# Quantum Dot-Infused Nanocomposites: Revolutionizing Diagnostic Sensitivity

Zahra Amiri<sup>1</sup>, Parsa Taromi<sup>2</sup>, Keyvan Alavi<sup>3</sup>, Parto Ghahramani<sup>4</sup>, William C. Cho<sup>5</sup>, Marzieh Ramezani Farani<sup>6,\*</sup>, Yun Suk Huh<sup>6,\*</sup>

<sup>1</sup>Department of Medical Nanotechnology, School of Medicine, North Khorasan University of Medical Sciences, Bojnurd, 94149, Iran. <u>zahra.amiri.de@gmail.com</u>

<sup>2</sup>Department of Chemistry, Iran University of Science and Technology, Tehran, Iran. parsa taromipt@yahoo.com

<sup>3</sup>Department of science and technology, Science & Research Branch, Islamic Azad University, Tehran, Iran. <u>Keivan.alavi@gmail.com</u>

<sup>4</sup>Kermanshah university of medical sciences, Regenerative medicine research center. partoghahramani@gmail.com

<sup>5</sup>Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong SAR, China. williamcscho@gmail.com

<sup>6</sup>NanoBio High-Tech Materials Research Center, Department of Biological Sciences and Bioengineering, Inha University, Incheon 22212, Republic of Korea. <u>farani.marzi@gmail.com</u>; <u>yunsuk.huh@inha.ac.kr</u>

### \*Corresponding authors:

Marzieh Ramezani Farani (farani.marzi@inha.ac.kr) ORCID: 0000-0002-4184-5670

Yun Suk Huh (yunsuk.huh@inha.ac.kr) ORCID: 0000-0003-1612-4473

## Supplementary Material

Quantum Dot Type	Nanocomposite Material	Diagnostic Applicatio n	Sample Type	Detection Method	Limit of Detection (LOD)	Sensitivity Achieved	Key Findings	Ref.
CdSe/ZnS QDs	Protein- Conjugated Nanocomposite	Enzyme Activity Detection	In Vitro (buffer solution)	FRET-Based Fluorescence	10 nM	Nanomolar (nM) levels	Demonstrated QD-based FRET for detecting enzyme activities	1
CdSe/ZnS QDs	PEGylated Nanocomposite	Tumor Imaging	In Vivo (mouse models)	Near-Infrared Fluorescence Imaging	Not specified (High specificity)	High specificity	Developed QD nanocomposites for targeted in vivo tumor imaging	2
CdTe QDs	Au Nanoparticle Composite	DNA Detection	In Vitro (synthetic samples)	Electrochemical Sensing	0.5 fM	Femtomolar (fM) levels	Achieved ultra-sensitive DNA detection using QD-Au nanocomposites	3
CdSe/ZnS QDs	Graphene Oxide Composite	MicroRNA Detection	Serum Samples	Fluorescence Quenching	10 pM	Picomolar (pM) levels	Developed QD-GO nanocomposite for sensitive microRNA detection	4
Carbon QDs	Polymer Nanocomposite	Glucose Sensing	Blood Samples	Fluorescence Sensing	2 μΜ	Micromolar (µM) levels	Created biocompatible carbon QD nanocomposites for glucose sensing	5
CdSe/ZnS QDs	Magnetic Nanoparticle Composite	Bacteria Detection	Water Samples	Magnetofluorescent Imaging	Detection in 30 min	Rapid detection	Combined magnetic separation and fluorescence for bacterial detection	6
PbS QDs	Silica Nanocomposite	Deep Tissue Imaging	In Vivo (mouse models)	Near-Infrared II Imaging	Not specified (Enhanced depth)	Enhanced imaging depth	Developed NIR-II QD nanocomposites for deep tissue imaging	7
Perovskite QDs	Polymer Matrix Nanocomposite	Heavy Metal Ion Detection	Environment al Samples	Fluorescence Quenching	0.1 nM	Nanomolar (nM) levels	Used perovskite QD nanocomposites for sensitive metal ion detection	8
CdSeTe QDs	Hydrogel Nanocomposite	Wound Healing	In Vivo (animal	Fluorescence Imaging	Real-time monitoring	Real-time monitoring	Developed QD-infused hydrogels for monitoring	9

