Review Article

Nanotechnology-Enabled Medical Informatics: From Atomistic Mechanisms to Intelligent Nanosystems and Accountable Clinical Decisions

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Abstract

Nanotechnology and medical informatics are converging into a field in which engineered materials do not only treat or image disease but also generate health data. Nanoparticles, nanosensors, implantable interfaces and responsive carriers convert biochemical events into optical, electrical, magnetic or mechanical signals, and informatics systems turn these signals into clinical decisions. This review follows that information path from end to end. We first explain how atomistic features such as crystal facets, surface defects, ligand packing, interfacial water and protein-corona formation determine what a nanomaterial reports in the body. We then examine nine platform classes (gold, silver, magnetic, quantum dot, carbon, metal-oxide and MXene, lipid, polymeric and dendrimer, and mesoporous silica nanomaterials) and identify, for each, the descriptors that must be recorded for its data to be reproducible. Next, we describe nanosensor transduction, analytical calibration, interoperable data pipelines, artificial intelligence, federated learning, digital twins and closed-loop therapy, followed by applications in oncology, cardiometabolic disease, infection, neurology, regenerative medicine, dentistry and point-of-care testing. Finally, we propose the NanoMed-Info framework, a seven-layer evidence model with explicit decision gates that links atomistic identity to clinical utility and lifecycle governance, together with a minimum reporting checklist for nanosystem-derived clinical data. The main barriers are incomplete metadata, batch variability, uncertain long-term safety, biased datasets, weak interoperability, cybersecurity risk and fragmented regulation. Progress will depend less on making devices smaller than on keeping every measurement traceable, calibrated and clinically meaningful from the atom to the bedside.

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1. Introduction

Good clinical decisions depend on detecting biological change early, combining different kinds of evidence and acting on it in time **(Bate *et al.* 2012)**. Medical informatics has traditionally worked with data at the level of the patient and the health system: electronic health records (EHRs), laboratory results, images, prescriptions and registries. Nanotechnology pushes this information environment down to the molecular and cellular scale **(Ratwani 2017)**. A gold nanoparticle that changes colour when it binds a biomarker, a magnetic nanoparticle that alters an MRI signal when it clusters around a target, or a lipid carrier whose distribution can be tracked in tissue is both a material and a source of data **(Dreaden *et al.* 2012)**. The main challenge is therefore not simply to build smaller devices. It is to keep the meaning of a nanoscale event intact as it passes through a series of transformations **(Zhou *et al.* 2015)**. Molecular binding must produce a stable physical signal; the signal must be calibrated and labelled with metadata; software must separate true biological change from device drift; and the final result must support a specific clinical action. A failure at any step can create false confidence **(Chen and Chen 2026)**. A highly sensitive sensor has little clinical value if its readings cannot be compared across manufacturing batches, patient groups, hospitals or time points **(Bao *et al.* 2026)**. Nanomaterials also depend on context in ways that conventional health data systems do not capture. Size distribution, shape, porosity, crystal defects, ligand density, surface charge, local pH and ionic strength can all change biological behaviour. Once a nanoparticle enters blood or tissue fluid, it is coated by a dynamic layer of proteins and other biomolecules, the biomolecular corona, which can redefine how cells recognize it **(Zhou *et al.* 2015)**. Even manufacturing history and storage conditions can change the data that a nanosystem produces in the body. Unless informatics systems record these variables, nanosystem measurements cannot be reproduced or interpreted reliably.

Previous reviews have usually treated nanomedicine, nanosensing and clinical artificial intelligence (AI) as separate topics **(Pant *et al.* 2021)**. We treat them as one multiscale information system. This review first maps the atomistic mechanisms for nine major nanoplatform classes to the specific descriptors that must be recorded for their data to be trusted. Second, it connects nanosensor physics to analytical calibration and interoperable clinical data standards **(Zhou *et al.* 2026)**. Third, it maps these capabilities onto clinical use cases and the evidence each requires. Fourth, it proposes the NanoMed-Info framework, a seven-layer evidence model with decision gates, and a minimum reporting checklist for nanosystem-derived clinical data **(Zhao *et al.* 2023)**. The review is organised to follow the data: from definitions and the information lifecycle, through atomistic mechanisms, sensing and data systems, and AI, to clinical applications, translation and governance **(Dewanjee *et al.* 2026)**, and future directions. The score of the review is given below.

1.1. Scope of the review

A literature search was performed in a systematic manner for studies on nanotechnology, nanomedicine, nanoinformatics, nanosensors, protein corona, molecular simulation, artificial intelligence, digital twins and clinical informatics **(Zheng *et al.* 2026)**. Studies were retrieved from the most relevant scientific e-databases and based on the study of reports and articles considering their nature, availability, scope and application in areas related to nanoscale mechanisms, nanomaterial characterisation and sensing, data integration, artificial intelligence and clinical applications including translational governance **(Maojo *et al.* 2012)**. Only peer-reviewed journal articles, reviews and relevant standards or position papers were selected and studies outside the scope of nano-enabled medical informatics were excluded.

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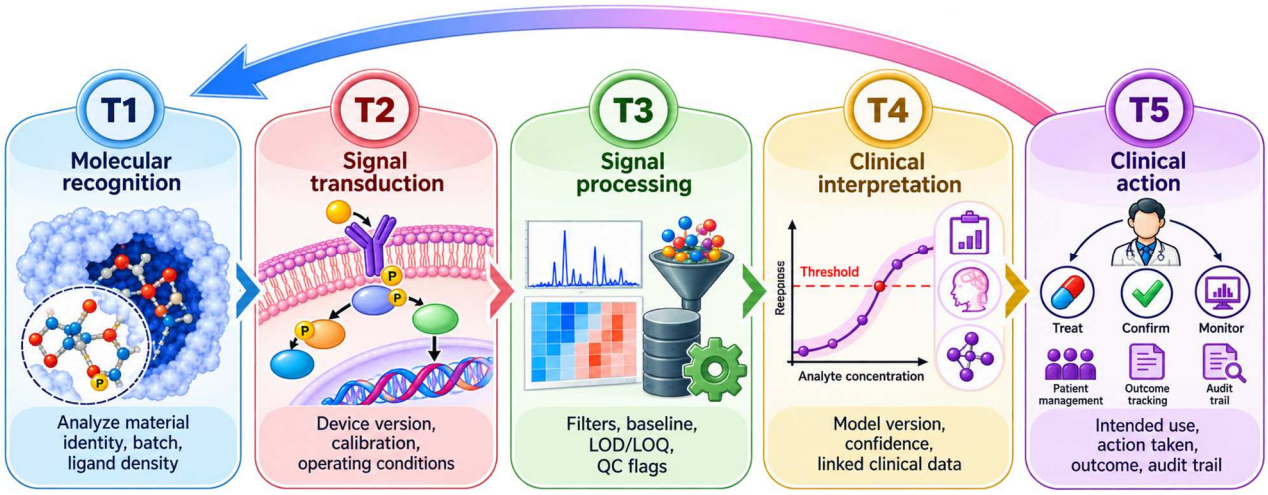

Figure 1. From a nanoscale molecular event to a clinical decision through five information transformations: T1, molecular recognition; T2, signal transduction; T3, signal processing; T4, clinical interpretation; and T5, clinical action. At each stage, key metadata, measurement conditions, model information, and clinical context are recorded and propagated to support reproducibility and traceability. Provenance, units, and uncertainty should travel with the measurement throughout the workflow, while clinical outcomes feed back into material, device, and model redesign.

2. Foundations of Nano–Medical Informatics

2.1. Definition and scope

We define nano–medical informatics as the acquisition, representation, integration, analysis and responsible use of health information that is generated by, or about, nanoscale systems. Its data sources include nanoparticle characterisation, molecular simulation, nanosensors, nanocarriers, implantable interfaces, omics platforms, imaging probes and therapeutic monitoring **(Maojo *et al.* 2012)**. Its purpose goes beyond storing experimental results: it aims to keep an unbroken, traceable link from material composition and atomic interactions to patient outcomes.

The field lies at the intersection of five disciplines meet. Nanoinformatics provides structured descriptions of materials and their biological effects. Bioinformatics connects nanoscale interventions to genes, proteins, pathways and cell states **(Kazi *et al.* 2025)**. Clinical informatics places outputs within diagnoses, care workflows and outcomes. Materials informatics predicts how synthesis conditions shape structure and properties. Computational medicine turns these relationships into patient-specific models and decisions **(Liu and Cohen 2015)**. None of these disciplines alone can carry a measurement from the atom to the bedside.

2.2. The information lifecycle

The lifecycle starts with material identity. Primary descriptors include elemental composition, molecular architecture, particle-size distribution, morphology, crystallinity, surface area, porosity, surface charge, ligand chemistry and stability. Contextual descriptors include synthesis route, purification, sterilization, storage, dispersion medium, temperature and instrument settings **(Sharma *et al.* 2026)**. Biological descriptors include corona composition, cellular uptake, intracellular trafficking, immune activation, biodistribution, degradation, clearance and dose–response behavior. These descriptors then pass through five transformations **(Figure 1)**. In T1, this molecular recognition step is performed by the nanosystem. In T2, the molecular event elicits an optical, electrical, magnetic, mechanical or electrochemical signal from the nanosystem. In T3, the raw signal is pre-processed (baseline correction, denoising, calibration and quality control, and feature extraction, are applied). In T4, the measured value is interpreted in the context of patient history, laboratory tests, radiology or omics. In T5, the clinical action that results from such interpretation may involve screening, diagnosis, the choice of treatment, dose adjustment, monitoring or escalation of care **(Jin *et al.* 2020)**.

2.3. FAIR and interoperable data

Data that are findable, accessible, interoperable and reusable (FAIR) matter especially in nanomedicine, because nanoscale experiments are highly sensitive to protocol details. A dataset without provenance cannot reliably train a model or support comparison between laboratories. Each measurement should carry machine-readable metadata describing the specimen source, nanomaterial batch, preparation protocol, device version, calibration status, operator, environment, uncertainty and preprocessing history **(Rush *et al.* 2024)**. Community resources such as ISA-TAB-Nano, the eNanoMapper ontology and ISO/TS 80004 nanotechnology vocabularies provide useful starting points for this material-side description. Clinical exchange also requires mapping nanosystem outputs onto recognised clinical standards. In practice, this means representing results as HL7 FHIR Observation and Device resources, coding the measured quantity with LOINC or SNOMED CT, expressing units in UCUM and recording provenance explicitly. A nanosensor result should never enter a clinical record as an unexplained number **(Inau *et al.* 2023)**. It should state the measurand, specimen, sensing mechanism, analytical range, limit of detection, confidence interval, quality flags and intended use. This discipline allows decision-support software to interpret values consistently and allows later audit.

