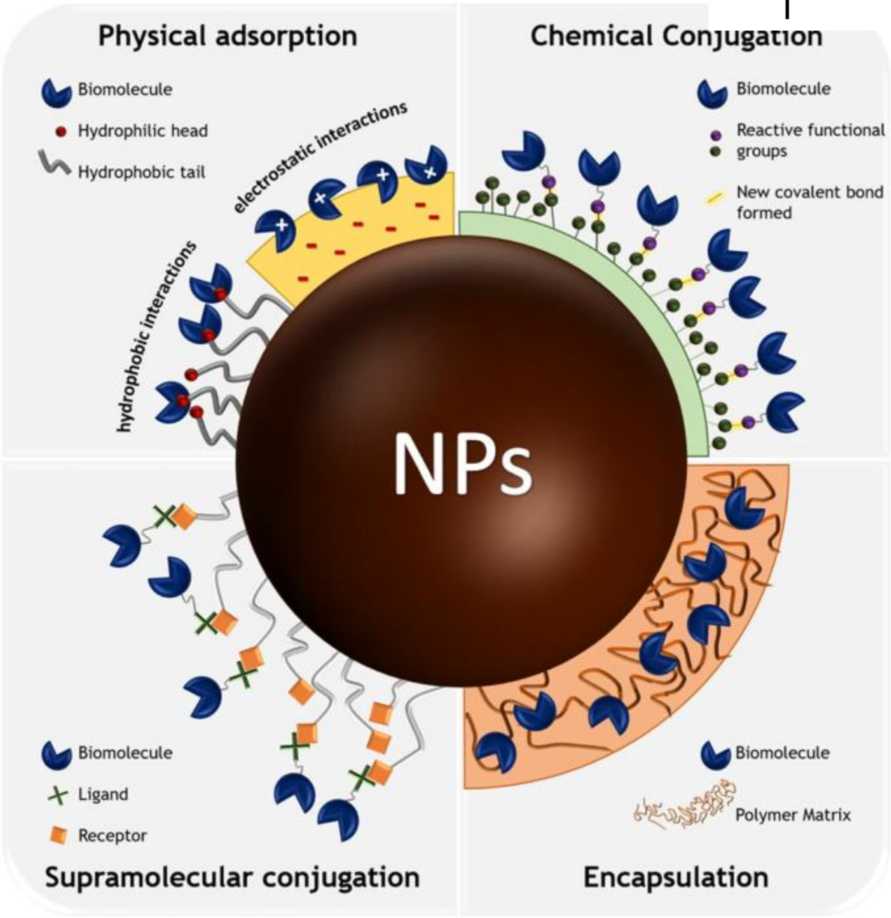


1+2. Bioreceptor Sensitivity and Specificity and Materials Science

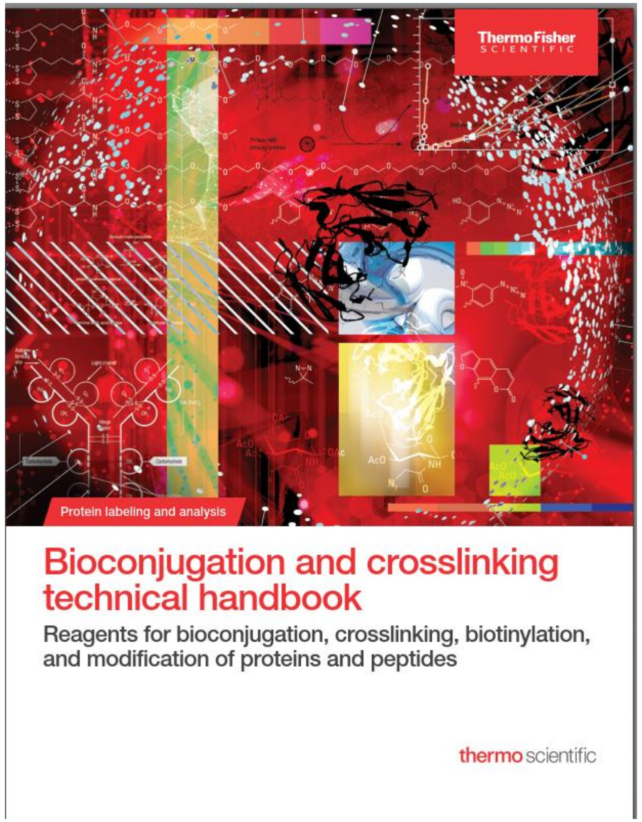
- Surface Chemistry: Optimizing the surface to which bioreceptors are attached can enhance the interaction with the target analyte, improving sensitivity and specificity.



a-k Functional groups with high affinity to the surfaces of NPs.
a Thioesters, b thiols, c dithiocarbamates, d thioureas, e phosphine oxides, f amines, g phosphates, h catechins, i trimethoxysilane, j carboxylic acids, k alcohols



Strategies of Bioconjugation



https://assets.thermofisher.com/TFS-Assets/BID/Handbooks/bioconjugation-technical-handbook.pdf