## Supplementary Table 1. Summary of Key Studies on Quantum Dot-Infused Nanocomposites for Ultra-Sensitive Diagnostics

		Monitoring	models)				wound healing processes	
Carbon QDs	MOF Nanocomposite	Cancer Biomarker Detection	Serum Samples	Electrochemiluminesce nce	0.3 fM	Femtomolar (fM) levels	Created CQD-MOF composites for ultra-sensitive detection of cancer biomarkers	10
CdSe/ZnS QDs	DNA-Au Nanocomposite	Pathogen Detection	Clinical Samples	FRET-Based Fluorescence	50 aM	Attomolar (aM) levels	Developed a QD-DNA-Au nanocomposite for ultra- sensitive pathogen detection	11
InP QDs	Silica-Coated Nanocomposite	Live Cell Imaging	Cell Cultures	Confocal Fluorescence Microscopy	Not specified (High resolution)	High resolution	Synthesized biocompatible InP QD nanocomposites for long- term live cell imaging Developed COD MOE	12
Carbon QDs	MOF Nanocomposite	Antibiotic Detection	Water Samples	Fluorescence Sensing	5 nM	Nanomolar (nM) levels	composites for sensitive detection of antibiotics in water samples	13
CdS QDs	Polymer Nanocomposite	Neurotrans mitter Detection	Cerebrospina l Fluid Samples	Electrochemical Sensing	0.1 pM	Picomolar (pM) levels	Achieved highly sensitive detection of neurotransmitters using QD-polymer nanocomposites Developed perovskite OD	14
Perovskite QDs	Graphene Nanocomposite	Viral RNA Detection	Clinical Samples	Photoluminescence Sensing	0.2 fM	Femtomolar (fM) levels	graphene nanocomposites for ultra-sensitive detection of viral RNA	15
Carbon Nitride QDs (CNQDs)	CNQD s/Poly aniline (PANI )	Non- invasiv e glucos e monito ring	Biolog ical sample s	Electro chemic al assay	0.1 μM	High		16

Graph GQDs ene with QDs Au5Ir (GQDs nanopa ) rticles	Atrazi ne detecti on in enviro nment al water	Enviro nment al water sample s	Electro chemic al biosen sor	0.02 nM	Very High	Au5Ir@GQDs nanocomposite combined with DNA walker enabled highly sensitive and selective atrazine detection.	17
--	--	---	--	------------	--------------	---	----

Overview of key works on quantum dot-infused nanocomposites for ultra-sensitive diagnostics, including types, applications, and detection methods.

## Supplementary Table 2. Comparative Analysis of Quantum Dot Materials for Ultra-Sensitive Diagnostic Applications.

Quantum Dot Material	Core Composition	Shell Compositi on	Emission Waveleng th Range (nm)	Quantu n Yield (%)	Surface Functionaliza tion	Biocompatibi lity	Stabilit y	Diagnostic Application	Ref.
-------------------------	---------------------	--------------------------	--	--------------------------	----------------------------------	----------------------	---------------	------------------------	------

CdSe/ZnS QDs	CdSe	ZnS	450–650	Up to 80%	PEGylation	Moderate	High	Cancer Imaging	2
InP/ZnS QDs	InP	ZnS	500–700	Up to 60%	Carboxyl Groups	Good	Modera te	Cellular Imaging	18
Carbon QDs	Carbon	None	350-550	Up to 30%	Amino Groups	Excellent	High	Glucose Sensing	5
PbS QDs	PbS	None	1000– 1400	Up to 50%	Thiol Groups	Low	Modera te	Deep Tissue Imaging	19
Perovskite CsPbBr <sub>3</sub> QDs	CsPbBr <sub>3</sub>	None	450–550	Up to 90%	Ligand Exchange	Poor	Low	Metal Ion Detection	20
Silicon QDs	Silicon	None	400–700	Up to 20%	Hydroxyl Groups	Excellent	High	Biosensing	21
CdTe QDs	CdTe	None	550–750	Up to 70%	Mercaptoaceti c Acid	Moderate	Modera te	DNA Detection	22
ZnO QDs	ZnO	None	350-400	Up to 40%	Silanization	Good	High	Pathogen Detection	23
CuInS <sub>2</sub> QDs	CuInS <sub>2</sub>	ZnS	550-800	Up to 50%	Polymer Coating	Good	Modera te	Fluorescence Imaging	24
CdSeTe QDs	CdSeTe	ZnS	650-800	Up to 85%	Hydrogel Embedding	Moderate	High	Wound Healing Monitoring	25
Graphene Quantum Dots	Graphene	None	400–600	Up to 25%	Nitrogen Doping	Excellent	High	Neurotransmitter Detection	26
Mn-Doped ZnS QDs	s ZnS	None	580	Up to 50%	Silica Coating	Good	High	Multiplexed Detection	27
Ag <sub>2</sub> S QDs	$Ag_2S$	None	900–1300	Up to 15%	PEGylation	Good	Modera te	NIR-II Imaging	28
Cd-free InAs QDs	InAs	ZnSe	800-1000	Up to 40%	Phospholipid Coating	Moderate	Modera te	In Vivo Imaging	29
ZnSe QDs	ZnSe	ZnS	450–550	Up to 30%	Carboxyl Groups	Good	High	Biosensing	30
Au Nanocluster QDs	s Gold	None	600–800	Up to 10%	BSA Conjugation	Excellent	High	Cancer Biomarker Detection	31
CdS QDs	CdS	ZnS	500–600	Up to 65%	Polymer Encapsulation	Moderate	Modera te	Environmental Sensing	26

