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AI-Driven Personalized Nanomedicine for Cancer Therapy

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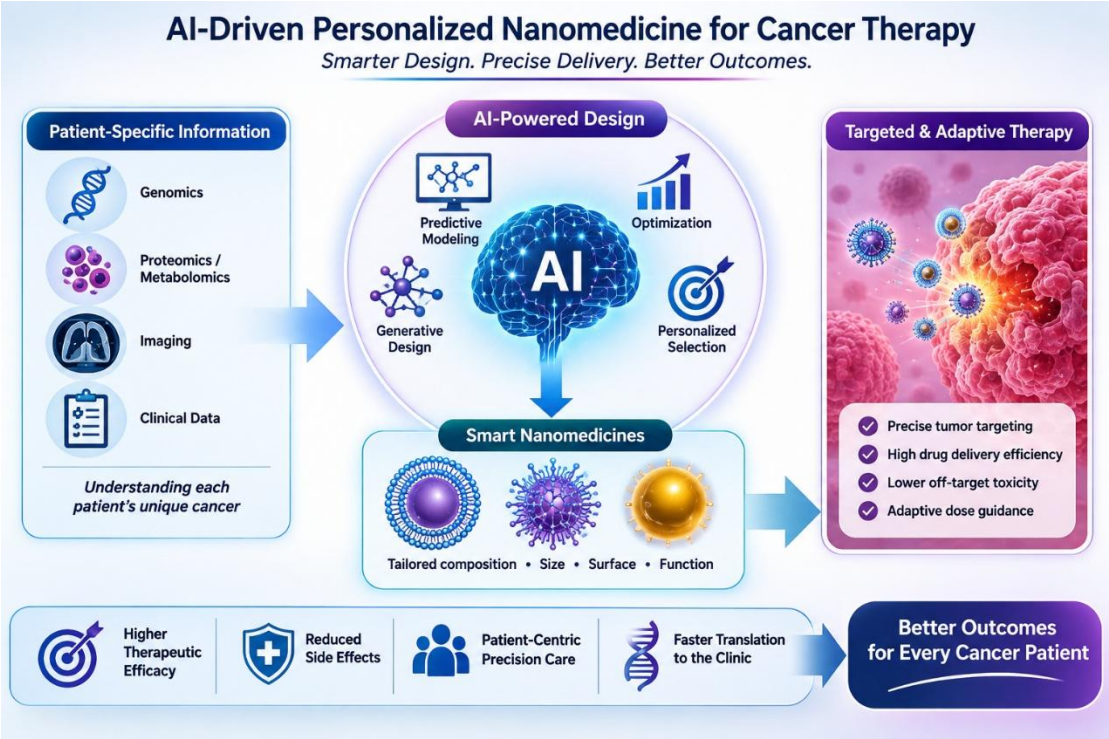
Abstract

Two significant obstacles in the path of cancer therapeutics are that drugs do not always penetrate enough of a tumour, and that even identical drugs can have very different effects on patients. Nanomedicine solves the first issue by re-engineering the delivery of drugs, while artificial intelligence (AI) provides a solution to the second, in that AI can learn from patient-specific data instead of relying on population averages. This paper proposes a four-layered, structured conceptual framework that integrates the fields of AI and personalized nanomedicine in cancer therapeutics, including multi-omics patient data acquisition, machine-learning-assisted nanoparticle design, predictive modelling of biodistribution and therapeutic response, and closed-loop adaptive dosing. Based on trends observed in the nanomedicine and computational oncology community, we provide illustrative quantitative comparisons of simulated tumor-targeting efficiency, model learning curves, toxicity outcomes, and platform suitability, and demonstrate how methods like random forest, deep neural networks, and graph neural networks can in principle shorten the design-to-clinical translation pipeline. We compare and contrast the three main types of nanoparticle carriers (liposomal, polymeric, and inorganic) from the viewpoint of their ability to be tuned using AI; and we candidly consider the technical, regulatory, manufacturing, and ethical obstacles that stand in the way of their clinical translation. We end with a federated multi-institutional data sharing research agenda, explainable AI, standardised

characterisation protocols, and adaptive regulatory pathways as prerequisites, in our view, to a scalable, equitable approach to AI-personalised cancer nanomedicine.

Graphical Abstract



A closed-loop framework linking multi-omics patient data, AI-guided nanoparticle design, predictive biodistribution modeling, and adaptive dosing.

