biosensors

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Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1,

Table S1. List of commonly used nanomaterials in biosensors development. Each nanoparticle category is associated with a non-comprehensive set of biosensing applications, as well as their reported properties for enhanced device performance, and detection modes.

Nanomaterial	Biosensing Applications	Reported properties	Operation Modes /References
Nanometal			
Copper	Detection of biological molecules, viruses, pathogens	Low cost and affordable Ease of preparation Optical properties (strong fluorescence, MegaStokes shifting, surface plasmon resonance (SPR)) Electrochemical properties (high sensitivity, rapid response), small size, high surface to volume ratio	Fluorescence: [282,283] Electrochemical: [284–286] Colorimetric: [287] References: [288–290]
Gold	Detection of pathogens (bacterial zoonosis, viruses, etc.) biological molecules (hormones, etc.), cancer cells, food pathogens (Staphylococcus aureus)	Optical properties (plasmonic resonance, rapid equipment-free detection, etc.) Simple framework Low-cost Chemical and physical stability Biocompatibility Conductivity Water solubility Facile conjugation to biomolecules Sensitive	Electrochemical: [286,291,292] Plasmonic Resonance: [293–295] Colorimetric: [296,297] Fluorescence: [298,299] References: [300–302]
Platinum	Detection of medication (heparin, dipyrone), biologically relevant molecules (enzymes, glucose), food pathogens (Staphylococcus aureus)	Ease of preparation Catalytic properties (redox reactions, hybridization) Resistant to corrosion and oxidation High-sensitivity Low-detection limits	Electrochemical: [303–305] Colorimetric: [306–308]
Silver	Biologically relevant molecules (α-fetoprotein (AFP), C-reactive protein (CRP), dopamine, MicroRNA, etc.); Medication (Ethambutol and Pyrazinamide)	Optical properties (high plasmon resonance in visible and near infrared regions, high brightness, and photostability) Chemical instability and oxidation Ease of preparation of nanoparticles and hybridized composites Easy conversion to silver ions Low cost Abundant	Plasmonic Resonance: [309–311] Fluorescence: [312,313] Electrochemical: [314]

		Poor adhesion on dielectric surfaces Electrical conductivity Stability Low sintering temperatures	
Palladium	Biologically relevant molecules (dopamine)	Effective catalytic properties High affinity towards H2 Reversibility	Electrochemical: [315,316] Optical: [317] References: [318,319]
Nanometal Oxide			
Copper Oxide	Biologically relevant molecules (glucose, HPV16 DNA), Fungi (*Aspergillus niger*)	Semiconductor metal oxide Ease of preparation Catalytic properties Antimicrobials Cytotoxic to cancer cell lines Cost-effective dye-degraders	Electrochemical: [320–322] Colorimetric: [323] References: [324–326]
Iron Oxide(s)	Food pathogens (Salmonella); Clinically relevant pathogens *Serratia marcescens*); Enzymes (arginase)	Unique magnetic properties (response to an externally applied magnetic field, Superparamagnetic) Biocompatible and biodegradability Facile to functionalize	Low field nuclear magnetic resonance: [327] Electrochemical: [328,329] Fluoresces: [330] References: [325,331]
Titanium Dioxide	Bacteria (E. coli O157:H7), biological temperature, biologically relevant molecules (HPV16 DNA)	Biocompatibility High conductivity Low cost	Electrical: [332] Electrochemical: [333] Optical: [334] References: [325]
Zinc oxide	Biologically relevant molecules (HPV16 DNA); Viruses (SARS-CoV-2)	Wide band gap Binding energy Biocompatibility low-cost Stability Semiconducting material Relatively high refractive index Biocompatibility Electrostatic affinity towards biomolecules	Electrochemical: [292,335,336] References: [325,337]

Table S2. Studies on the toxicity of 0-D, 1-D, 2-D, and 3-D nanocarbon materials in zebra fish (*Danio rerio*) embryos.

Material	Concentration (μg/L)	Endpoint	Reported outcomes	Ref
Fullerenes (0-D)	100 to 500	Cellular Death	• Cell death (concentration dependent) significant at concentrations greater than or equal to 100 μg/L • 100 percent mortality at 200 μg/L exposure	[338]
Multi-walled carbon nanotubes (MWCNTs) (1-D)	0, 3400, 7600, 12500, 25,000 and 50,000	Cellular Death; hatching	• Increase in overall cellular apoptosis (concentration-dependent) significant at 50000 μg/L • Significantly delayed hatching	[339]
Graphene oxide (GO) sheets (2-D)	0, 3400, 7600, 12500, 25,000 and 50,000	Cellular Death; hatching	• Cellular apoptosis (forehead and eye region) • Minor cell growth inhibition • Slight hatching delay (50000 μg/L)	[339]
Laser-induced graphene (3-D)	5000, 10000, 50000 and 100000	Growth; hatching; embryo development	• Biocompatibility • No toxic effects • No effect on development	[340]

Table S3. Studies on the size-dependent toxicity of nanometal, nanometal oxide, and nanocarbon materials used in biosensing. Studies, where smaller-sized nanomaterials induced higher toxicity, are labeled ↓ size = ↑ toxicity while studies, where larger-sized materials induce higher toxicity, are labeled ↑ size = ↑ toxicity.