2.4. Human-centered design

A nanosystem's clinical value depends on how its information is presented. Alert fatigue, ambiguous risk scores and badly timed notifications can cancel out excellent analytical performance. Interfaces should show trends, uncertainty, device condition and the reason behind any recommendation **(Ray *et al.* 2026)**. Clinicians need to be able to inspect the supporting evidence, see what data are missing and override automation with a documented reason **(Martin-Contreras *et al.* 2022)**. Patients need plain explanations of what is being measured, how often, who can see the data and what actions may follow.

3. Atomistic Insights into Nanotechnology

3.1. Computational methods across scales

Atomistic modelling explains why small chemical changes can produce large differences in how a nanosystem behaves. Density functional theory

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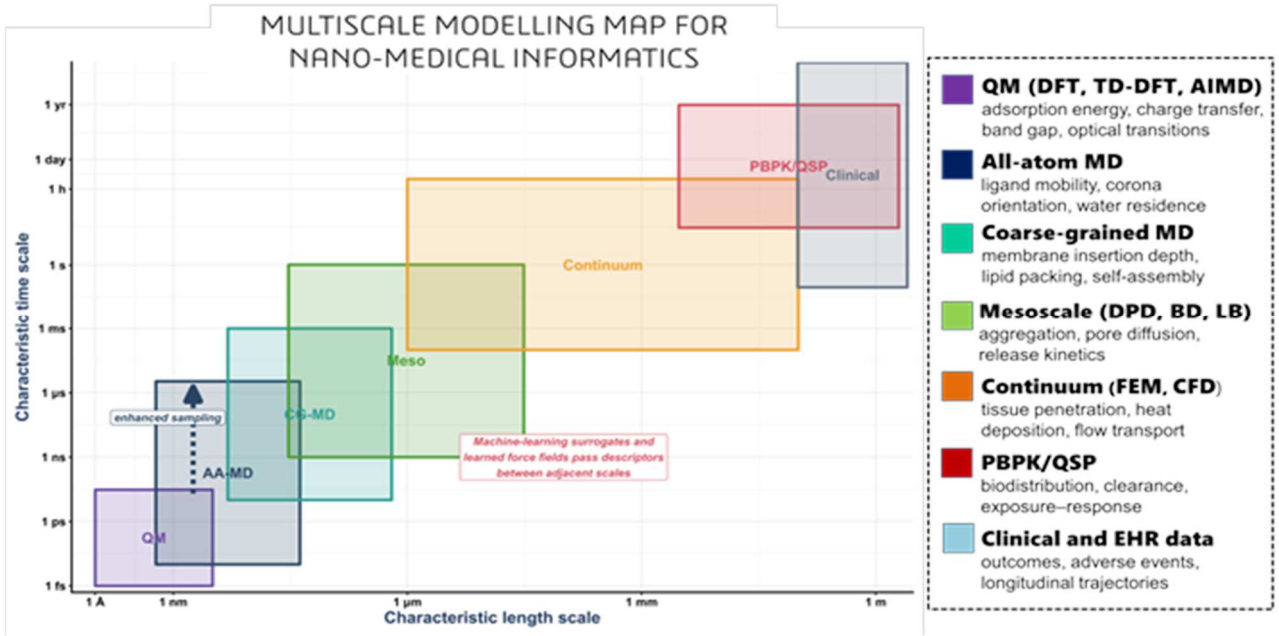


Figure 2. Multiscale modelling map for nano–medical informatics. Each box shows the approximate length and time scales accessible to a class of method, from quantum mechanics to clinical and EHR data streams. The right-hand panel lists typical outputs that can be used as informatics descriptors. Machine-learning surrogates and learned force fields pass information between adjacent scales. Boundaries are indicative and shift with hardware and algorithms. AIMD, ab initio molecular dynamics; BD, Brownian dynamics; CFD, computational fluid dynamics; DPD, dissipative particle dynamics; FEM, finite-element method; LB, lattice Boltzmann; PBPK, physiologically based pharmacokinetics; QSP, quantitative systems pharmacology.

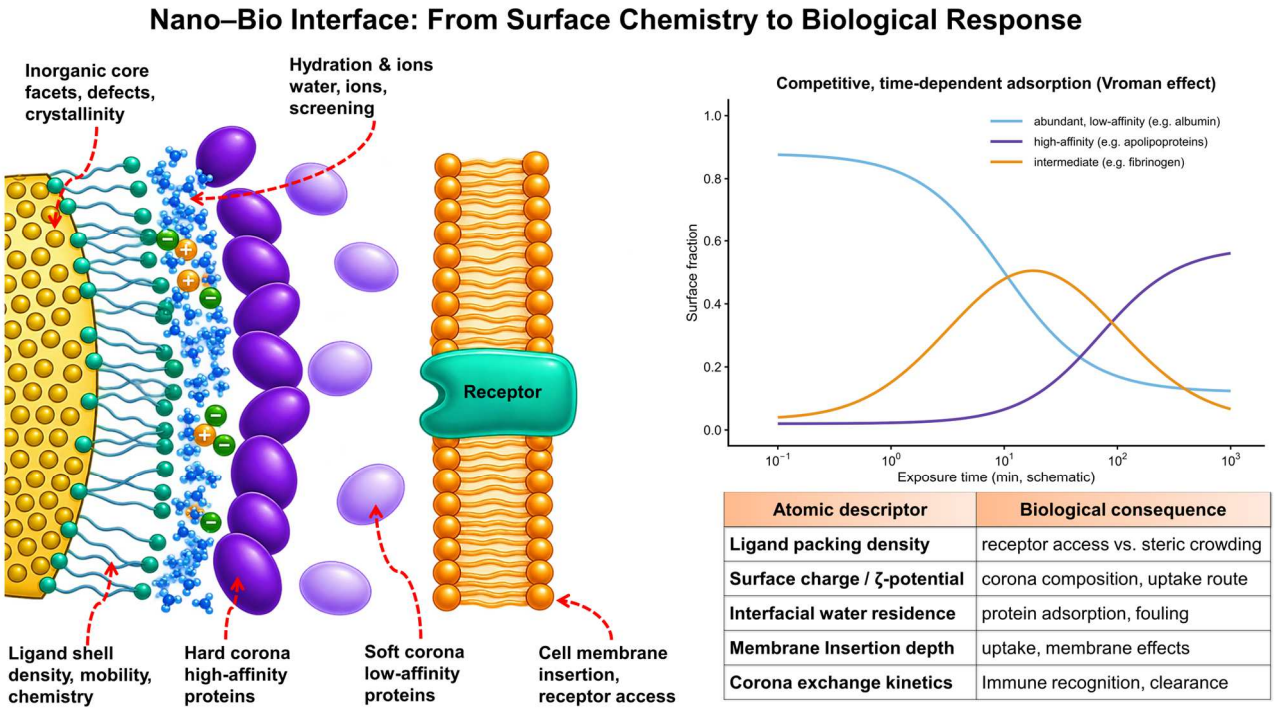
(DFT) and its time-dependent form estimate electronic structure, adsorption energies, charge transfer, catalytic sites and optical transitions. All-atom molecular dynamics (MD) follows solvent, ions, lipids, ligands, proteins and drug molecules with explicit time resolution, typically over nanoseconds to microseconds **(Zwier and Chong 2010)**. Enhanced-sampling methods such as umbrella sampling and metadynamics reach rare events, including membrane crossing, ligand exchange, conformational change and payload release. Coarse-grained Molecular dynamics (CG-MD) extends the accessible length and time scales, and dissipative particle dynamics represents self-assembly and mesoscale transport **(Bernardi *et al.* 2015)**. No single method can cover the whole path from molecule to patient **(Figure 2)**. Quantum methods give electronic accuracy but are limited to a few hundred atoms. Classical MD captures detailed interfaces but is only as good as its force field. Coarse-grained models reach larger scales at the cost of chemical detail **(Su *et al.* 2026)**. Continuum and physiologically based pharmacokinetic (PBPK) models connect nanoscale mechanisms to organ-level transport and whole-body exposure. Machine-learning surrogates and learned force fields increasingly pass information between adjacent scales **(Herring and Montemore 2023)**. For informatics purposes, simulation outputs should not be treated as direct observations. Their assumptions, parameter sets, boundary conditions, sampling length, convergence criteria and uncertainty must be stored alongside them **(Wan *et al.* 2021)**.

3.2. The nano–bio interface and the protein corona

Across all nanomaterial classes, the biomolecular corona is the central bridge between atomistic design and clinical behaviour **(Figure 3)**. When a nanoparticle enters a biological fluid, proteins, lipids and metabolites compete to adsorb on its surface. Abundant but weakly binding proteins such as albumin arrive first and are gradually replaced by less abundant, higher-affinity proteins such as apolipoproteins, a process known as the Vroman effect **(Saei and Mahmoudi 2024)**. The result is often described as a tightly bound, slowly exchanging hard corona and a loosely bound, rapidly exchanging soft corona. This layer can hide targeting ligands, expose new recognition motifs, change aggregation and drive immune clearance **(Bashiri *et al.* 2023)**. Beneath the corona, atomistic features set the terms of this competition. Crystal facets and defects fix surface energy; ligand density and mobility control whether receptors can reach targeting groups; the structured water and ion layer controls protein adsorption and electrostatic screening; and surface charge shapes both corona composition and uptake route. Corona composition also varies with the patient's physiology, disease state, medication, specimen handling and exposure time, which is why the concept of a 'personalised corona' has emerged **(Kay *et al.* 2026)**. A clinically useful informatics framework should therefore treat the corona as conditional metadata rather than a fixed material property. Both abundant and high-affinity components may matter, and exchange kinetics can matter as much as the final composition **(Aliyandi *et al.* 2020)**. Combining corona proteomics with simulation-derived surface descriptors may allow biological identity to be predicted, provided that models account for platform, protocol and population differences **(Hou *et al.* 2026)**.