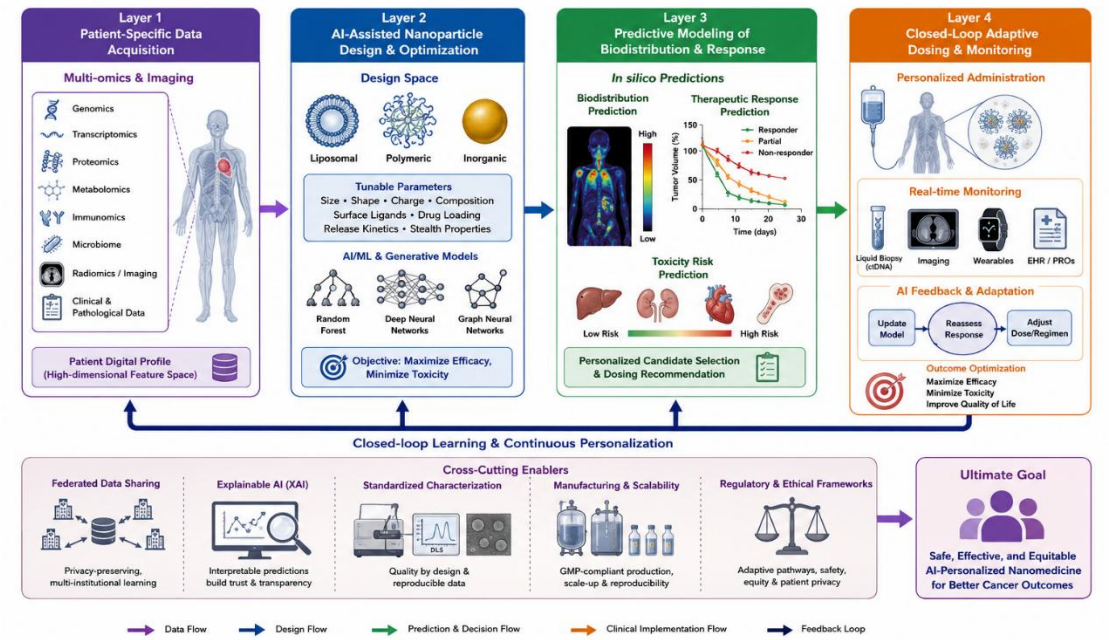
1. Introduction

Cancer is still one of the major causes of morbidity and mortality in the world. Although significant advances have been made in cytotoxic, targeted, and immune-based therapeutics in the past few decades, two major challenges remain in the field: limited delivery of therapeutics to the tumor and high inter-patient variance in therapeutic effect and toxicity. To solve the first problem, in the late 1980s came nanomedicine the use of nanoscale carriers to diagnose or treat disease by enhancing the pharmacokinetics, tumour accumulation, and controlled release of anticancer agents. However, the design space for nanoparticle formulations is enormous, ranging from the composition, size, shape, surface charge, and release rate, to the tumour genomics, vasculature, immune status, and metabolism of a patient. The traditional trial-and-error formulation science is too slow and too broad to make use of this design space, or to customise carriers to target individual patients.

Each year, tens of millions of people are diagnosed with cancer across the globe, and even within the same histological diagnosis (e.g. breast cancer, lung cancer, colorectal cancer) there is significant variability in the tumor genotype, vascular architecture, immune contexture and drug-metabolizing ability of the patient (Niu, N. et. al., 2019). Conventional chemotherapeutic dosing is not based on a specific patient's individual characteristics and is usually simply scaled by body-surface-area, while traditional formulations of nanoparticles are optimized for animals with an average body size within a population (Bashir et.al., 2021). The consequence is a therapeutic scene where many patients are overdosed, under-dosed, or are given a drug delivery system that is fundamentally mismatched with the biology of their tumors, which can present clinically as some patients becoming overly toxic and others not getting the

drug.