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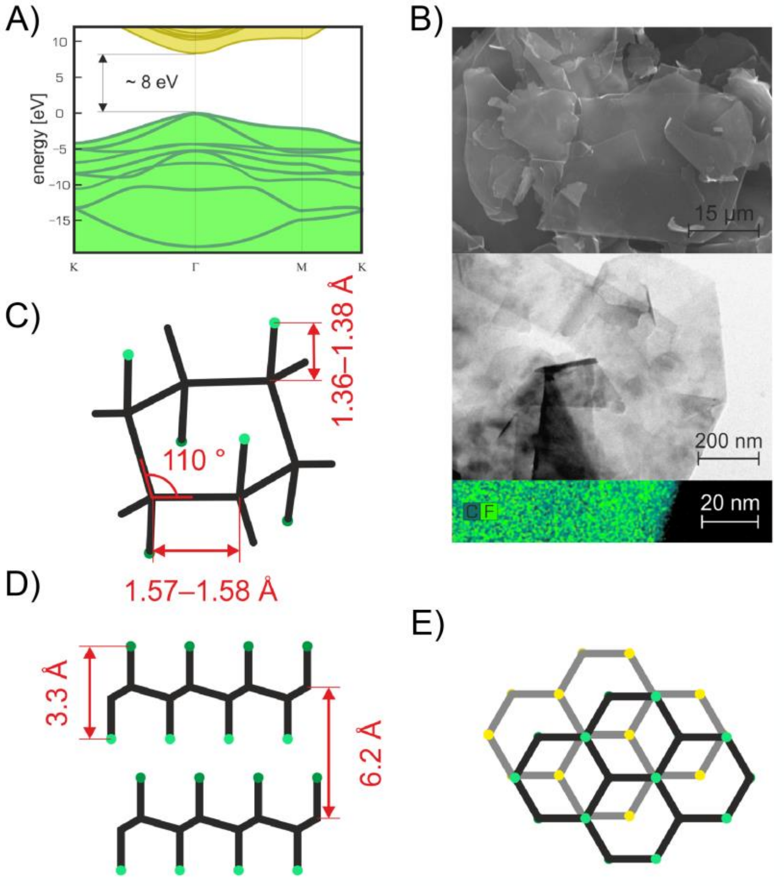
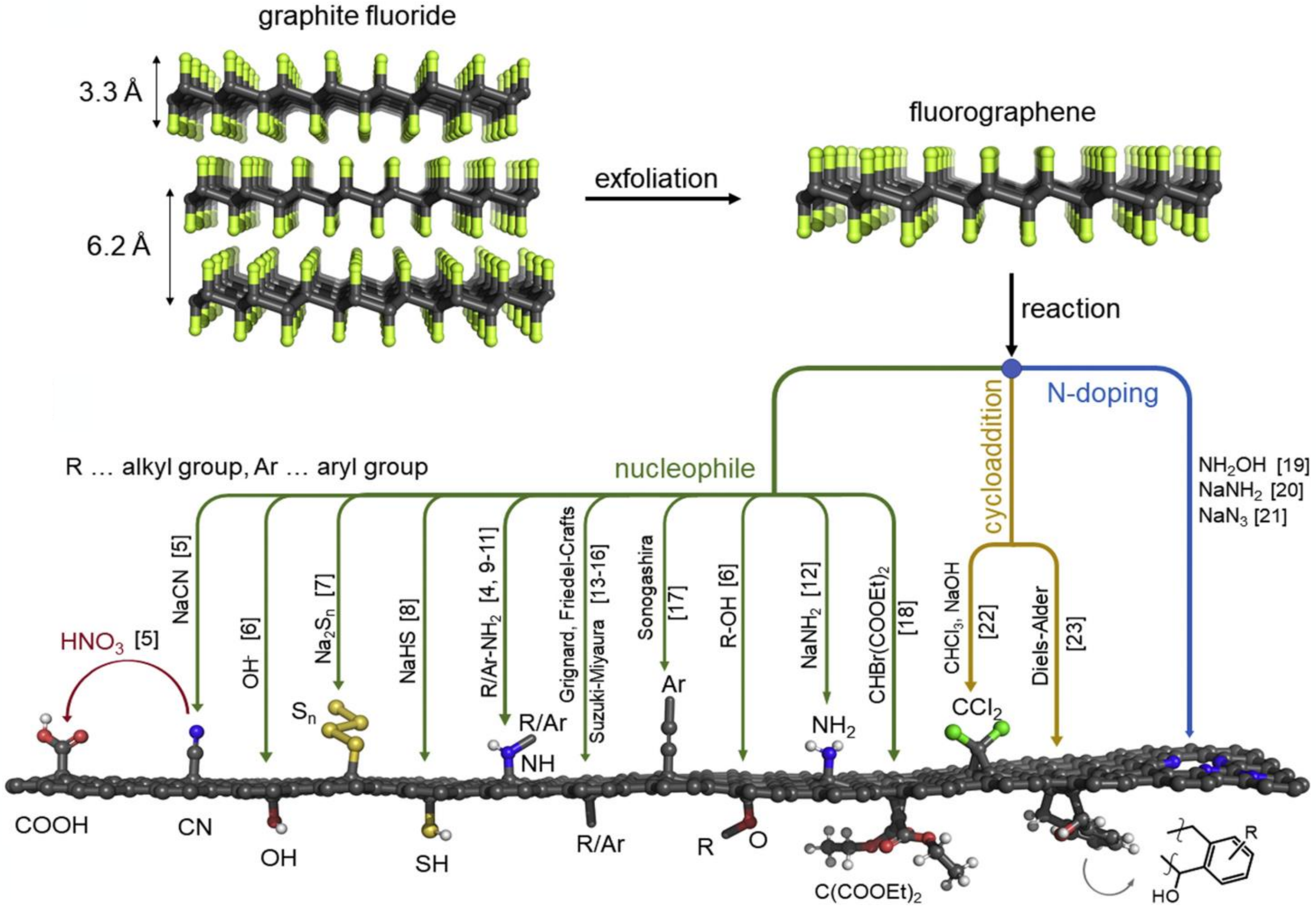
1+2. Bioreceptor Sensitivity and Specificity and Materials Science

- Surface Chemistry: Optimizing the surface to which bioreceptors are attached can enhance the interaction with the target analyte, improving sensitivity and specificity.