3.3. Gold nanoparticles

Gold nanoparticles are valued for their tunable localised surface plasmon resonance (LSPR), chemical stability and simple thiol-based functionalisation **(Figure 4a)**. Spherical particles of about 10–20 nm absorb strongly near 520 nm, which gives colloidal gold its red colour. When particles aggregate, the plasmon band shifts to longer wavelengths and the solution turn blue or purple, a change that underlies colorimetric assays and lateral-flow tests. At the atomic level, particle size and exposed facets alter surface energy and ligand packing **(Lorenzana-Vazquez *et al.* 2023)**. Curvature changes the free volume available to each ligand, which affects both receptor access and non-specific adsorption. Water and ions organise differently near the functionalised surface than in bulk solution **(Dai and Zhou 2015)**. The biological identity of a gold nanoparticle emerges as proteins and metabolites compete for its surface. A dense ligand layer can shield the core, but an overcrowded coating may also block recognition molecules. Atomistic simulations can compare the orientation, residence time and conformational stability of adsorbed proteins, which helps predict colloidal stability, immune recognition,



Atomic descriptor	Biological consequence
Ligand packing density	receptor access vs. steric crowding
Surface charge / ζ-potential	corona composition, uptake route
Interfacial water residence	protein adsorption, fouling
Membrane Insertion depth	uptake, membrane effects
Corona exchange kinetics	Immune recognition, clearance

Figure 3. Anatomy of the nano–bio interface. Left: schematic zoomed cross-section from the inorganic core through the ligand shell, hydration and ion layer, and hard and soft protein corona to a cell membrane receptor. Targeting ligands (triangles) can be partly masked by adsorbed proteins. Upper right: schematic time course of competitive protein adsorption (Vroman effect), in which abundant low-affinity proteins are progressively displaced by high-affinity proteins. Lower right: atomic descriptors and the biological consequences they predict.

sensor accessibility and cellular uptake. Informatics records should always distinguish the core diameter measured by electron microscopy from the hydrodynamic diameter measured by light scattering and should state whether measurements were made before or after exposure to biological fluid **(Dykman and Khlebtsov 2011)**.

3.4. Silver nanoparticles

Silver nanoparticles combine strong plasmonic properties, useful for surface-enhanced Raman scattering (SERS), with antimicrobial activity driven by the release of silver ions **(Figure 4b)**. Their effects depend on oxidation state, surface defects, capping chemistry, dissolved oxygen, chloride concentration, pH and nearby biomolecules **(Sati *et al.* 2025)**. In sulfide-rich environments, silver surfaces convert to poorly soluble silver sulfide, which sharply reduces ion release. Atomistic descriptions must therefore account for both the particle and the dissolved ions **(Duman *et al.* 2024)**. A nominal mass dose can hide large differences in reactive surface area and dissolution rate. Molecular and electronic simulations can identify oxidation-prone sites, the binding of sulfur-containing biomolecules and interactions with membrane components **(Wu *et al.* 2026)**. The same reactivity that kills microbes can cause oxidative stress in human cells or disturb beneficial microbial communities **(Sati *et al.* 2025)**. Rather than assigning a single static toxicity label, medical-informatics models should integrate time-resolved dissolution, aggregation state, exposure route and tissue environment, so that risk estimates reflect the actual conditions of use.

3.5. Magnetic nanoparticles

Iron-oxide nanoparticles enable MRI contrast, magnetic separation, biosensing, hyperthermia and guided delivery **(Figure 4c)**. Below a critical size of roughly 20 nm, magnetite cores become superparamagnetic: they magnetise strongly in an applied field but retain little magnetisation once it is removed, which limits aggregation **(Wahajuddin and Arora 2012)**. Their magnetic response depends on core composition, size, crystallinity, defects, magnetic anisotropy and coupling between neighbouring particles. Coatings affect colloidal stability and the spacing between magnetic cores, and therefore the transverse relaxivity (r_2) that determines MRI contrast and the specific absorption rate (SAR) that determines heating. Atomistic and spin-resolved calculations can relate lattice organization to these measurable properties **(Wroblewski *et al.* 2026)**. At the biological interface, coating mobility and protein adsorption change hydrodynamic behavior and recognition. In an alternating magnetic field, heating depends on field amplitude and frequency, aggregation, viscosity and local confinement, so a heating rate measured in a simple dispersion may not predict performance in tissue **(Ghazi *et al.* 2025)**. The intrinsic loss power, which normalizes SAR to the applied field conditions, is a more comparable metric. Informatics platforms should link material descriptors to field strength, frequency, exposure time, local temperature, imaging sequence and physiological context, so that patient-level models can estimate benefit while monitoring thermal injury and off-target accumulation **(Yazdani *et al.* 2026)**.

3.6. Quantum dots

Quantum dots are semiconductor nanocrystals whose band gap widens as their size reduces, because electrons and holes are confined in space **(Figure 4d)**. As a result, smaller dots emit blue light and larger dots emit redd light, with narrow emission peaks and allow several targets to be imaged at once. Core–shell structure, surface vacancies, lattice mismatch and surface passivation determine brightness, photostability, blinking and potential toxicity **(Hamidu *et al.* 2023)**. Zinc sulfide shell can protect a reactive CdSe core, but incomplete coverage or degradation can open leakage pathways. Ligand exchange to improve water solubility can introduce surface traps that reduce the quantum yield **(Son *et al.* 2026)**. Electronic-structure calculations can map how defects and adsorbed molecules affect fluorescence, and molecular simulations describe ligand organisation, hydration and biomolecular interactions. In diagnostic systems, every optical signal must be linked to its excitation conditions, spectral correction, photobleaching history and particle composition

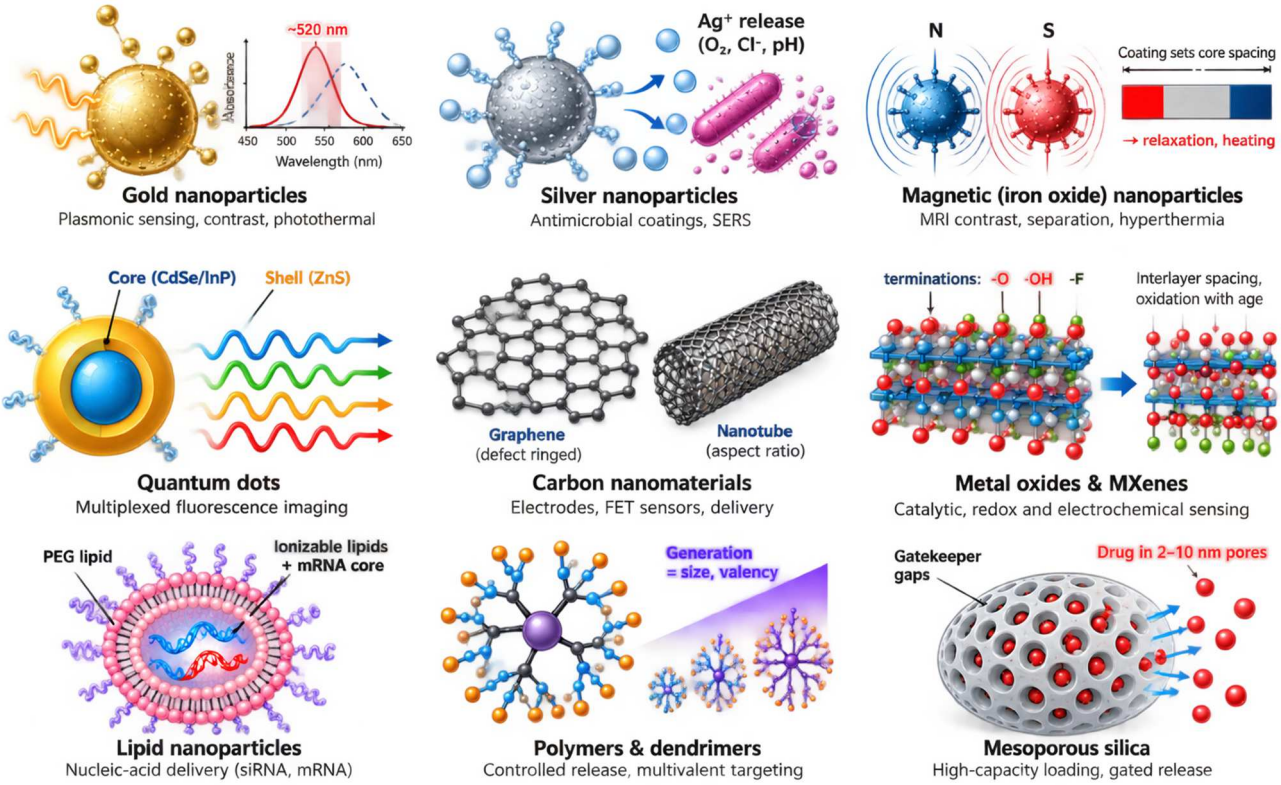


Figure 4. Nine nanoplatform classes viewed as information sources. Each panel shows a schematic of the structure, its main role and the descriptors that must be recorded for its data to be reproducible. (a) Gold nanoparticles and plasmon shift on aggregation; (b) silver nanoparticles and ion release; (c) superparamagnetic iron-oxide cores whose coatings set inter-core spacing; (d) core–shell quantum dots with size-tuned emission; (e) graphene with a defect site and a carbon nanotube; (f) layered MXene or oxide sheets with mixed surface terminations; (g) lipid nanoparticle with PEG-lipid surface and nucleic-acid core; (h) dendrimer generations; (i) mesoporous silica with loaded pores and gatekeeper caps.

(Smith and Nie 2010). For clinical translation, data models should clearly separate cadmium-containing formulations from lower-toxicity alternatives such as indium phosphide and carbon dots and should represent how particles transform over time rather than only their initial characterization **(Kah and Abrahamse 2026)**.