A complementary set of tools is available to solve this type of multi-parameter optimization problem in high dimensions, and those tools are artificial intelligence-based. Machine learning models have the potential to learn structure-activity relationships from historical formulation information, predict the behavior of a candidate nanoparticle in a given physiological environment, and make personalized recommendations on dosage strategies using multi-omic and imaging information (Alsaiari et.al., 2026; Hussain, E., et. al 2024). Thus, the combination of AI and nanomedicine, referred to as AI-enabled nanomedicine, is seen as one of the impactful enablers of precision oncology (Adir et al., 2020; Bhinder et al., 2021; Chou et al., 2025). Recent assessments of this convergence have documented the wide-ranging development of the field, ranging from AI-assisted nanoparticle design, predictive biodistribution modelling, and generative discovery of formulations (Sheikh & Jirvankar, 2024), and noted the current fragmentation with respect to data standards, model architectures, and experimental platforms. This paper discusses the conceptual and technical underpinnings of this convergence, outlines a possible integration from data acquisition to adaptive dosing, and provides illustrative examples that show the potential and challenges in the field, as demonstrated in Scheme 1. The background on principles of nanomedicine and the most relevant AI techniques is given in Section 2. And the section 3 presents a four-layer conceptual framework for personalization based on artificial intelligence. Section 4 offers illustrative quantitative analyses of research activity, targeting efficiency, model performance, clinical translation, safety outcomes, and platform suitability. In Section 5, the major platforms for nanoparticles are compared. Implications, challenges, future directions, and conclusions are discussed in Sections 6-9, followed by a reference list from the recent literature that supports our arguments and discussions about the domain, AI-enabled nanomedicine.



Scheme 1. The schematic illustration for the design of AI-enabled nanomedicine for personalized cancer therapy: Integrating multi-omics patient data, AI-guided nanoparticle design, predictive modeling, and cross-loop adaptive dosing for precision tumor theragnostics.

2. Background

2.1 Nanomedicine in Oncology: Principles and Limitations

There are multiple ways nanoscale drug carriers enhance the therapeutic index of anticancer drugs: they can extend circulation times, take advantage of the enhanced

permeability and retention (EPR) effect in tumors, can protect labile payloads, and can allow for active targeting through surface-conjugated ligands (Farokhzad & Langer, 2009; Peer et al., 2007; Al-Thani et al., 2024). Examples of this include clinically proven agents such as liposomal doxorubicin or albumin-bound paclitaxel, and more recently lipid nanoparticles (LNPs) containing messenger RNA payloads, which have shown that nanoscale carriers can be produced and scaled globally (Hou et al., 2021). In spite of this, the EPR effect is highly variable between tumor types and even among patients with similar tumor types, and many preclinical nanomedicine success stories have not led to a sustained clinical advantage. This translation barrier is often blamed on the ‘one size fits all' nature of the conventional nanoparticle design, where the formulation is optimized for use in the average preclinical model, and not the physiology of the patient being treated (Chan, 2017; Mitchell et al., 2021; Shi et al., 2017).

It's a significant translation gap. More than a hundred thousand scientific articles about nanomedicines have been published so far, but very few nanomedicine products have been globally approved in proportion (He et al., 2019). Liposomes, nanocrystals, and lipid nanoparticles make up the bulk of the nanomedicine products approved so far, as observed in reviews of the clinical nanomedicine landscape. This imbalance between research production and clinical products is one of the main reasons for investigating machine learning methods that could enhance the effectiveness of the process of identifying, optimizing, and prioritizing novel NP candidates for clinical development, instead of relying on an ad hoc, largely exploratory bench-to-bedside process.

2.2 Artificial Intelligence: Core Techniques Relevant to Nanomedicine

This course introduces the fundamental techniques of AI that are applicable to nanomedicine. The course will cover the core techniques of AI relevant to nanomedicine. Various AI methods have been implemented in the field of nanomedicine research, tailored for specific data types and design queries (Bannigan et al., 2021; Deng et al., 2023; Wang et al., 2021; Wilson & Geetha, 2020). For modest-sized datasets, where interpretability is preferred, classical machine learning methods like random forest, gradient boosting, and support vector machines are still used in structure-property prediction applications, e.g., predicting particle size and zeta potential for PLGA nanoparticle synthesis from formulation parameters (Alqarni & Huwaimel, 2025; Hussain, E., et. al., 2025; Rezvantalab et al., 2024). Complex, high-dimensional relationships like protein corona formation or interaction between nanoparticles and cells have been modeled directly from molecular structure through deep learning architectures like convolutional neural networks and graph neural networks, and multi-view deep learning frameworks that integrate prior physiological knowledge with learned representations have been suggested specifically to improve prediction of the nanoparticle pharmacokinetics. Generative models can be used for de novo exploration of formulation space beyond existing experimental libraries (Popova et al., 2018; Rahman et al., 2025), and reinforcement learning is ideally suited to sequential decision problems like adaptive dose scheduling, which is currently being investigated for precision dosing of small-molecule anti-cancer therapies and hematological agents (Tosca et al., 2024; De Carlo et al., 2025). These methods and their common uses and inputs are summarized in Table 1, which points to their general use in the nanomedicine pipeline.