Chronopoulos D. D. et al. Applied Materials Today 9, 2017



Hrubý V. et al. Power Electronic Devices and Components 7, 2024

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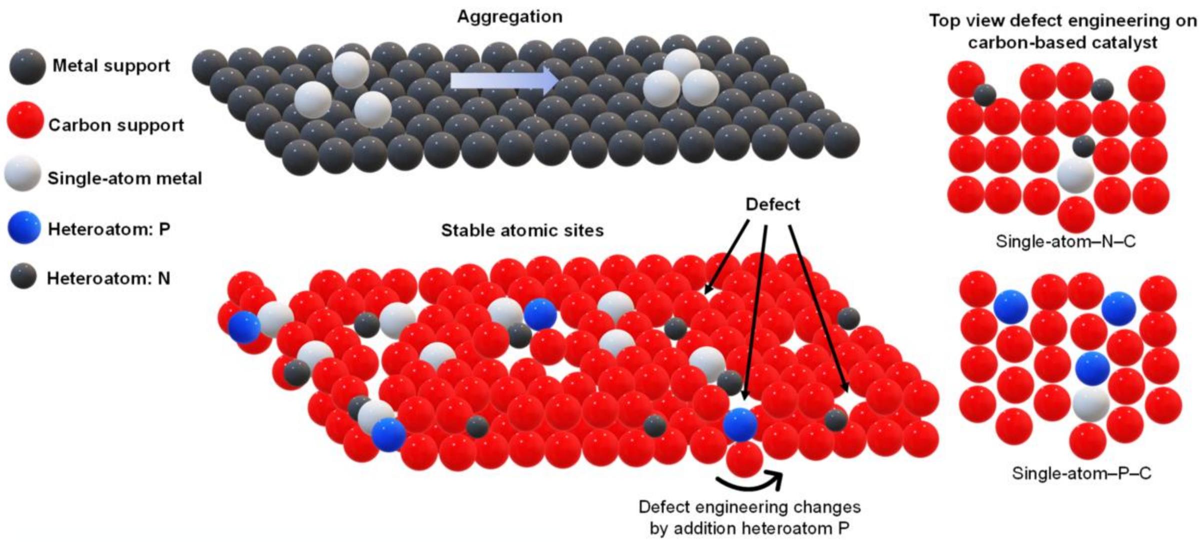
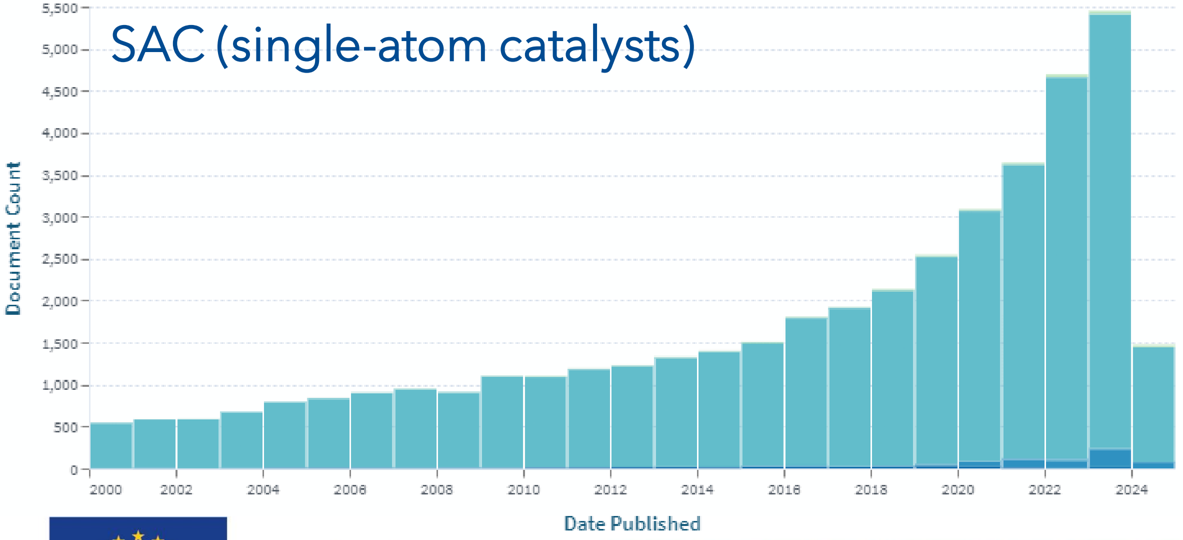
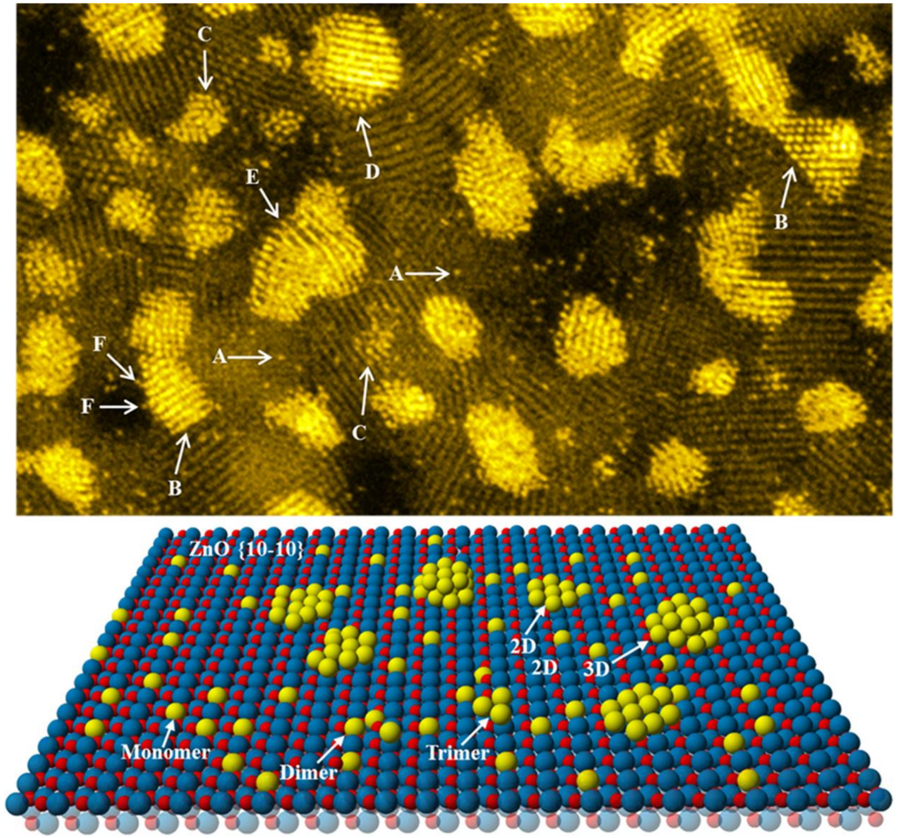