Nitrogen-Doped Carbon QDs	Carbon	None	450–550	Up to 35%	Amino Groups	Excellent	High	Antibiotic Detection	32
MoS <sub>2</sub> Quantum Dots	$MoS_2$	None	400–500	Up to 20%	PEGylation	Good	Modera te	Biosensing	33
Cd-Free ZnTe QDs	ZnTe	ZnS	450–550	Up to 25%	Thiol Groups	Good	Modera te	Cellular Imaging	34
CdSeZnS/ZnS QDs	CdSeZnS	ZnS	500-650	Up to 98%	Polymer Coating	Excellent	High	cellular Imaging, Cancer Detection	35
CdSe/ZnS QDs	CdSe	ZnS	600-650	Up to 75%	Carboxylation	Good	High	Detection of CP4-EPSPS protein in genetically modified crops	36

Comparative studies of different quantum dot materials are presented, underlining their core-shell composition, emission wavelength, functionalization, biocompatibility, stability, and application in diagnostics. The qualitative terms 'high', 'moderate', and 'low' for biocompatibility and stability are based on reported experimental data, including cytotoxicity, immune response, and degradation behavior. 'High biocompatibility' indicates low toxicity and good biological interaction, while 'low' implies adverse effects. Similarly, 'high stability' refers to good resistance to degradation and aggregation. These labels are used for comparative purposes only, not as quantitative metrics.

#### References

1. Medintz, I. L.; Uyeda, H. T.; Goldman, E. R.; Mattoussi, H., Quantum dot bioconjugates for imaging, labelling and sensing. *Nature materials* **2005**, *4* (6), 435-446.

2. Gao, X.; Cui, Y.; Levenson, R. M.; Chung, L. W.; Nie, S., In vivo cancer targeting and imaging with semiconductor quantum dots. *Nature biotechnology* **2004**, *22* (8), 969-976.

3. Zhou, H.; Liu, J.; Xu, J.-J.; Chen, H.-Y., Ultrasensitive DNA detection based on Au nanoparticles and isothermal circular double-assisted electrochemiluminescence signal amplification. *Chemical Communications* **2011**, *47* (29), 8358-8360.

4. Freeman, R.; Willner, I., Optical molecular sensing with semiconductor quantum dots (QDs). *Chemical Society Reviews* **2012**, *41* (10), 4067-4085.

5. Yang, S.-T.; Wang, X.; Wang, H.; Lu, F.; Luo, P. G.; Cao, L.; Meziani, M. J.; Liu, J.-H.; Liu, Y.; Chen, M., Carbon dots as nontoxic and high-performance fluorescence imaging agents. *The Journal of Physical Chemistry C* **2009**, *113* (42), 18110-18114.

6. Chen, O.; Riedemann, L.; Etoc, F.; Herrmann, H.; Coppey, M.; Barch, M.; Farrar, C. T.; Zhao, J.; Bruns, O. T.; Wei, H., Magneto-fluorescent core-shell supernanoparticles. *Nature communications* **2014**, *5* (1), 5093.

7. Jun, B. H.; Hwang, D. W.; Jung, H. S.; Jang, J.; Kim, H.; Kang, H.; Kang, T.; Kyeong, S.; Lee, H.; Jeong, D. H., Ultrasensitive, Biocompatible, Quantum-Dot-Embedded Silica Nanoparticles for Bioimaging. *Advanced Functional Materials* **2012**, *22* (9), 1843-1849.

8. Halali, V. V.; Sanjayan, C.; Suvina, V.; Sakar, M.; Balakrishna, R. G., Perovskite nanomaterials as optical and electrochemical sensors. *Inorganic Chemistry Frontiers* **2020**, *7* (14), 2702-2725.