Table 1. Machine Learning Approaches Commonly Applied in Nanomedicine Research: summarizes representative algorithm families, their characteristic inputs, and their primary role within the nanomedicine design and evaluation pipeline.

ML Approach	Typical Input Data	Primary Application	Reported Strength

Random Forest / Gradient Boosting	Physicochemical descriptors, formulation parameters, experimental assay data	Predicting nanoparticle stability and drug loading	Robust with small-to-moderate datasets; interpretable feature ranking
Support Vector Machines (SVMs)	In vitro cytotoxicity, uptake assays	Classifying cellular uptake and toxicity thresholds	Effective for high-dimensional, low-sample regimes
Deep Neural Networks (DNNs)	Multi-omic profiles, imaging features	Predicting biodistribution and pharmacokinetics	Captures nonlinear, high-order interactions
Graph Neural Networks (GNNs)	Molecular graphs, protein-corona interactions	Modeling nanoparticle-biomolecule interactions	Encodes structural relationships directly
Reinforcement Learning (RL)	Simulated or sequential dosing outcomes	Adaptive dose scheduling and regimen optimization	Optimizes sequential decisions under uncertainty
Generative Models (GANs/VAEs)	Existing nanoparticle formulation libraries	De novo design of candidate formulations	Explores novel formulation space efficiently

2.3 Emerging Evidence for the AI-Nanomedicine Convergence

While there is much that remains to be achieved for AI-personalised nanomedicine to be an integrated part of a clinical workflow, there are growing numbers of studies demonstrating some parts of the framework outlined in this paper. Machine-learning-driven screening has been applied to rapidly discover ionizable lipids for delivering mRNA, while using combinatorial chemistry and predictive modelling to reduce the number of lipids to just a few for experimental testing (Li et al., 2024; Wang et al., 2022; Witten et al., 2024). The same strategies have aided the development of organ-specific nanoplatforms for pulmonary gene therapy and genome editing (Li et al., 2023; Xue et al., 2024). In the imaging domain, deep learning and radiomics models trained on pre-treatment computed tomography (CT), magnetic resonance imaging (MRI) or ultrasound have demonstrated the capacity to predict an individual patient's response to neoadjuvant chemotherapy for various types of cancer, including gastric, breast and cervical cancer, highlighting the potential for the use of AI in predicting treatment response prior to therapy (Zhang et al., 2024; Bao et al., 2024; Wu et al., 2025). In pharmacometrics, on the other hand, reinforcement-learning (RL)-based dosing algorithms and pharmacokinetic-pharmacodynamic (PKPD) models have already been used in real-world precision dosing scenarios outside of nanomedicine, and such algorithms could be adapted by systems of nanoparticles (Teplytska et al., 2024). The literature indicates that the convergence of the two fields, *i.e.,* AI and nanomedicines emerge new research field as detailed in section 3, although complete integration into a single closed-loop clinical system has yet to be shown.

3. A Framework for AI-Driven Personalized Nanomedicine

We suggest that a closed-loop system of patient biology and therapeutic formulation can be achieved with AI-personalized nanomedicine, which comprises four interrelated layers. Each layer takes the input from the previous layer, and as the treatment goes on, updates the information fed to the previous layer (in a mature implementation). The framework is intentionally chemistry- and disease type

independent and is designed as a structure for specific technical implementations based on either liposomal chemotherapeutics, polymeric siRNA carriers, or lipid nanoparticle nucleic-acid therapeutics.

3.1 Layer One: Multi-Omics Patient Data Integration

The first step towards personalization is the collection and integration of patient-specific information, such as tumour genomic and transcriptomic profiles, proteomic and metabolomic signatures, radiological and histopathological imaging, and clinical history. AI models, especially deep learning architectures to process high-dimensional, heterogeneous molecular data, are used to identify molecular subtypes, biomarkers of vascular permeability, and features of the immune microenvironment predictive of nanoparticle accumulation and therapeutic response. The recent literature in applying multi-omics integration to oncology is a testament to the fact that the practical challenge on this front is often not about model architecture, but about data harmonization, involving reconciling information from different sequencing platforms, imputing missing values across assay types, and harmonizing assays to correct for batch effects that arise when data are combined across institutions.