Asikin-Mijan N et al. Catalysts 11, 2021





Aberration-corrected HAADF-STEM image of a Pt/ZnO nanobelt model catalyst shows the presence of Pt single atoms (A), faceted Pt clusters (B), highly disordered Pt subnano clusters (C), reconstructed surface atoms of Pt nanoparticles (D), strained lattices of Pt (E), and highly unsaturated Pt atoms attached to the Pt nanocrystal (F);

Liu J. ACS Catalysis 7, 2017

https://www.lens.org/lens/search/scholar/analysis?q=single-atom-catalyst&dateFilterField=publishedYear&publishedYear.from=2000

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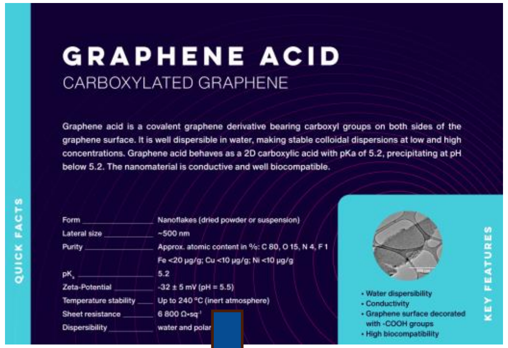

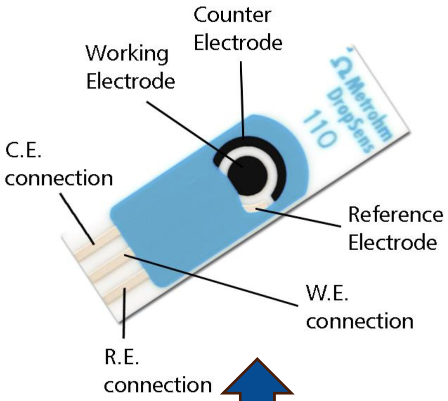

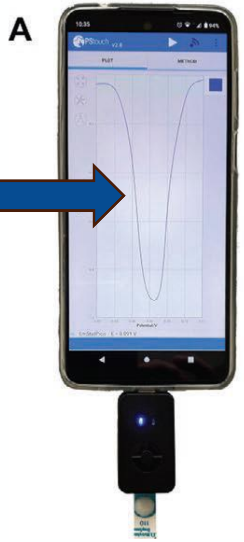