9. Gandla, K.; Kumar, K. P.; Rajasulochana, P.; Charde, M. S.; Rana, R.; Singh, L. P.; Haque, M. A.; Bakshi, V.; Siddiqui, F. A.; Khan, S. L., Fluorescent-Nanoparticle-Impregnated Nanocomposite Polymeric Gels for Biosensing and Drug Delivery Applications. *Gels* **2023**, *9* (8), 669.

10. Ibrahim, M. R.; Greish, Y. E., MOF-based biosensors for the detection of carcinoembryonic antigen: A concise review. *Molecules* **2023**, *28* (16), 5970.

11. Yang, B.; Zhang, S.; Fang, X.; Kong, J., Double signal amplification strategy for ultrasensitive electrochemical biosensor based on nuclease and quantum dot-DNA nanocomposites in the detection of breast cancer 1 gene mutation. *Biosensors and Bioelectronics* **2019**, *142*, 111544.

12. Zhou, J.; Yang, Y.; Zhang, C.-y., Toward biocompatible semiconductor quantum dots: from biosynthesis and bioconjugation to biomedical application. *Chemical reviews* **2015**, *115* (21), 11669-11717.

13. Velmurugan, S.; Traiwatcharanon, P.; Jiwanti, P. K.; Cheng, S.-H.; Wongchoosuk, C., Highly selective carbendazim fungicide sensing performance of nitrogen-doped carbon quantum dots encapsulated aminated-UiO-66 zirconium metal-organic framework electrocatalyst. *Electrochimica Acta* **2024**, *479*, 143911.

14. Soylemez, S.; Erkmen, C.; Kurbanoglu, S.; Toppare, L.; Uslu, B., Fabrication of quantum dot-polymer composites and their electroanalytical applications. In *Electroanalytical Applications of Quantum Dot-Based Biosensors*, Elsevier: 2021; pp 271-306.

15. Kundu, S.; Patra, A., Nanoscale strategies for light harvesting. *Chemical Reviews* **2017**, *117* (2), 712-757.

16. Chiu, Y.-H.; Rinawati, M.; Chang, L.-Y.; Guo, Y.-T.; Chen, K.-J.; Chiu, H.-C.; Lin, Z.-H.; Huang, W.-H.; Haw, S.-C.; Yeh, M.-H., Carbon Nitride Quantum Dots/Polyaniline Nanocomposites for Non-Invasive Glucose Monitoring Using Wearable Sweat Biosensor. *ACS Applied Nano Materials* **2025**.

17. Schwendt, G.; Borisov, S. M., Achieving simultaneous sensing of oxygen and temperature with metalloporphyrins featuring efficient thermally activated delayed fluorescence and phosphorescence. *Sensors and Actuators B: Chemical* **2023**, *393*, 134236.

18. Liu, W.; Howarth, M.; Greytak, A. B.; Zheng, Y.; Nocera, D. G.; Ting, A. Y.; Bawendi, M. G., Compact biocompatible quantum dots functionalized for cellular imaging. *Journal of the American Chemical Society* **2008**, *130* (4), 1274-1284.

19. Gines, G.; Zadorin, A.; Galas, J.-C.; Fujii, T.; Estevez-Torres, A.; Rondelez, Y., Microscopic agents programmed by DNA circuits. *Nature nanotechnology* **2017**, *12* (4), 351-359.

20. Liu, D.; Wang, J.; Gu, C.; Li, Y.; Bao, X.; Yang, R., Stirring Up Acceptor Phase and Controlling Morphology via Choosing Appropriate Rigid Aryl Rings as Lever Arms in Symmetry-Breaking Benzodithiophene for High-Performance Fullerene and Fullerene-Free Polymer Solar Cells. *Advanced Materials* **2018**, *30* (8), 1705870.

21. Morozova, S.; Alikina, M.; Vinogradov, A.; Pagliaro, M., Silicon quantum dots: synthesis, encapsulation, and application in light-emitting diodes. *Frontiers in chemistry* **2020**, *8*, 191.

22. Zhang, Y.; Wang, T.-H., Quantum dot enabled molecular sensing and diagnostics. *Theranostics* **2012**, *2* (7), 631.

23. Asadi, F.; Jannesari, A.; Arabi, A., Synthesis and Characterization of Well-dispersed Zinc Oxide Quantum Dots in Epoxy Resin Using Epoxy Siloxane Surface Modifier. *Progress in Color, Colorants and Coatings* **2023**, *16* (4), 399-408.