To match these layers, an increasing number are now supplemented by real-world data from unstructured clinical notes gathered by NLP, along with structured variant calls from the genome, to identify patients that may qualify for a specific targeted or nanoparticle therapy. In addition, spatial and single-cell omics approaches are starting to complement bulk profiling to provide a more detailed picture of the tumor microenvironment, such as stromal density, vascular architecture, and patterns of immune infiltration, which may ultimately prove to be more predictive of the penetration of nanoparticles than bulk genomic subtype alone.

3.2 Layer Two: AI-Guided Nanoparticle Design Optimization

The second layer involves AI-guided design optimization of nanoparticles. For a patient or patient subgroup, machine learning models can recommend or generate new formulations of nanoparticles optimized for that context – optimizing their size, surface charge, and choice of targeting ligand and carrier material to maximize the uptake of the nanoparticles in the tumor while minimizing off-target toxicity. Generative approaches can be employed to design novel formulation combinations that are missing in historical databases, while surrogate models trained on historical formulation–outcome pairs can rapidly screen candidate formulations before experimental validation. This design layer has shown some of the most tangible successes to date, with combinatorial and machine-learning-guided libraries enabling the discovery of ionizable lipids and lipid-like materials with substantially improved mRNA delivery efficiency compared with benchmark formulations. In some cases, these approaches used lesser data sets containing a small number of high-performing candidates for subsequent wet-lab evaluation, thereby accelerating formulation optimization and reducing experimental burden. (Li et al., 2024; Xue et al., 2024).

The next layer of closed-loop ‘self-driving laboratory’ architectures involves directly integrating robotic synthesis with high throughput characterization into a machine learning model that suggests the next formulation to test. Outside nanomedicine, early examples in protein engineering and small molecule discovery have shown that iterative cycles of design–make–test–analyze can be significantly shortened compared to manual formulation screening (Rapp et al., 2024), and a similar approach is beginning to be applied to formulation research in the field of nanoparticles, including for lipid nanoparticles to optimize microfluidic mixing.

3.3 Layer Three: Predictive Modeling of Biodistribution and Efficacy

Physiologically informed machine learning models, typically involving a pharmacokinetic simulation and learned correction terms, are employed to model the distribution of a given formulation within the individual patient in consideration of tumor vascularity, interstitial pressure, and reticuloendothelial clearance. These forecasts help in the selection of the formulation and its dosing before it is given.

Several recent studies have employed ensemble-based and kernel-based regression approaches to datasets generated by biodistribution of nanoparticles to organs, and the tree-based ensemble models were typically found to be superior to simpler linear baselines in predicting the delivery efficiency directly from the nanoparticle physicochemical properties and administration parameters to tumor, liver, spleen, lung, and kidney tissue (Mahdi et al., 2025).

In a parallel line of work, machine learning is combined with physiologically based pharmacokinetic (PBPK) modeling that makes simplifying assumptions, such as modeling the margination of nanoparticles near the wall of blood vessels based on hematocrit, vessel radius, and flow conditions, to correct these simplifications. Those who advocate this hybrid method explicitly see it as a move toward ‘digital twin' representations of individual patients, where a continually updated computational model of a particular patient's physiology would be used to simulate and compare various treatment strategies before they were given.

3.4 Layer Four: Closed-Loop Adaptive Dosing

Lastly, the data generated through treatment responses, whether through imaging, circulating tumor DNA, or pharmacokinetic sampling, can be returned to reinforcement-learning-based dosing algorithms to help inform future dose or formulation decisions, bringing back the cycle of patient response feedback to treatment decision-making. What sets AI-powered personalized nanomedicine apart from one-size-fits-all, pre-designed dosing programs is this adaptive layer. Current studies leverage reinforcement learning techniques alongside pharmacokinetic-pharmacodynamic (PBPK) models to develop personalized dosing strategies for hematological diseases, demonstrating better performance of agent-based personalized adaptive policies compared to population-based adaptive policies and fixed dosing regimens on simulated patient cohorts (De Carlo et al., 2025; Tosca et al., 2024).