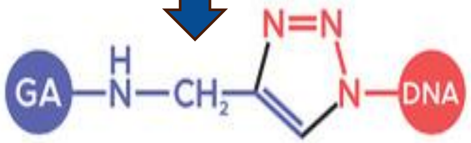

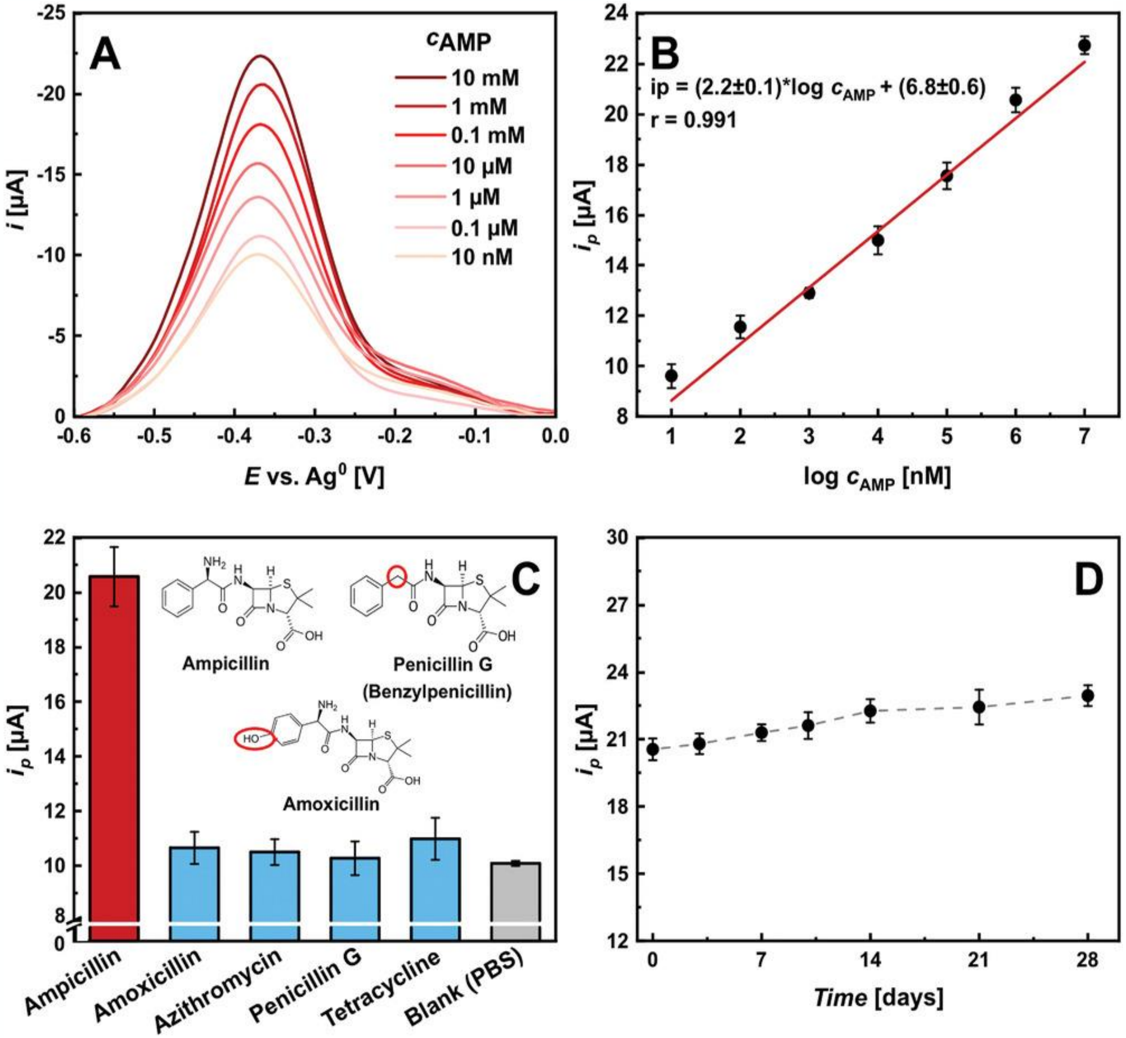

Highlights

- using click chemistry, an aptamer is immobilized and used as a platform for the **selective determination of antibiotic ampicillin** in real samples
- **detection limit of 1.36 nM** eight-fold lower than the European maximum residue limits in milk (4 µg L^{-1})
- the **storage stability of 4 weeks**, high selectivity among other antibiotics

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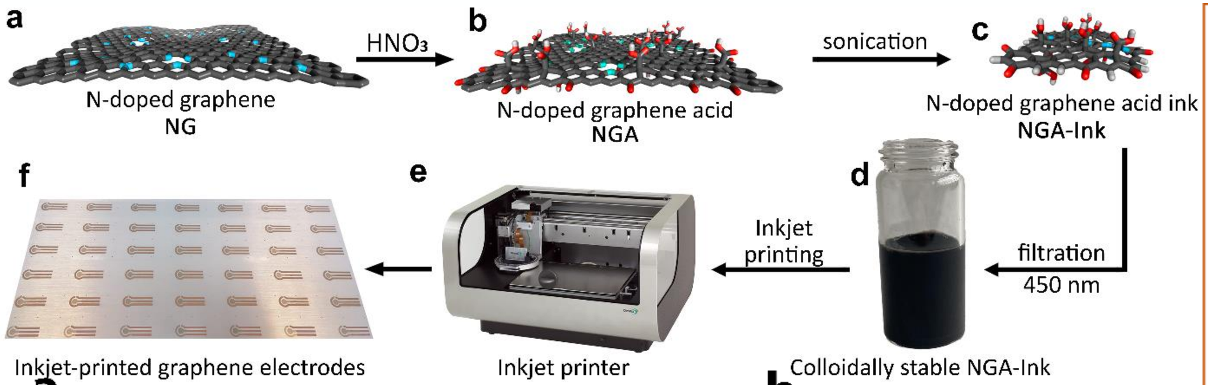
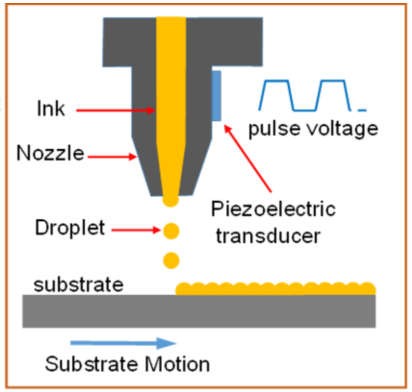
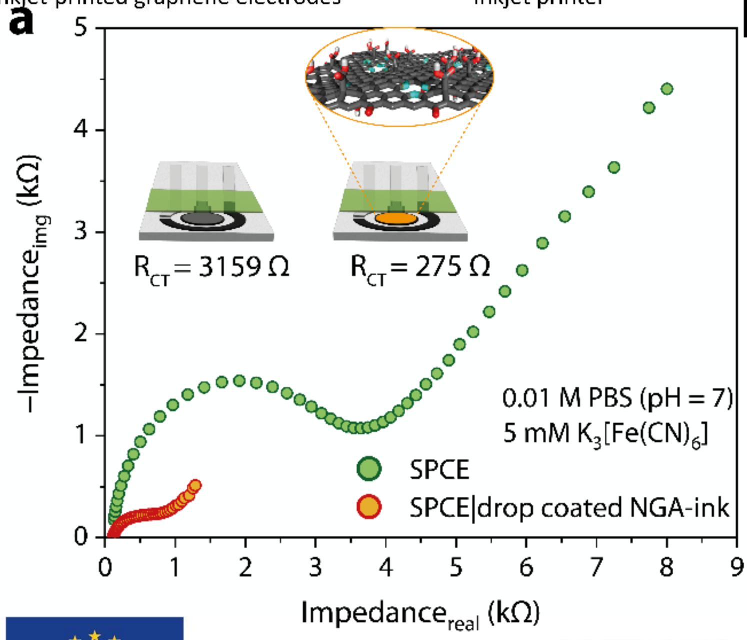
Antibiotic Sensing in the 21st Century: Innovations and Future Directions