3.7. Carbon nanomaterials

Graphene, graphene oxide, carbon nanotubes, nanodiamonds and carbon dots offer distinct electrical, mechanical, optical and adsorption properties **(Figure 4e)**. Their biological behaviour depends strongly on layer number, chirality, edge structure, defect density, degree of oxidation, residual metal catalyst, length and functionalisation. Flat graphene surfaces bind aromatic biomolecules through π–π stacking and dispersion forces, which makes them sensitive electrode and field-effect transistor (FET) materials **(Xiao *et al.* 2023)**. For nanotubes, curvature and aspect ratio influence how they contact membranes and how macrophages process them; long, rigid fibres raise particular concern because they can resist clearance. Atomistic simulation helps characterise protein orientation, lipid extraction, membrane deformation and drug adsorption on carbon surfaces **(Brossell *et al.* 2026)**. These interactions are useful in sensing and delivery but harmful when they disrupt membranes. Data systems should therefore not treat 'carbon nanomaterials' as one category **(Speranza 2021)**. Ontologies should encode geometry, defect state, oxygen-to-carbon ratio, aggregation and contaminant profile, so that safety and performance evidence is only compared between genuinely similar materials.

3.8. Metal oxides, MXenes and related 2D materials

Metal-oxide nanoparticles and emerging two-dimensional materials provide catalytic, semiconducting, photothermal and electrochemical functions **(Figure 4f)**. Cerium oxide, for example, switches between Ce^{3+} and Ce^{4+} states and can act as an antioxidant enzyme mimic, whereas zinc oxide dissolves readily to release zinc ions. Surface hydroxylation, oxygen vacancies, exposed facets, oxidation state and ion dissolution determine how these materials interact with biological media **(Ahmed *et al.* 2025)**. In MXenes such as $Ti_3C_2T_x$, surface terminations (–O, –OH, –F), interlayer spacing, oxidation and sheet size control conductivity, stability and molecular adsorption. MXenes also oxidise gradually in water, so their properties drift during storage. Electronic-structure calculations can identify active sites and charge-transfer pathways, while molecular simulations describe water layers, ion transport, biomolecule adsorption and membrane interactions **(Iqbal *et al.* 2021)**. Because these materials change during storage and use, informatics records should include ageing, oxidation and environmental history. Device models must also separate the intrinsic sensitivity of the material from gains that come from electrode design, signal amplification chemistry or data preprocessing.

3.9. Lipid nanoparticles

Lipid nanoparticles (LNPs) are dynamic assemblies rather than rigid particles **(Figure 4g)**. Clinical formulations typically combine four components: an ionizable lipid, a helper phospholipid, cholesterol and a polyethylene glycol (PEG)-lipid. The ionizable lipid is designed with an apparent pKa of roughly 6–7, so that it is nearly neutral in blood but becomes positively charged in the acidic endosome, where it helps disrupt the membrane and release nucleic-acid cargo. This design principle underpins approved siRNA therapeutics and mRNA vaccines **(Han *et al.* 2021)**. Mixing conditions and pH during formulation determine self-assembly, and after administration protein adsorption and lipid exchange can reshape the particle before it reaches its target cell. Only a small

Table 1. Nanoplatform classes: atomistic determinants, descriptors to record and main risks to track

Platform	Key atomistic determinants	Descriptors to record	Main clinical roles	Key risk to track
Gold	Facets, curvature, thiol ligand packing	Core vs. hydrodynamic size, ligand density, LSPR peak	Colorimetric and lateral-flow assays, photothermal therapy, contrast	Corona masking; aggregation-driven signal errors
Silver	Oxidation sites, capping, sulfidation	Dissolution rate, Ag+ fraction, medium composition	Antimicrobial coatings, SERS sensing	Ion toxicity; microbiome disruption
Iron oxide	Crystallinity, anisotropy, core spacing	Core size, coating, r2, SAR/ILP	MRI contrast, hyperthermia, magnetic separation	Off-target heating; iron overload
Quantum dots	Core–shell mismatch, surface traps	Composition, quantum yield, photobleaching	Multiplexed fluorescence imaging	Heavy-metal leakage on degradation
Carbon	Layers, chirality, defects, oxidation	O/C ratio, length, catalyst residue	Electrodes, FET sensors, delivery	Membrane damage; poor clearance of long fibres
Metal oxides and MXenes	Terminations, vacancies, redox state	Oxidation state, ageing history	Catalytic, redox and electrochemical sensing	Drift from oxidation during storage
Lipid nanoparticles	Ionizable-lipid protonation, lipid packing	Molar ratios, apparent pKa, encapsulation, PEG content	siRNA and mRNA delivery	Reactogenicity; anti-PEG immunity
Polymers and dendrimers	Chain mobility, generation, end groups	Mw, dispersity, surface groups, release conditions	Controlled release, multivalent targeting	Cationic toxicity; burst release
Mesoporous silica	Silanol density, pore curvature, gatekeeper	Pore size and volume, loading, release medium	High-capacity loading, triggered release	Incomplete degradation; premature release

fraction of internalised cargo is thought to escape the endosome, which makes this step a key target for design **(Hald Albertsen *et al.* 2022)**. Atomistic and coarse-grained simulations can examine lipid packing, cargo condensation, membrane fusion, endosomal interactions and pH-dependent structural transitions. Informatics systems should link formulation parameters to structural descriptors, encapsulation efficiency, potency, biodistribution, immune response and storage stability **(Xu *et al.* 2025)**. Batch comparability requires more than matching the mean diameter: it requires evidence that internal organisation and functional behaviour remain within an accepted range. Repeated dosing also calls for monitoring of anti-PEG antibodies, which can accelerate clearance.

3.10. Polymeric nanoparticles and dendrimers

Polymeric nanoparticles can be engineered for controlled degradation, targeted delivery, imaging and stimulus-responsive release **(Figure 4h)**. For widely used polyesters such as poly(lactic-co-glycolic acid) (PLGA), the lactide-to-glycolide ratio and molecular weight control the rate of hydrolysis and hence drug release. More generally, molecular weight, dispersity (Đ), monomer ratio, branching, tacticity, end groups, cross-linking and residual solvent influence chain mobility and cargo retention **(Makadia and Siegel 2011)**. Dendrimers add generation-dependent size, many terminal groups and internal cavities. Their dense surface groups improve loading and multivalent binding, but cationic surfaces can damage membranes and cause toxicity unless they are modified. Simulations reveal polymer–drug association, water penetration, swelling, erosion and interactions with proteins and membranes. Protonation and local ionic strength can change dendrimer conformation and binding **(Elmowafy *et al.* 2023)**. Informatics systems should preserve full polymer-distribution data rather than only nominal composition. Release profiles should always be linked to the release medium, pH, enzymes, temperature and sink conditions, so that machine-learning models do not combine fundamentally different experiments.

3.11. Mesoporous silica nanoparticles

Mesoporous silica nanoparticles offer a high surface area, adjustable pore geometry and chemically modifiable surfaces **(Figure 4i)**. Pores in the mesoporous range (2–50 nm by IUPAC definition; typically, 2–10 nm in drug carriers) can hold large amounts of drug. Their behaviour is governed by silanol density, pore curvature, hydration, ionic environment and the chemistry of 'gatekeeper' groups that cap the pore openings. Drug molecules interact with pore walls according to their charge, hydrogen-bonding capacity and competition with solvent **(Zhang *et al.* 2024b)**. Gatekeepers can be designed to open in response to pH, enzymes, redox state, light or magnetic fields. Molecular simulation can estimate diffusion, adsorption, confinement and release, while continuum models extend these findings to tissue transport. Dissolution and biodegradation depend on the degree of silica condensation and the surrounding environment **(Narayan *et al.* 2018)**. Informatics records should include pore-size distribution, accessible pore volume, surface modification, loading protocol, release medium and degradation products. These descriptors allow fair comparison between studies and support prediction of dose, stability and safety.

3.12. From atomistic descriptors to predictive models

Atomistic descriptors can serve as inputs to machine learning. Useful examples include adsorption free energy, solvent-accessible surface area, ligand flexibility, interfacial water residence time, membrane-insertion depth, ion coordination, electrostatic potential and payload-binding energy. When these are linked to measured uptake, toxicity or release, they support mechanism-based prediction. However, models trained on small or chemically narrow datasets can mistake correlation for a transferable physical law **(Chi *et al.* 2021)**. **Table 1** summarises, for each platform, the atomistic determinants, the descriptors that should be recorded and the main risk that informatics systems must track.

4. Nanosensors and Connected Data Systems

4.1. Transduction modalities

Nanosensors convert molecular events into measurable physical changes **(Figure 5a–e; Table 2)**. Plasmonic sensors detect shifts in optical resonance. Field-effect devices detect changes in surface charge as a shift in threshold voltage. Electrochemical sensors monitor current, potential, impedance or capacitance. Magnetic relaxation sensors detect how target-induced clustering of magnetic particles changes the MRI relaxation time T_2. Nanomechanical resonators detect added mass as a shift in resonance frequency. Nanostructuring increases surface area and amplifies signals, but greater sensitivity can also mean greater susceptibility to fouling,

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Table 2. Nanosensor transduction modalities and their informatics requirements

Modality	Measured change	Typical nanomaterials	Main strengths	Main confounders to model
Plasmonic / optical	Resonance shift (Δλ), intensity, colour	Gold, silver, quantum dots	Label-free, visual read-out, multiplexing	Aggregation, turbidity, ambient light
Field-effect (FET)	Threshold voltage (ΔVth), conductance	Graphene, carbon nanotubes, silicon nanowires	High sensitivity, miniaturisation	Debye screening, ionic strength, drift
Electrochemical	Current, potential, impedance (ΔRct)	Carbon, metal oxides, MXenes, metal nanoparticles	Low cost, wearable, quantitative	Fouling, temperature, reference-electrode drift
Magnetic relaxation	T2 relaxation time (ΔT2)	Iron-oxide nanoparticles	Works in turbid samples such as whole blood	Field inhomogeneity, viscosity, non-specific clustering
Nanomechanical	Resonance frequency (Δf) or deflection	Cantilevers, nanowires, graphene membranes	Label-free mass sensing	Damping in liquid, temperature, vibration