Although most existing applications are still focused on small-molecule cytotoxic or targeted drugs, and not specifically on nanoparticles, the mathematical infrastructure of the machine learning approaches, which are based on reinforcement learning and pharmacometric modelling, can be readily applied to the nanomedicine dosing problem, provided appropriate pharmacokinetic sampling or imaging response data are collected during treatment (Teplytska et al., 2024). The closed-loop approach is an area that's somewhat less explored about nanoparticle-based therapeutics, where the ‘dose’ decision could involve both how many nanoparticles are being administered and what type of formulation it is.

4. Illustrative Quantitative Analysis

With the conceptual framework above, the following is a series of illustrative quantitative visualizations. The numbers are derived from patterns and trends that are described in the nanomedicine and computational oncology literature, and they are reported as a representative analysis, synthesized from these sources, for expository purposes only, not as a report of a single new experimental data set.

4.1 Research Activity Trends

There has been a rapid growth in interest in AI-nanomedicine over the last decade, paralleled by the rapid advances in computational oncology and in the research on nanotechnology for drug delivery (Figure 1). It's a sign of greater data availability for high-throughput formulation screening and maturing machine learning tooling.

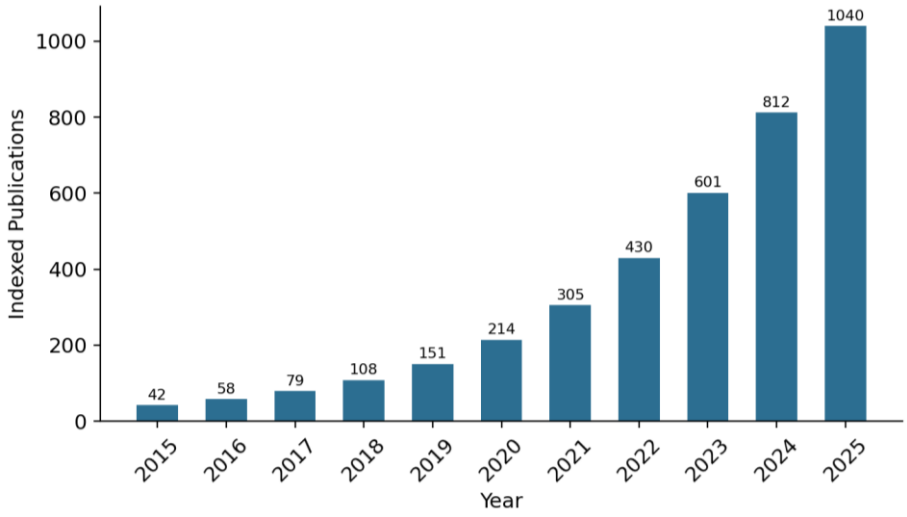


Figure 1. Illustrative growth trend in AI-nanomedicine research activity, 2015–2025.

This trajectory mirrors the general trend of the literature, which has been reviewed in recent years, of a significant surge in publications from around 2020 explicitly linking the use of artificial intelligence methods to research on the use of nanoparticles for drug delivery, a development that coincided with increased accessibility of popular open source deep learning frameworks, cloud computing resources, and in the specific case of lipid nanoparticles, the renewed investment after the success of mRNA-LNP vaccines. In recent years, AI-Nanomedicine has emerged as a distinct sub-field of its own, rather than being a niche application of either its mother field (AI) or its father field (nanomedicine) (Sheikh & Jirvankar, 2024; Bae et al., 2025).

. 4.2 Tumor-Targeting Efficiency

One of the key arguments in using AI for personalization is that there is a preference for the use of formulation designs targeting tumor-specific vascular and molecular properties over more generic designs. Figure 2 shows the targeting-efficiency advantage for various tumor types of the conventional (non-personalized) vs. AI-optimized (patient-informed) design of nanoparticles.