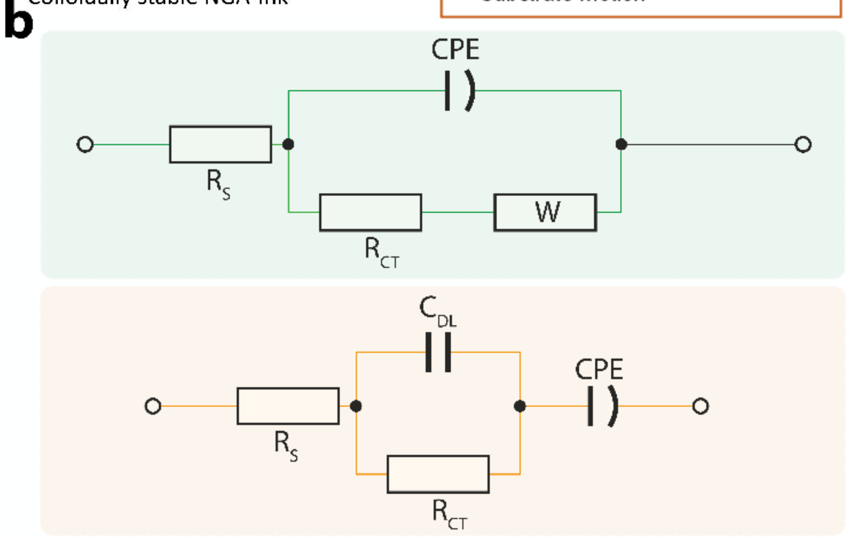
3. Transducer Technology

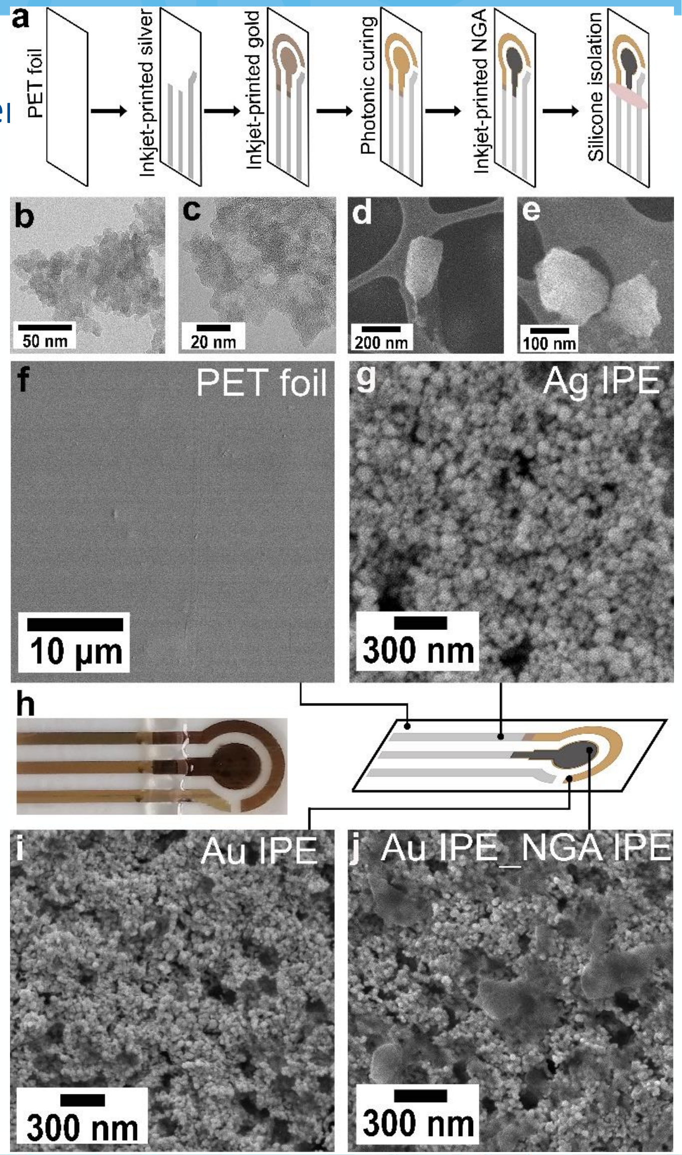
- Signal Transduction Enhancement: Innovations in optical, electrochemical, and piezoelectric transducer