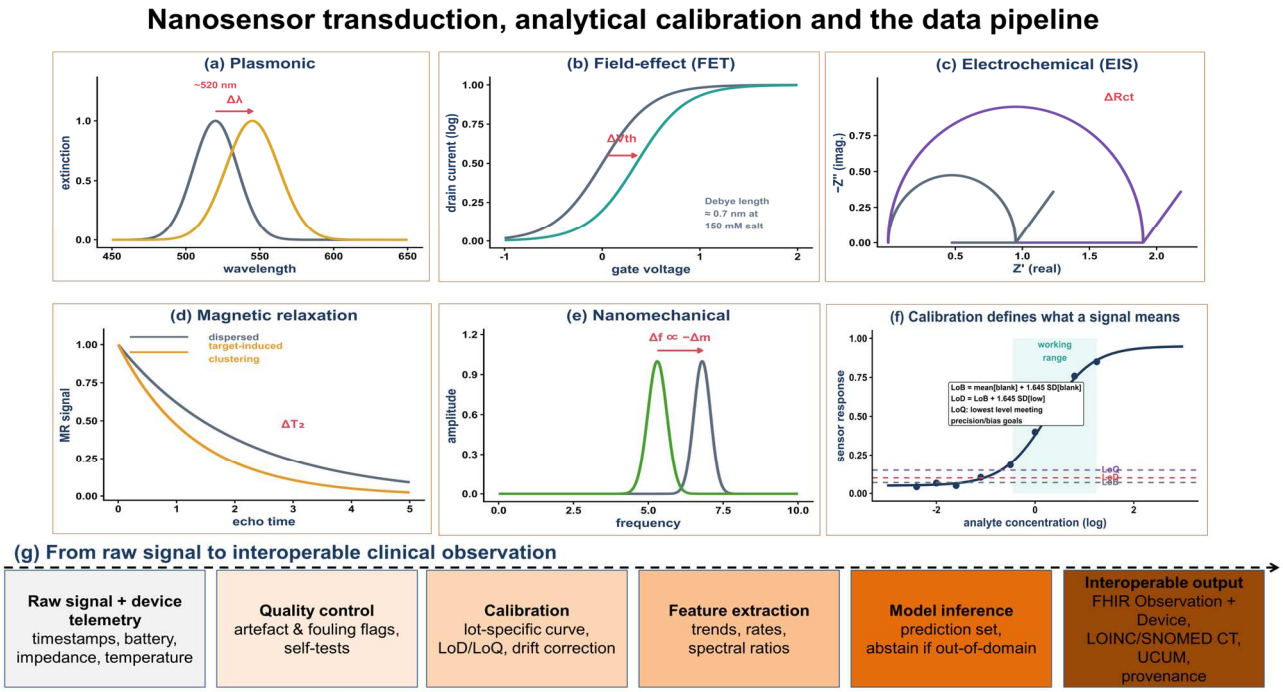

Figure 5. Nanosensor transduction, calibration and data pipeline. (a–e) Schematic read-outs for five transduction modalities before (grey) and after (colour) target binding: plasmonic wavelength shift, field-effect threshold-voltage shift (with the Debye screening length in physiological saline), electrochemical charge-transfer resistance in a Nyquist plot, magnetic T2 relaxation changes on target-induced clustering, and nanomechanical resonance shift with added mass. (f) A calibration curve with limit of blank (LoB), limit of detection (LoD), limit of quantification (LoQ) and working range. (g) Data pipeline from raw signal and device telemetry to an interoperable clinical observation.

environmental noise and manufacturing variation **(Swierczewska *et al.* 2012)**. Each modality has its own physical limits. Field-effect sensors illustrate this well: in physiological fluids with about 150 mM salt, the Debye screening length is only about 0.7 nm, so charges beyond this distance from the surface are largely invisible. Receptor size, sample dilution and surface engineering therefore directly determine what an FET biosensor can detect **(Dehghandehnavi *et al.* 2024)**. Informatics systems must record such conditions, because the same device can give different readings in buffer, serum and sweat. Analytical performance should be reported using established metrics: calibration range, selectivity, response time, limit of blank (LoB), limit of detection (LoD), limit of quantification (LoQ), drift, carry-over, recovery and stability **(Figure 5f)**. Following common clinical laboratory practice, LoB is the highest signal expected from a blank sample, LoD is the lowest concentration reliably distinguished from the blank, and LoQ is the lowest concentration measured with acceptable precision and bias **(Armbruster and Pry 2008)**. Clinical performance requires further measures, including sensitivity and specificity at a defined threshold, predictive values, likelihood ratios and effect on patient outcomes. The distinction matters: a nanosensor may detect an analyte at very low concentration without improving diagnosis or treatment **(Shreffler and Huecker 2023)**.

4.2. Wearable and implantable nanosystems

Nanoscale coatings, flexible electrodes, microneedles and miniaturised transducers support continuous or minimally invasive monitoring **(Wang *et al.* 2023)**. Possible targets include metabolites, electrolytes, inflammatory mediators, gases, pressure, temperature and electrophysiological signals. Measurements from sweat, tears, interstitial fluid, blood and tissue are not interchangeable. Interstitial glucose, for example, typically lags blood glucose by several minutes, and sweat composition changes with sweat rate. Transport delay, local physiology, contamination, motion and environmental exposure must therefore be modelled explicitly. Implants add the challenges of biofouling, the foreign-body response, fibrous encapsulation, power supply, communication and long-term calibration. A slowly changing signal may reflect disease progression, sensor drift, fibrotic isolation or a failing battery. Device-status telemetry should therefore accompany every biological observation **(Min *et al.* 2023)**. Algorithms can use redundant channels, reference

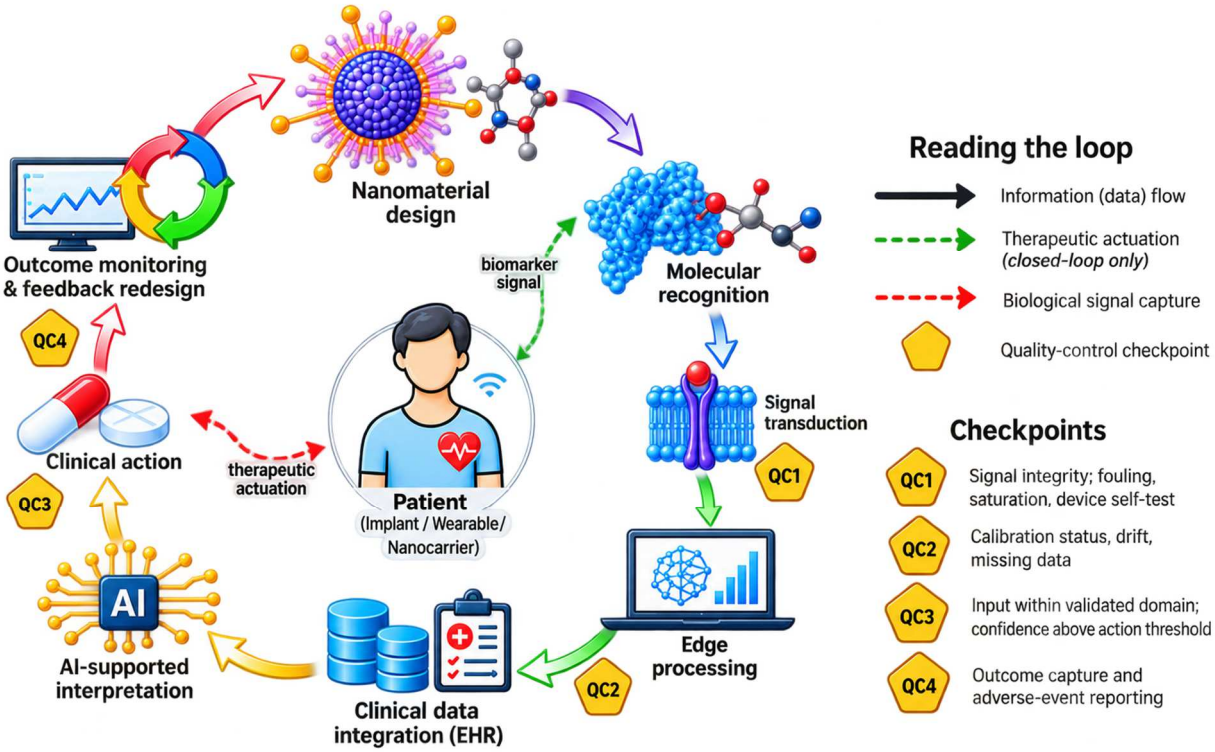

Figure 6. The nano–digital clinical loop. Information flows clockwise from nanomaterial design through molecular recognition, signal transduction, edge processing, clinical data integration and AI-supported interpretation to clinical action, outcome monitoring and redesign. Biological signals are captured from the patient (dotted line) and, in closed-loop systems only, therapeutic actuation returns to the patient (dashed line). Hexagons mark four quality-control checkpoints (QC1–QC4). Actuation requires independent dose limits, a fail-safe mode and clinician override.

electrodes, self-tests and change-point detection to separate physiological trends from hardware failure.

4.3. Internet of Nano-Things and bio-nano networks

The Internet of Nano-Things describes networks in which nanoscale or microscale devices communicate with gateways and larger information systems. In the body, communication may be electromagnetic, optical, acoustic, chemical or molecular. The concept enables distributed sensing and responsive intervention, but practical systems must overcome severe limits on power, bandwidth, localisation, biocompatibility and signal attenuation in tissue **(Elzein 2024)**. A safe architecture keeps sensing, local preprocessing, transmission, clinical interpretation and actuation as separate functions. Edge computing can save bandwidth and protect privacy by transmitting features or alerts rather than raw data streams, but on-device models must be version-controlled and monitored for degradation **(Alabdulatif *et al.* 2023)**. Closed-loop actuation should use conservative thresholds, independent safety limits, manual override and auditable event logs.

4.4. Data pipeline and interoperability

A complete pipeline begins with time-stamped raw data and quality indicators **(Figure 5g)**. Preprocessing may include filtering, baseline correction, normalization, artefact removal and conversion using a lot-specific calibration. Feature engineering then derives trends, rates of change, spectral ratios, event counts or learned representations. Raw measurements should be kept whenever possible, because future algorithms may need information that early processing discarded. Interoperability depends on shared identifiers, units, timestamps, specimen descriptions and provenance **(Yan 2025)**. Device data should map to clinical observations without losing nanoscale context. Application programming interfaces, ideally FHIR-based, can connect nanosystems with EHRs, laboratory information systems, imaging archives (DICOM) and research repositories **(Mihailescu *et al.* 2025)**. Versioning is essential: a change in firmware, coating, calibration or algorithm can change what a measurement means even when its displayed name stays the same. **Figure 6** summarizes how these elements form a continuous clinical loop, with quality-control checkpoints at the points where errors most often enter.