24. Liu, S.; Hu, J.; Zhang, H.; Su, X., CuInS2 quantum dots-based fluorescence turn off/on probe for detection of melamine. *Talanta* **2012**, *101*, 368-373.

25. Zhu, X.; Zhou, Y.; Yan, S.; Qian, S.; Wang, Y.; Ju, E.; Zhang, C., Herbal Medicine-Inspired Carbon Quantum Dots with Antibiosis and Hemostasis Effects for Promoting Wound Healing. *ACS Applied Materials & Interfaces* **2024**, *16* (7), 8527-8537.

26. Li, R.; Chen, M.; Yang, H.; Hao, N.; Liu, Q.; Peng, M.; Wang, L.; Hu, Y.; Chen, X., Simultaneous in situ extraction and self-assembly of plasmonic colloidal gold superparticles for SERS detection of organochlorine pesticides in water. *Analytical Chemistry* **2021**, *93* (10), 4657-4665.

27. Chantada-Vázquez, M. P.; Sánchez-González, J.; Peña-Vázquez, E.; Tabernero, M. J.; Bermejo, A. M.; Bermejo-Barrera, P.; Moreda-Piñeiro, A., Simple and sensitive molecularly imprinted polymer–Mn-doped ZnS quantum dots based fluorescence probe for cocaine and metabolites determination in urine. *Analytical chemistry* **2016**, *88* (5), 2734-2741.

28. Zhang, Y.; Hong, G.; Zhang, Y.; Chen, G.; Li, F.; Dai, H.; Wang, Q., Ag2S quantum dot: a bright and biocompatible fluorescent nanoprobe in the second near-infrared window. *ACS nano* **2012**, *6* (5), 3695-3702.

29. Bentolila, L. A.; Ebenstein, Y.; Weiss, S., Quantum dots for in vivo small-animal imaging. *Journal of nuclear medicine* **2009**, *50* (4), 493-496.

30. Jang, E.-P.; Han, C.-Y.; Lim, S.-W.; Jo, J.-H.; Jo, D.-Y.; Lee, S.-H.; Yoon, S.-Y.; Yang, H., Synthesis of alloyed ZnSeTe quantum dots as bright, color-pure blue emitters. *ACS applied materials & interfaces* **2019**, *11* (49), 46062-46069.

31. Liang, Z.; Khawar, M. B.; Liang, J.; Sun, H., Bio-conjugated quantum dots for cancer research: detection and imaging. *Frontiers in Oncology* **2021**, *11*, 749970.

32. Skeeters, S. S.; Rosu, A. C.; Divyanshi; Yang, J.; Zhang, K., Comparative determination of cytotoxicity of sub-10 nm copper nanoparticles to prokaryotic and eukaryotic systems. *ACS applied materials & interfaces* **2020**, *12* (45), 50203-50211.

33. Coloma, A.; Del Pozo, M.; Martínez-Moro, R.; Blanco, E.; Atienzar, P.; Sánchez, L.; Petit-Domínguez, M. D.; Casero, E.; Quintana, C., MoS2 quantum dots for on-line fluorescence determination of the food additive allura red. *Food Chemistry* **2021**, *345*, 128628.

34. Gao, T.; Wang, X.; Yang, L.-Y.; He, H.; Ba, X.-X.; Zhao, J.; Jiang, F.-L.; Liu, Y., Red, yellow, and blue luminescence by graphene quantum dots: syntheses, mechanism, and cellular imaging. *ACS applied materials & interfaces* **2017**, *9* (29), 24846-24856.

35. Kim, J.; Hwang, D. W.; Jung, H. S.; Kim, K. W.; Pham, X.-H.; Lee, S.-H.; Byun, J. W.; Kim, W.; Kim, H.-M.; Hahm, E.; Ham, K.-m.; Rho, W.-Y.; Lee, D. S.; Jun, B.-H., High-quantum yield alloy-typed core/shell CdSeZnS/ZnS quantum dots for bio-applications. *Journal of Nanobiotechnology* **2022**, *20* (1), 22.

36. Zeng, H.; Zhang, M.; Zhang, Y.; Liu, H.; Liu, J.; Zhu, L.; Wang, J., A Signal Enhanced Lateral Flow Immunoassay Based on Core-Shell Qds Labeled Antibody and Antigen for Sensitive Detection of Cp4-Epsps Protein. *Available at SSRN 4968483*.

CNQDs/PANI nanocomposite exhibited outstanding electrochemical performance, suitable for non-invasive glucose monitoring.