Nalepa M.-A. et al. Biosensors and Bioelectronics, 2020

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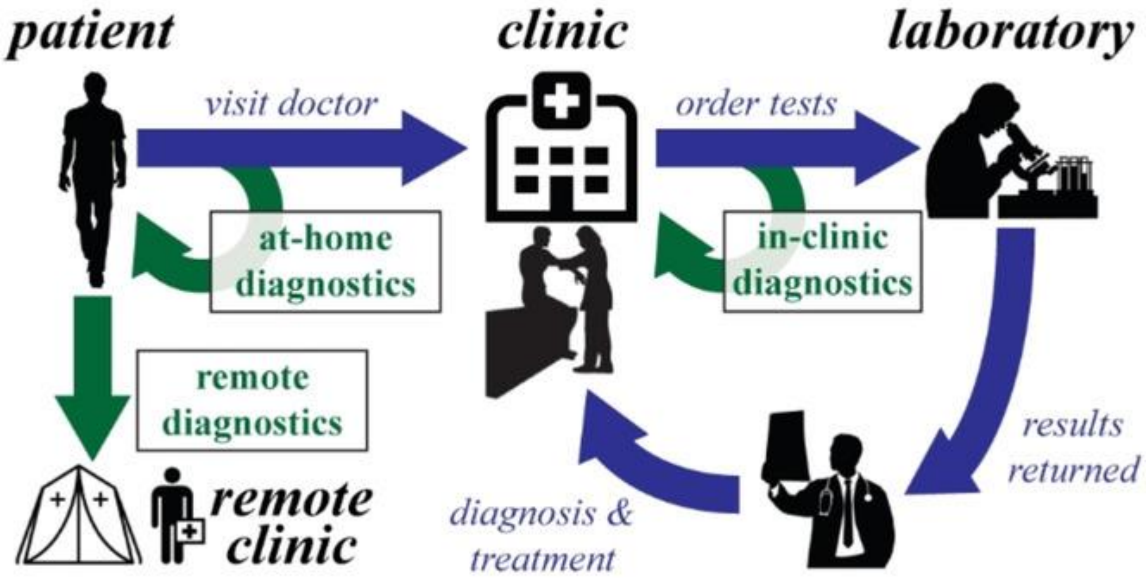
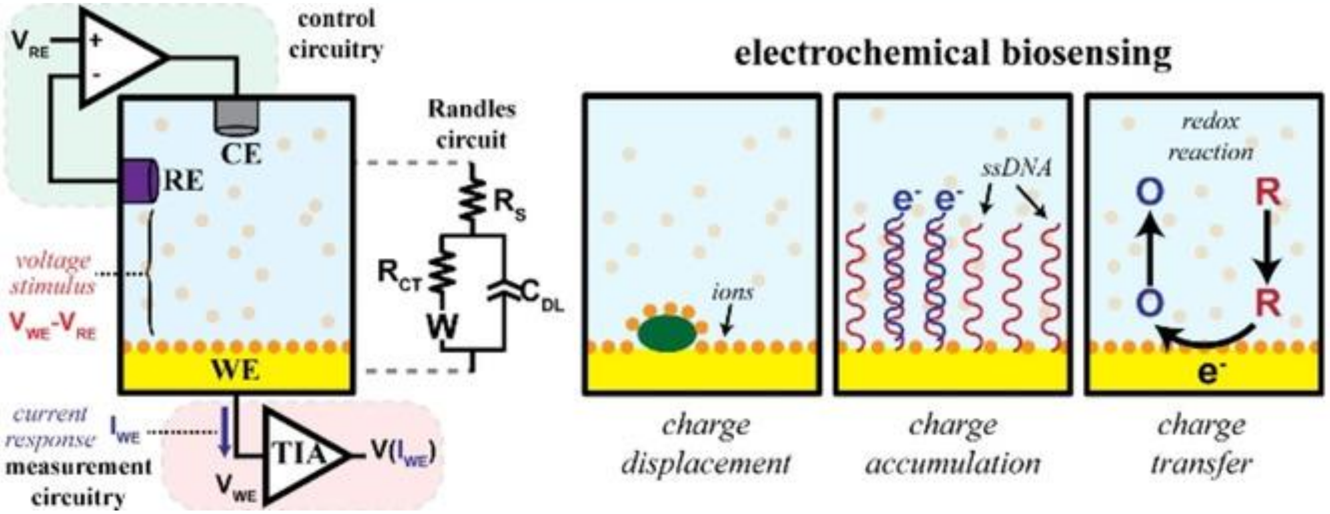
4. Data Analysis and Connectivity

- Data Processing Algorithms: Advanced algorithms and machine learning techniques can extract more information from the biosensor data, improving accuracy and enabling the detection of complex patterns.
- Wireless Connectivity: Incorporating IoT (Internet of Things) capabilities can enable real-time monitoring and remote data analysis, expanding the applicability and efficiency of biosensors.