Nanomaterial	Nanoparticle Parameters	Size	Model Organism	End point and results	Reference
Nanometal					
Copper	Shape: Spherical Zeta Potential: Not Reported Surface Functionalization: Not Reported	30 nm 50 nm 80 nm 1 μm	Male Sprague Dawley rats	Acute (LD50): ↓ size = ↑ toxicity Short Term: ↑ size = ↑ toxicity	[182]
Gold	Shape: Spherical Zeta Potential: 5-nm (−10.33 mV), 20-nm (−4.58 mV) and 50-nm (−12.32 mV)	5 nm 20 nm 50 nm	HepG2 cells and L02 cells BALB/c mice	Cytotoxicity assay: ↓ size = ↑ toxicity Hemolysis test: No significant differences ROS Generation: ↓ size = ↑ toxicity Cytokines release: ↓ size = ↑ toxicity Western blot analysis: ↓ size = ↑ toxicity	[185]

Platinum	Shape: Spherical Zeta Potential: 5 nm (–54.20±0.44 to –11.40±0.40 mV) and 70 nm (–39.43±0.62 to –10.04±0.17 mV)	5 nm 70 nm	Neonatal mice ventricular cardiomyocytes	Cardiomyocyte function: No significant differences ROS Generation: No significant differences Extracellular lactic dehydrogenase (LDH): No significant differences	[37]
Silver	Shape: Spherical Zeta Potential: Not reported	10 nm 60 nm	Human hepatocarcinoma cells (HepG2)	Cell Viability Assay: ↓ size = ↑ toxicity	[341]
Palladium	Shape: Spherical Zeta Potential: Not reported	2.0±0.1 nm 2.5±0.2 nm and 3.1±0.2 nm	Gram negative *E. coli* Gram positive *S. aureus*	Inhibitory growth effects *E. coli*: ↓ size = ↑ toxicity Inhibitory growth effects *S. aureus:* mid-sized (2.5 nm) particles most toxic and smaller (2.0 nm) and larger (3.1 nm) less toxic	[197]
Nanometal Oxide					
Copper Oxide	Shape: Not reported Zeta Potential: Not reported	4 nm 24 nm	A549 human lung cell line	Cell toxicity assay: ↑ size = ↑ toxicity	[342]
Iron Oxide(s)	Shape: Spherical Zeta Potential: −3.99 ± 0.70 mV and −12.43 ± 1.21 mV	10 nm 30 nm	Bone marrow cells Female C57BL/6 mice	mRNA transcription of inflammation-related genes in macrophages: ↑ size = ↑ toxicity	[343]
Titanium Dioxide	Shape: Square Zeta Potential: Not Reported	100 nm 50 nm 30 nm 10 nm	Human umbilical vein endothelial cells (HUVECs)	Comet assay (DNA damage): ↓ size = ↑ toxicity Micronucleus test: ↓ size = ↑ toxicity ROS Generation: ↓ size = ↑ toxicity Glutathione (GSH) assay: ↑ size = ↑ toxicity (antioxidative ability) Western Blot (levels of Nrf2 protein): ↓ size = ↑ toxicity	[344]
Zinc oxide	Shape: Spherical Zeta Potential: -10.3 and -10.0 mV	50 nm 200 nm	Human lung adenocarcinoma A549 cell line	Cell viability (MTS assay): ↓ size = ↑ toxicity	[345]

				Mitochondrial damage and oxidative stress: ↓ size = ↑ toxicity Autophagic process: ↓ size = ↑ toxicity Autophagic dysfunction: ↓ size = ↑ toxicity Lysosomal function: ↓ size = ↑ toxicity	
Carbon					
Graphene	Shape: Not Reported Zeta Potential: Not Reported	S-G (avg 29.31 nm) M-G (307.56 nm) L-G (not reported)	Zebrafish (Danio rerio) HEK 293T cells	Cell viability: Toxicity S-G < L-G < M-G DNA damage (HEK 293T): Toxicity M-G < L-G < S-G Hatching rate: S-G < M-G <L-G Body length: M-G < S-G < L-G Body weight: S-G < M-G and L-G ROS Generation (Zebrafish): S-G < M-G < L-G	[346]
Graphene oxide (GO)	Shape: Not Reported Zeta Potential: GO- L > GO-S	GO-Large (thickness 0.8–1.2 nm, size 500–5000 nm) GO-Small (thickness 0.8–1.2 nm, size < 500 nm	Macrophages (THP-1 monocytes)	Cytotoxicity: ↑ size = ↑ toxicity	[347]
Multi-walled carbon nanotubes	Shape: Nanotube Zeta Potential: Not reported	Diameter (constant): 40 to 60 nm Length (Varied): 3 to 14 μm or 1.5 μm	RAW264.7 cells MCF-7 cells	Cell viability assays: ↑ Length = ↑ toxicity	[348]
Fullerenes (buckyball)	Shape: Small: smooth and round	Hydrodynamic diameter:	GFP-Bax stable MCF7 cells	Cytotoxicity: ↓ size = ↑ toxicity	[349]

	Larger: amorphous and angula Zeta Potential: Not reported	108.6 ± 3.5 to 228.2 ± 7.5	A549 cells	Bax translocation: ↓ size = ↑ toxicity