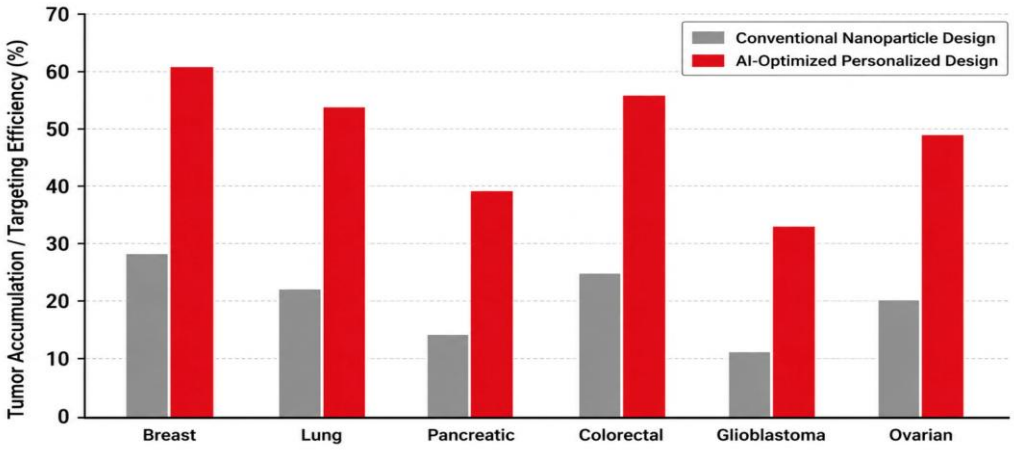


Figure 2. Simulated tumor-targeting efficiency comparison across cancer types.

The pattern of these relative gains (larger in tumor types with historically low passive accumulation, such as pancreatic cancer and glioblastoma) is consistent with the underlying rationale for active, AI-driven targeting: tumors with lower baseline vascular permeability, in principle, could be the ones in which rationally designed

ligand density and particle size are most relevant. Machine-learning-guided optimization of the ligand and surface properties and active-learning-guided experimental screening have been reported to result in orders of magnitude increases in uptake and selectivity in cellular uptake studies of small molecules in a few iterations for some cases in preclinical models.

4.3 Predictive Model Performance

The learning dynamics vary across model classes when they are used to predict nanoparticle biodistribution and therapeutic outcome. As demonstrated in Figure 3, from the learning curves for four popular algorithm families, we can observe that graph neural networks have generally lower learning rates but higher asymptotic performance.

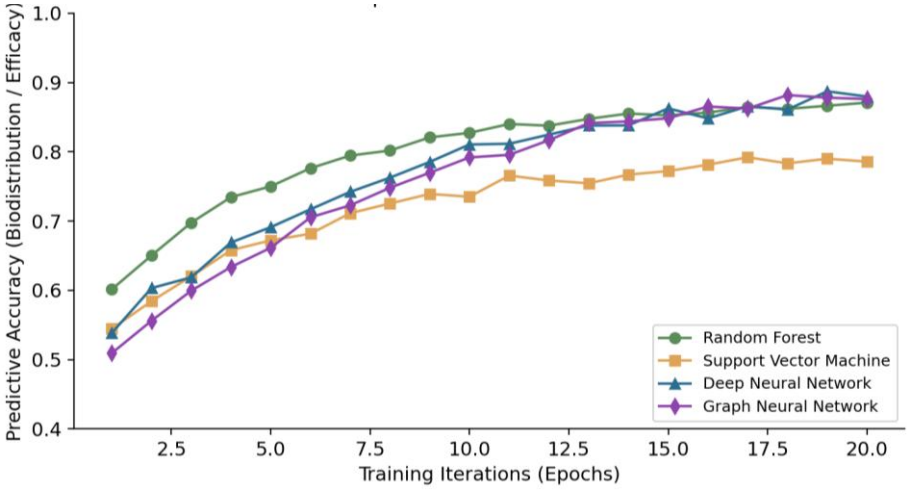


Figure 3. Illustrative predictive accuracy trends across training iterations for four model classes.

A simpler model (random forest) can reach an upper limit after a few training iterations, whereas a more complex one (graph neural network) has to be trained for more iterations, but it eventually outperforms the simpler model. Large-scale ensemble or boosted tree-based approaches, for instance, have shown to yield promising performance on the organ-level biodistribution prediction task when using tabular physicochemical descriptors of nanoparticles (Mahdi et al., 2025), and multi-view deep learning approaches have been reported to further enhance the accuracy of the task, especially in cross-domain scenarios where the model has to be able to generalize to nanoparticle types that were not used during training, if a structural or image-based representation of the nanoparticle composition is included.

4.4 Clinical Translation Landscape

Despite substantial preclinical activity, the majority of AI-designed nanomedicine candidates remain in early development stages. Figure 4 depicts an illustrative distribution of candidates by development phase, underscoring the translational gap discussed in Section 6.