5. Artificial Intelligence and Multiscale Informatics

AI in this field must work across scales, from electronic structure to health systems. **Figure 7** summarizes the data types, computational methods, sources of uncertainty and validation endpoints at each level. Information passes upward as mechanistic prediction and downward as calibration and constraint, and uncertainty must be propagated at every interface rather than discarded.

5.1. Materials discovery and formulation optimization

Machine learning can relate synthesis variables and physicochemical descriptors to stability, loading, targeting, toxicity or sensor response **(Seal *et al.* 2025)**. Supervised models work well when the endpoint is clearly defined, while unsupervised learning can group material families or flag unusual batches. Bayesian optimisation and active learning choose the most informative next experiment and avoid exhaustive screening. Generative models can propose new structures, but their outputs must be constrained by chemistry, manufacturability and biological plausibility. Data quality limits every approach **(van den Broek *et al.* 2025)**. Nanomedicine datasets often contain inconsistent names, missing negative results, variable assay conditions and small sample sizes. If records are split randomly, near-identical formulations from one study can appear in both training and test sets, which inflates apparent performance **(Collins *et al.* 2024)**. Evaluation should therefore use grouped, temporal or external validation that matches how the model will actually be used.

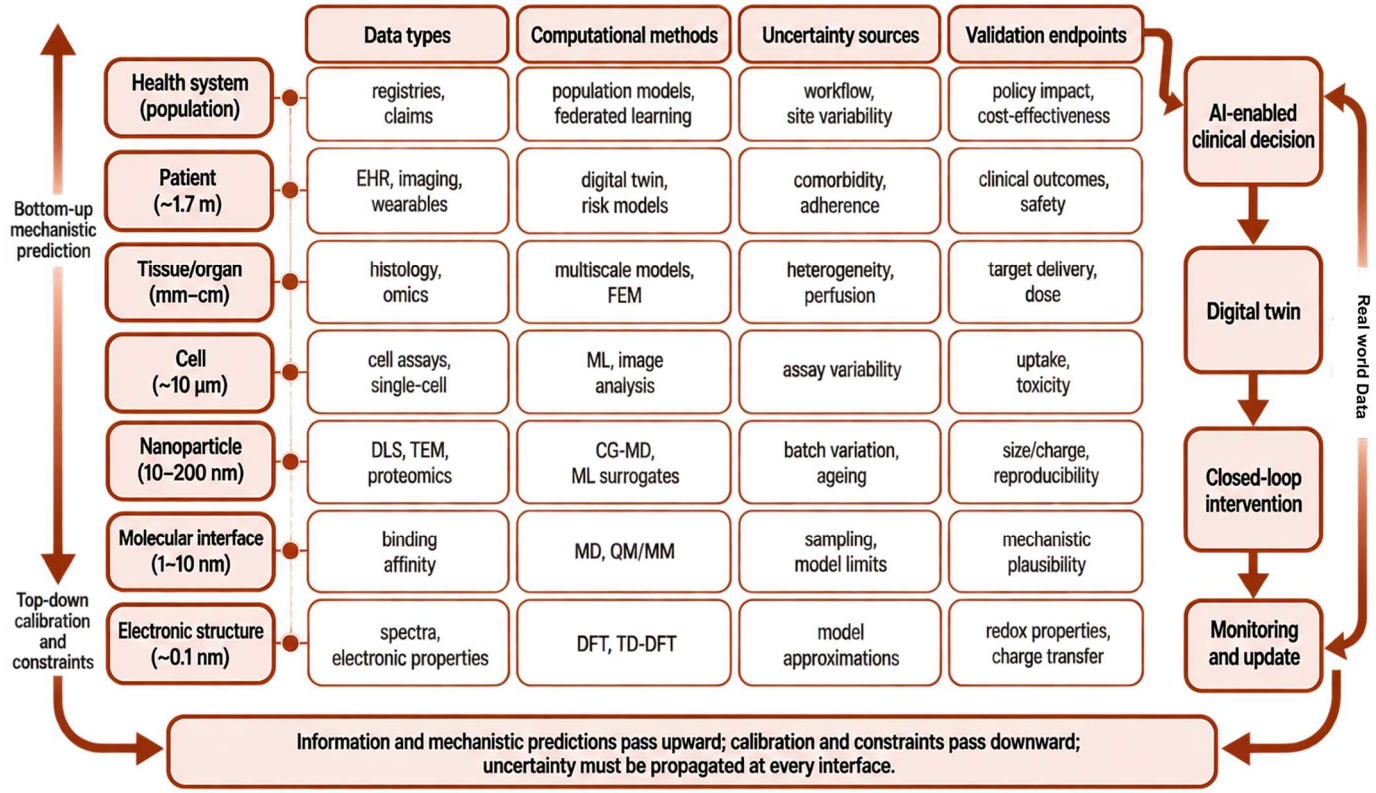

Figure 7. Multiscale architecture linking atomistic mechanisms to clinical decisions. For each of seven levels, from electronic structure to the health system, the figure lists representative data types, computational methods, uncertainty sources and validation endpoints. Bottom-up arrows represent mechanistic prediction; top-down arrows represent calibration and constraints from clinical and experimental data. DLS, dynamic light scattering; FEM, finite-element method; MD, molecular dynamics; PBPK, physiologically based pharmacokinetics; QM/MM, quantum mechanics/molecular mechanics; QSP, quantitative systems pharmacology; TEM, transmission electron microscopy; DFT, density functional theory; TD-DFT, time-dependent density functional theory; CG-MD, coarse-grained molecular dynamics; ML, machine learning.

5.2. Signal analytics and multimodal fusion

Nanosensor streams can be high-frequency, noisy and context-dependent. Time-series models detect trends and short events, while anomaly detection flags rare patterns or device malfunction. Combining nanosensor data with laboratory values, imaging, genomics, medication history, symptoms and environmental exposure can improve interpretation **(Ma *et al.* 2025)**. Fusion can take place at the level of raw data, features, learned representations or final decisions, depending on how well the sources are aligned in time and how often data are missing. In clinical systems, missing data carry meaning. A gap may indicate that the device was removed, that communication failed, that the patient did not adhere or that the patient became unstable. Models should not silently fill all gaps as if they were random. They should represent uncertainty and be able to abstain when inputs fall outside the validated range **(Pana *et al.* 2026)**. Calibration, the agreement between predicted and observed risk, matters as much as discrimination, because clinical decisions depend on whether a predicted probability can be taken at face value.

5.3. Explainability and uncertainty

Explanations should answer clinically relevant questions: which signals drove the output, whether the result is stable, how uncertainty was estimated and what alternative interpretation is plausible. Feature-attribution methods such as SHAP can mislead when inputs are correlated or when preprocessing hides device artefacts **(Aravindkumar *et al.* 2026)**. Mechanistic constraints from atomistic modelling and pharmacology can make models more credible by ruling out predictions that violate known physical behavior. Uncertainty arises from biological variability, measurement error, model parameters and distribution shift, and these components should be separated where possible. Confidence intervals, conformal prediction sets, quality flags and out-of-distribution warnings are more useful to clinicians than an isolated score **(Clegg and Mac Gabhann 2015)**. A model should be allowed to defer to laboratory confirmation or expert review instead of forcing a decision in every case.

5.4. Federated and privacy-preserving learning

Federated learning lets institutions or devices contribute model updates without pooling raw data. This supports multicentre development when privacy, ownership or bandwidth limits prevent data sharing. It does not guarantee privacy on its own, because model updates can leak information (for example, through gradient-inversion attacks), and institutions often differ in patient population, device version and workflow **(Loftus *et al.* 2022)**. Secure aggregation, differential privacy, access control, encryption and governance agreements reduce these risks. Performance should be reported separately for each site and for relevant demographic groups. The system must record model provenance, participation history and update validation, and must be able to roll back a faulty update **(Horst *et al.* 2025)**. For nanosystems, harmonisation should include material batch and device metadata as well as the usual clinical variables.

5.5. Digital twins and closed-loop therapy

A digital twin is a computational representation of a patient or biological process that is updated continuously with new data. Nanosensors can supply molecularly resolved inputs, while imaging, physiology, laboratory tests and clinical events constrain the larger model. The twin may simulate disease progression, drug exposure, tissue response or device behaviour. Its usefulness depends on update frequency, parameter identifiability, validation and the specific decision it supports **(Khoshfekr Rudsari *et al.* 2025)**. Credibility frameworks for computational models used in medical devices, such as ASME V&V 40, provide a structured way to decide how much verification and validation a given decision requires. Closed-loop

systems move from prediction to action. A responsive carrier, implant or external controller may adjust therapy according to the measured state. Such systems need layered safety: validated sensing, robust control logic, dose limits, fail-safe modes, independent monitoring and clinician override (**Zhang *et al.* 2024a**). Every recommendation and actuation event should be logged with the model version, inputs, confidence and outcome.

6. Clinical Applications

Table S1 summarizes how nanosystems and informatics combine in seven clinical areas, and the key question that validation must answer in each.

6.1. Oncology

Cancer is a leading case because tumours show molecular heterogeneity, abnormal blood vessels, changing treatment responses and important spatial variation. Nanoprobes support biomarker detection, image enhancement, multiplexed profiling and guided therapy, while nanocarriers change pharmacokinetics or co-deliver several agents (**Negahdary *et al.* 2026**). Informatics connects these functions with pathology, radiology, genomics, treatment history and outcomes (**Samadzadeh *et al.* 2025**). Precision-oncology platforms should not assume that target expression alone predicts nanoparticle delivery. Analyses of preclinical studies have estimated that a median of less than 1% of an injected nanoparticle dose reaches a solid tumour, and the enhanced permeability and retention effect varies widely between tumours and patients (**Bhujel *et al.* 2025**). Perfusion, stromal density, immune composition, lesion size, prior therapy and organ function all affect exposure. Longitudinal models can compare molecular signals before and during treatment, identify early non-response and trigger confirmatory testing. Clinical evaluation should measure survival, toxicity, quality of life, workflow burden and resource use, not only imaging contrast or biomarker sensitivity (**Peeters *et al.* 2025**).