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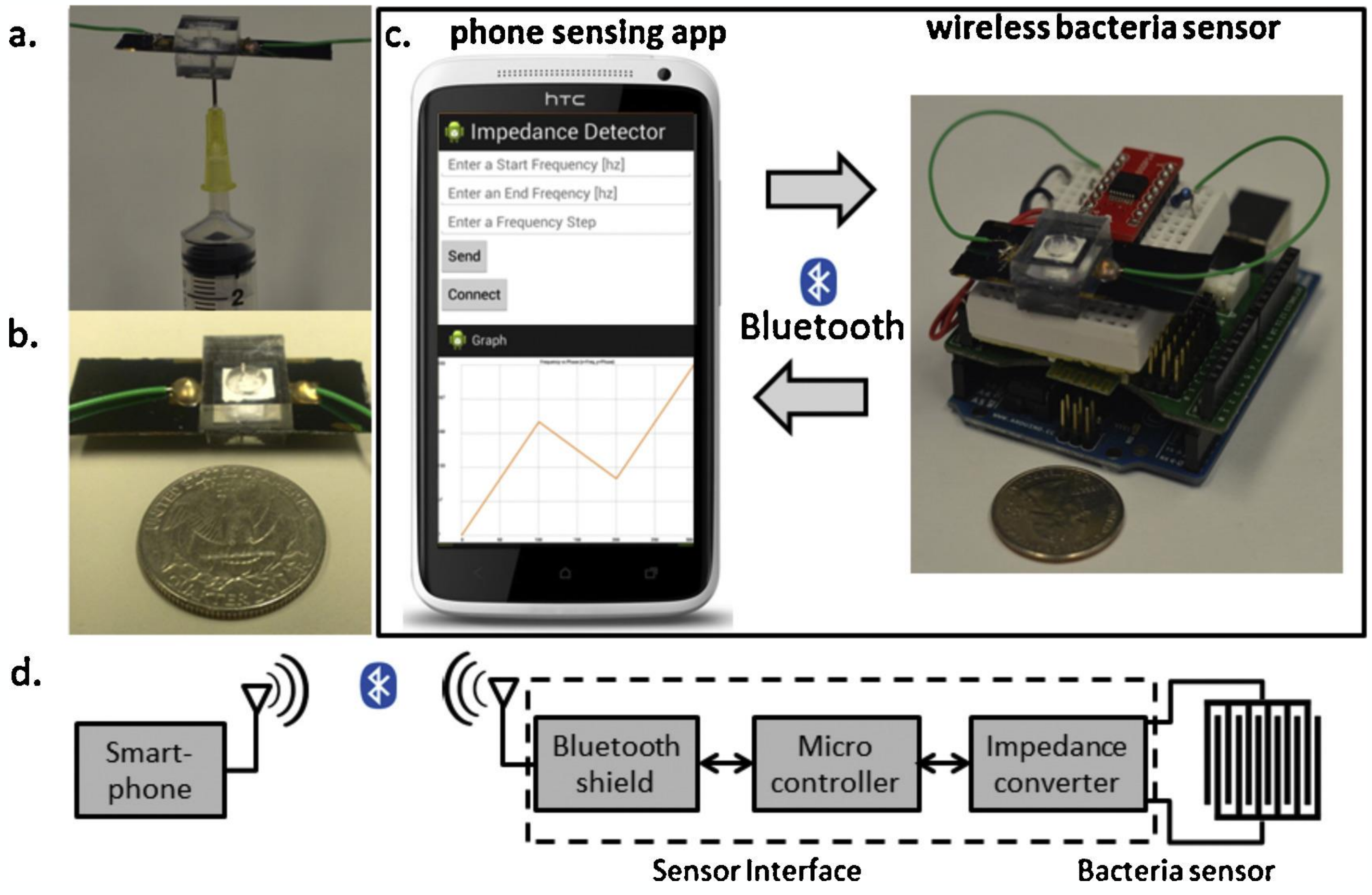

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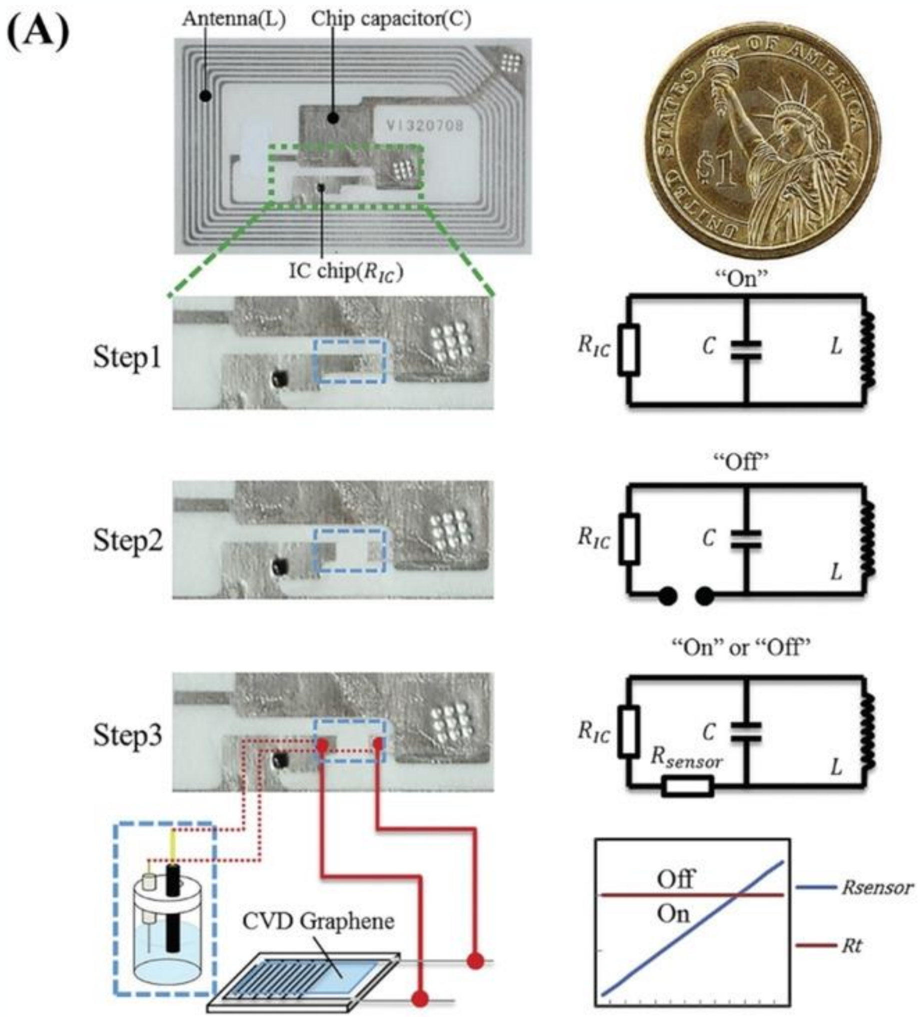

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Thank you for attention

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