6.2. Cardiovascular and metabolic medicine

Nanosensors can measure cardiac biomarkers, glucose, lactate, electrolytes, lipids, inflammatory mediators and coagulation-related signals. Nanostructured electrodes improve electrochemical sensitivity, and targeted imaging agents can characterise vascular inflammation and plaque biology. Continuous data can reveal patterns that occasional testing misses, but interpretation must account for physiological lag, exercise, diet, temperature, medication and the body compartment being sampled (**Hu *et al.* 2022; Ma *et al.* 2025**). Decision support should focus on trends and actionable thresholds. In metabolic monitoring, sensor error near a treatment threshold, such as the boundary for hypoglycaemia, can have immediate consequences (**Hu *et al.* 2022**). Systems need redundancy, calibration surveillance and clear instructions for confirmatory testing. Implanted or intravascular devices also require careful assessment of thrombogenicity, endothelial response, degradation products and long-term signal stability (**Babboni *et al.* 2025**).

6.3. Infectious disease and antimicrobial resistance

Nanotechnology supports rapid pathogen detection, multiplexed antigen and nucleic-acid assays, antimicrobial coatings and targeted delivery. Informatics can combine sensor results with symptoms, exposure history, imaging, host-response markers and local epidemiology (**Maojo *et al.* 2012**). At population level, connected tests can strengthen surveillance if their metadata are standardised and results are reported promptly. High analytical sensitivity can detect non-viable organisms or harmless colonisation, so algorithms must distinguish detection from disease (**Ioannou *et al.* 2024**). Antimicrobial nanomaterials need stewardship, because broad activity can disturb the normal microbiota or select for tolerance. Surveillance should track performance drift, false positives, environmental release and changes in local prevalence, since predictive values shift as prevalence changes.

6.4. Neurology and neurotechnology

Nanomaterials can improve neural recording, imaging, transport across the blood–brain barrier and local drug delivery (**Kulkarni *et al.* 2024**). Flexible and nanostructured interfaces reduce the mechanical mismatch with brain tissue and increase electrode surface area, which lowers impedance. However, neural tissue is highly sensitive to inflammation, heat, mechanical injury and chronic foreign-body responses, and signal quality can change as cells and extracellular matrix remodel around an implant. Neuroinformatics platforms should integrate device telemetry with electrophysiology, imaging, medication, behaviour and patient-reported outcomes (**Kozai *et al.* 2015**). Algorithms for seizure detection, stimulation or motor decoding need low latency and robust handling of uncertainty. Closed-loop neurotechnology also raises questions about autonomy, identity, consent and cybersecurity that go beyond conventional device performance (**Wesal *et al.* 2026**).

6.5. Regenerative medicine and tissue engineering

Nanofibres, patterned surfaces, nanoparticles and responsive scaffolds influence cell adhesion, differentiation, vascularization and matrix organization (**Gupta *et al.* 2014**). These effects come from chemical signals and also from geometry, stiffness, charge, degradation and the spatial arrangement of cues. Informatics can relate manufacturing parameters and local microenvironments to cell states and tissue outcomes. Spatial omics, microscopy, biomechanical testing and scaffold-embedded sensors can together produce high-dimensional maps of regeneration. Models may identify combinations of structure and signalling that promote repair, but causal validation remains essential. Long-term studies should assess immune response, tissue integration, mechanical durability, degradation and functional recovery (**Barthes *et al.* 2014**).

6.6. Dentistry and oral health

Dental and oral applications include antimicrobial surfaces, remineralisation agents such as nano-hydroxyapatite, restorative composites, implant coatings, salivary nanosensors, image enhancement and targeted delivery (**El-Morsy *et al.* 2025**). The mouth is a demanding environment, with rapid changes in pH, temperature, mechanical load, diet, microbial ecology and saliva composition, but it is also rich in accessible data. Digital dentistry can combine intraoral imaging, three-dimensional scans, periodontal measurements, salivary biomarkers, material history and patient behaviour (**Lam *et al.* 2026**). Predictive models may support caries risk assessment, periodontal monitoring, implant surveillance and maintenance of restorations. Material informatics should capture wear particles, ion release, surface ageing, biofilm interactions and repeated exposure. Patient-facing tools must be simple to maintain and give patients clear control over their data (**Patel *et al.* 2022**).

6.7. Point-of-care and resource-constrained care

Paper-based, microfluidic, plasmonic and electrochemical nanosystems can bring testing closer to patients. Their clinical value depends on robustness, affordability, storage requirements, power needs, sample preparation, training and connectivity (**Shen *et al.* 2020**). A laboratory prototype may fail in the field if humidity, dust, heat, reagent instability or inconsistent sample collection changes the result (**de Oliveira Cardoso *et al.* 2026**). Offline operation, local-language interfaces, visual quality indicators and delayed synchronisation make deployment more practical. Smartphone reading of colorimetric tests can reduce subjective interpretation, but it introduces variation from cameras and lighting that

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must itself be calibrated (**Liu *et al.* 2025**). Algorithms should be validated in the setting where they will be used rather than transferred unchanged from tertiary hospitals. Equitable performance requires testing across the relevant range of disease prevalence, comorbidity, skin tone, age, sex and socioeconomic conditions (**Wang *et al.* 2024**).

7. Translation, Safety and Governance

7.1. Analytical and clinical validation

Translation begins with a clearly stated intended use. The target population, specimen, operator, setting, output and resulting clinical action must be defined before performance metrics are chosen (**Austin 2021**). Analytical validation shows that the system measures consistently under expected conditions. Clinical validation shows that the output corresponds to the relevant disease state or outcome (**Huang *et al.* 2023**). Clinical utility asks whether using the system actually improves decisions or patient outcomes compared with current care. Prospective studies should reflect the whole workflow, including failed measurements, repeat testing, user behaviour, missing data and maintenance (**Sutton *et al.* 2020**). The comparator matters: a nanosystem should not be judged only against no testing when an established laboratory or imaging pathway already exists (**Zhang *et al.* 2012**). External and multicentre evaluation is needed when materials, populations or workflows vary (**Cruchinho *et al.* 2024**). Established reporting guidelines should be followed, including STARD for diagnostic accuracy, TRIPOD+AI for prediction models, and SPIRIT-AI, CONSORT-AI and DECIDE-AI for trials and early clinical evaluation of AI systems (**Klontzas *et al.* 2023; Liu *et al.* 2020; Park and Suh 2024; Vasey *et al.* 2022**).

7.2. Nanotoxicology and lifecycle safety

Safety depends on dose, route, duration, persistence, transformation and individual susceptibility (**Paul and Sasidharanpillai 2025**). Mass concentration alone is often a poor basis for comparing particles of different sizes, because smaller particles present far more surface area per unit mass; surface-area and particle-number doses are frequently more informative (**Abbasi *et al.* 2023**). Relevant endpoints include membrane damage, oxidative stress, inflammation, complement activation (including infusion reactions), genotoxicity, thrombosis, organ accumulation, reproductive effects and immune changes (**Jacob *et al.* 2025**). Degradation products and excipients need separate assessments, following the biocompatibility principles of ISO 10993. Lifecycle assessment extends beyond the treated patient. Manufacturing workers, caregivers, waste handlers and the environment may all be exposed. Repeated low-level exposure and disposal routes are studied far less than therapeutic dosing. Safety databases should link batch, composition, exposure scenario, assay protocol and outcome, so that evidence can be pooled without losing important context (**Sharma *et al.* 2024**).

7.3. Bias, equity and accessibility

Bias can enter through material design, specimen collection, device adhesion, optical interaction, clinical labelling, missing data and model development. A sensor may perform differently because of sweat composition, skin properties, comorbidity, medication or environment. Optical sensors provide a clear warning: pulse oximeters have been shown to overestimate oxygen saturation more often in people with darker skin, and optical nanosensors could inherit similar problems. If training data under-represent such factors, an algorithm may widen rather than narrow health disparities. Equity evaluation should be planned from the start, not added after overall performance has been reported (**Sedighi *et al.* 2025**). It requires subgroup analysis, error analysis, accessibility testing, attention to affordability and deployment in under-served settings. Fairness does not mean forcing identical outputs when baseline risk and measurement quality genuinely differ. The goal is clinically justified performance for every relevant group, with limitations and mitigations stated openly (**Stanley *et al.* 2025**).

7.4. Privacy and cybersecurity

Connected nanosystems may collect continuous, intimate and behaviorally revealing data. Privacy protection requires data minimization, purpose limitation, consent management, encryption, access control, retention schedules and auditable sharing. Patients should know whether their data stays on the device, move to a phone, enter a cloud platform or become part of the clinical record. Cybersecurity is a patient-safety issue whenever software can influence diagnosis or therapy (**Ji *et al.* 2024**). Threats include spoofed signals, unauthorised commands, malicious updates, denial of service, re-identification and model manipulation. Secure boot, signed firmware, authenticated communication, network segmentation, vulnerability disclosure, timely patching and incident response should be built into the product lifecycle, in line with standards such as IEC 81001-5-1. Closed-loop devices need especially strict separation between monitoring and actuation privileges (**Nankya *et al.* 2023**).

7.5. Regulation and quality management

Regulatory evaluation becomes complex when one product combines a nanomaterial, a diagnostic function, software, AI and therapeutic action. The primary mode of action may not capture the system's full risk. Developers need an integrated evidence plan covering chemistry, manufacturing and controls; biocompatibility; analytical performance; software verification under IEC 62304; risk management under ISO 14971; human factors; clinical evaluation; and post-market surveillance (**Desai *et al.* 2025**). In the European Union, the Medical Device Regulation and the AI Act may apply together, and in the United States, AI-enabled devices can use a predetermined change control plan to define in advance which algorithm updates are permitted. Adaptive algorithms and formulation changes therefore require pre-specified change-control strategies. An apparently minor change in coating, supplier, preprocessing or model threshold can alter clinical behaviour. Quality systems should link requirements, hazards, verification tests, validation evidence and field performance (**Carvalho *et al.* 2025**). Post-market data should support rapid investigation without encouraging uncontrolled model updates.

7.6. The NanoMed-Info translational framework

We propose that evidence be organised into seven linked layers: atomistic identity, physicochemical product, biological interface, device or formulation performance, data and algorithm, clinical utility, and lifecycle governance (**Figure 8; Table S2**). A product should advance to the next layer only when traceability to the adjacent layer has been shown. For example, a change in ligand chemistry should be traced to its effect on corona behaviour, sensor calibration, model input distribution and ultimately clinical risk. Between layers, decision gates (G1–G6) specify the required evidence, the acceptable uncertainty, the accountable owner and the monitoring plan. The framework is designed to discourage isolated claims of innovation (**Weber *et al.* 2025**). Exceptional sensitivity cannot compensate for unstable manufacturing, and high model accuracy cannot compensate for biased labels or an unclear clinical action. Post-deployment signals flow back to the product and algorithm layers, so that the framework describes a learning cycle rather than a one-way pipeline. Current methods tend to treat nanomaterials identification and characterization, nano sensors, data management or integration, and clinical AI solutions as separate components (**Xie and Tummala 2025**). The Nano Med-Info platform unites them all in an overall evidence pathway that takes the new, nanoscale information from its atom identity through its physicochemical properties, biological interface, sensor device performance, data, algorithms, clinical utility, to the final life cycle

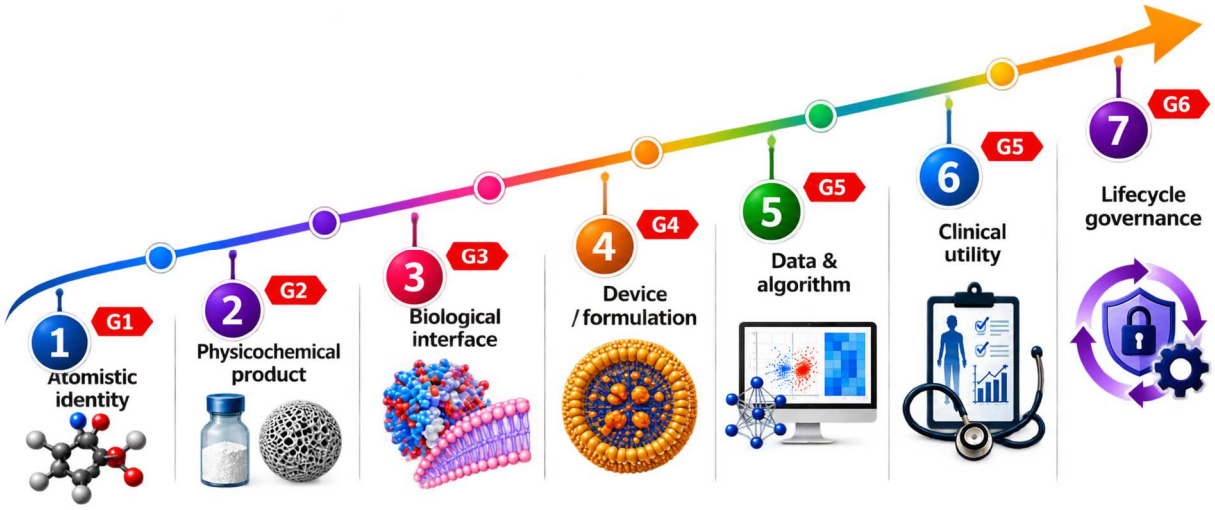

Figure 8. The seven-layer NanoMed-Info evidence framework. Each step lists example evidence and the key question it must answer. Gate markers (G1–G6) indicate decision points at which evidence, uncertainty, an accountable owner and a monitoring plan must be specified before advancing. Post-deployment signals provide feedback to the product and algorithm layers.

management. A key aspect of the evidence pathway is decision gates that require the availability of well-quantified evidence of traceability, uncertainty, and accountability before progress to the next stage **(Joseph *et al.* 2023)**.

8. Future Directions

8.1. Standardized representations

The next phase of the field needs shared vocabularies and minimum information standards covering nanomaterial identity, biological context, simulation conditions, sensor calibration and clinical deployment **(Fadeel 2022)**. Unique material and device identifiers would improve traceability across experiments and product versions. Knowledge graphs can connect particles, coatings, proteins, pathways, diseases, devices and outcomes while preserving provenance **(Khalid *et al.* 2025)**. As a practical starting point, Table S3 proposes a minimum reporting checklist for any study or product that feeds nanosystem-derived data into clinical decisions. Benchmark datasets should include negative results, repeated batches, realistic controls and external test sets **(Homeyer *et al.* 2022)**. Data-sharing mechanisms must respect intellectual property and patient privacy while still allowing independent validation. Community challenges can compare models, but their tasks should reflect real clinical decisions rather than convenient prediction targets **(Faria *et al.* 2018; Kwak and Kim 2025)**.

8.2. Mechanistic artificial intelligence

Mechanistic or physics-informed AI combines physical constraints with data-driven flexibility. Atomistic calculations can define descriptors or prior distributions, while clinical observations update patient-specific predictions. Such hybrid models tend to extrapolate better than purely statistical systems when they meet new formulations or populations. Their assumptions must remain open to inspection, and their uncertainty should increase when evidence is sparse **(Angelis *et al.* 2023; Seifert *et al.* 2021)**. Foundation models for molecules, materials, images and clinical text may speed up hypothesis generation and multimodal integration. They also bring risks: fabricated explanations, hidden data leakage and high computational cost **(Angelis *et al.* 2023)**. They should be used only in validated roles, with human review, version control and a clear separation between generated hypotheses and established evidence.

8.3. Autonomous laboratories and digital manufacturing

Robotic synthesis, automated characterization and active learning can explore formulation space far more efficiently than manual work. In a closed experimental loop, the system proposes a candidate, makes it, measures its key properties, updates the model and selects the next experiment. To be scientifically useful, such systems need calibrated instruments, standardised metadata, anomaly detection and retention of failed experiments. Digital manufacturing records could eventually support release testing and personalised production. This will require validated process models, secure transfer of recipes, control of raw materials and traceable links between digital instructions and physical batches **(Kim *et al.* 2026)**. Personalized products must meet the same quality requirements as mass-produced ones, even when made in very small numbers.

8.4. Clinical integration priorities

Near-term progress is most likely where a nano system addresses a clearly defined unmet need and fits an existing care pathway. Examples include rapid rule-in or rule-out tests, therapeutic monitoring where conventional sampling is burdensome, targeted imaging that changes the intervention, and formulations that measurably improve exposure and safety **(Baryakova *et al.* 2023)**. Development should start with the clinical decision and work backwards to the material, rather than starting with a novel particle and searching for an application. Implementation studies should measure training needs, maintenance, turnaround time, alert burden, confirmatory testing, cost and patient acceptance **(Zheng *et al.* 2026)**. Procurement decisions should consider the full lifecycle cost, including calibration, software, cybersecurity, replacement and waste management. Health-economic models should be updated with real-world outcomes rather than relying indefinitely on laboratory assumptions.

9. Conclusions

Nanotechnology-enabled medical informatics offers a coherent way to connect molecular design with accountable healthcare. Its central insight is that a nanomaterial is not only a physical object but also a context-dependent generator, carrier and modifier of information. Atomistic interactions determine biological identity, nano sensors convert molecular events into signals, and informatics systems turn those signals into decisions. The most valuable systems will not necessarily be the smallest or the most sensitive. They will be those that keep measurements traceable through synthesis, biological exposure, signal processing, algorithmic interpretation, clinical action and long-term surveillance. Achieving this requires standardized metadata, interoperable data structures, prospective validation, uncertainty-aware models, human-

centered interfaces and lifecycle governance. Each nanoplatform class, from gold and silver nanoparticles to lipid carriers and mesoporous silica, has distinctive strengths and failure modes. Their clinical relevance depends on representing these differences explicitly rather than grouping them into a generic 'nano' category. The Nano Med-Info framework and the proposed minimum reporting checklist provide a practical structure for doing so. With collaboration among materials scientists, computational chemists, biologists, clinicians, informaticians, engineers, regulators, ethicists and patients, the convergence of nanotechnology and medical informatics can deliver earlier detection, more precise intervention, adaptive monitoring and safer personalized care.

10. Disclosure Statements

10.1. Author Contribution

LAD: Conceptualization, methodology, literature investigation, data curation, writing - original draft, visualization, and project administration; **SS:** Literature investigation, data curation, and writing - original draft; **YEA:** Literature investigation, critical analysis, and writing - review and editing; **MME:** Literature investigation, interpretation, and writing - review and editing; **RV:** methodology, critical analysis, supervision, and writing - review and editing. **LAD:** Corresponding author and responsible for overall coordination of the manuscript, integration of contributions, and final approval of the submitted version. All authors contributed to the development and critical revision of the manuscript and approved the final version.

10.2. Declaration of Generative AI

The authors used generative artificial intelligence tools solely for language editing and grammatical correction. QuillBot was used solely for language correction and improvement of English expression. BioRender and Canva were used for the preparation, design, and formatting of scientific figures. The scientific content, interpretation, and final presentation were reviewed and approved by the authors. All content has been reviewed and approved by the authors, who take full responsibility for the integrity and accuracy of the work.

10.3. Ethics approval (for clinical/animal studies)

Ethical approval was not required for this study because it is a review article based exclusively on previously published literature and does not involve human participants, human-derived samples, animals, or experimental interventions.

10.4. Informed Consent Statement

Not applicable. This study did not involve human participants, human-derived samples, or clinical data; therefore, informed consent was not required.

10.5. Data Availability Statement

No new data were generated or analyzed in this study. All information discussed in this review was obtained from publicly available published literature and cited appropriately within the manuscript.

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10.8. Conflicts of Interest

The authors declare that they have no known financial, personal, academic, or other relationships that could inappropriately influence, or be perceived to influence, the work reported in this manuscript. All authors confirm that there are no competing interests to declare.

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10.10. Supplementary Information

The supplementary information associated with this manuscript is available in https://jomi.aayvu.com/SuppFile/240979/1/

10.11. Sustainable Development Goals (SDGs)

This article contributes to the following Sustainable Development Goals (SDGs):

SDG 3	Good Health and Well-being
SDG 9	Industry, Innovation and Infrastructure
SDG 12	Responsible Consumption and Production
SDG 13	Climate Action
SDG 16	Peace, Justice and Strong Institutions
SDG 17	Partnerships for the Goals

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