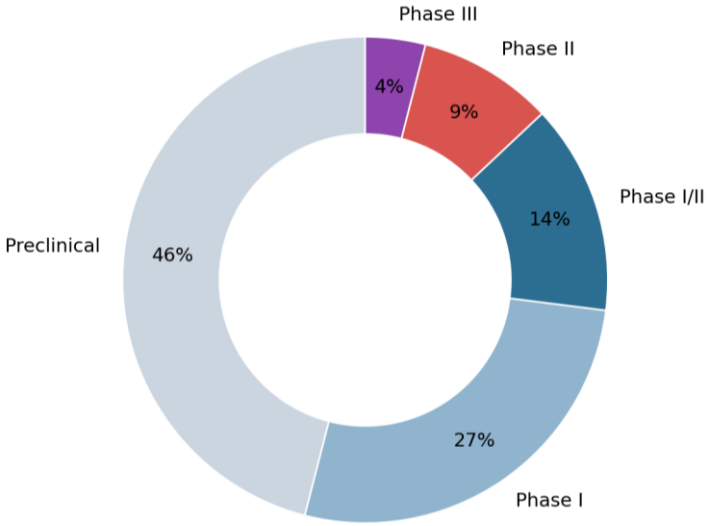


Figure 4. Illustrative distribution of AI-designed nanomedicine candidates by development stage.

The heavy focus on preclinical and early-phase development is not uncommon in the nanomedicine space, where only a small number of candidates have historically made it to regulatory approval (He et al., 2019), and is also driven by certain considerations about AI-designed candidates: there is a lack of clarity regarding the expectations of regulators when an AI-driven design process is used, and sponsors may not want to be the first to test an unknown review pathway.

4.5 Toxicity and Safety Outcomes

The hypothesis is that personalized dosing based on the genomic subtyping will have lower rates of adverse events compared to standard fixed dosing. Figure 5 depicts simulated incidence of adverse events at grade 2 or higher by the four different hypothetical genomic subtypes for both standard dosing and AI personalized dosing.

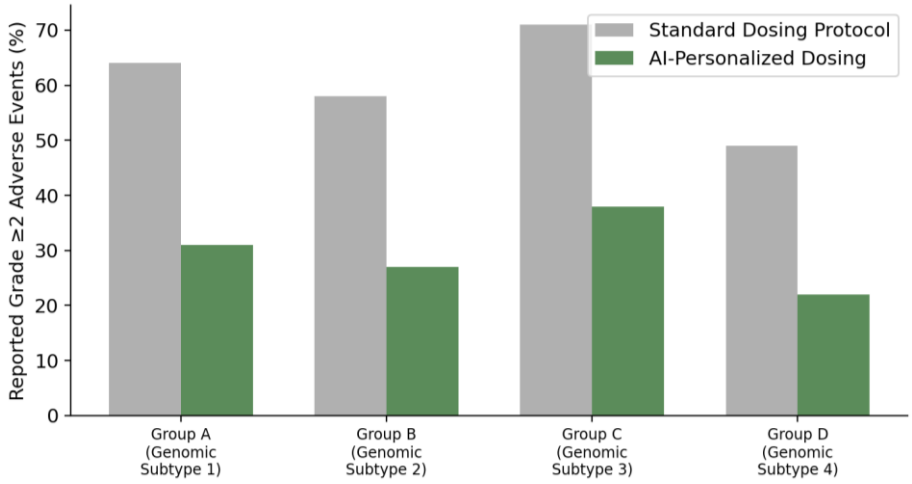


Figure 5. Simulated adverse-event rates: standard versus AI-personalized dosing.

This is consistent with initial findings for single-episode dosing agents developed using reinforcement learning that have demonstrated similar or greater efficacy with significantly lower toxicity when used for individual patients compared to fixed population-based dosing regimens in simulated patient cohorts (De Carlo et al., 2025). Will similar improvements be achieved for nanoparticle therapeutics? That will largely depend on the development of real-time or near-real-time biomarkers, such as circulating tumor DNA (ctDNA), or serial imaging, that are sufficiently sensitive to guide intra-treatment dose adjustment.

4.6 Platform Suitability for AI-Guided Personalization

Not every nanoparticle platform is suitable for tuning with AI. The three main

platform classes are compared on six criteria that are important to personalization (Figure 6), with an illustrative expert-weighted scale applied.

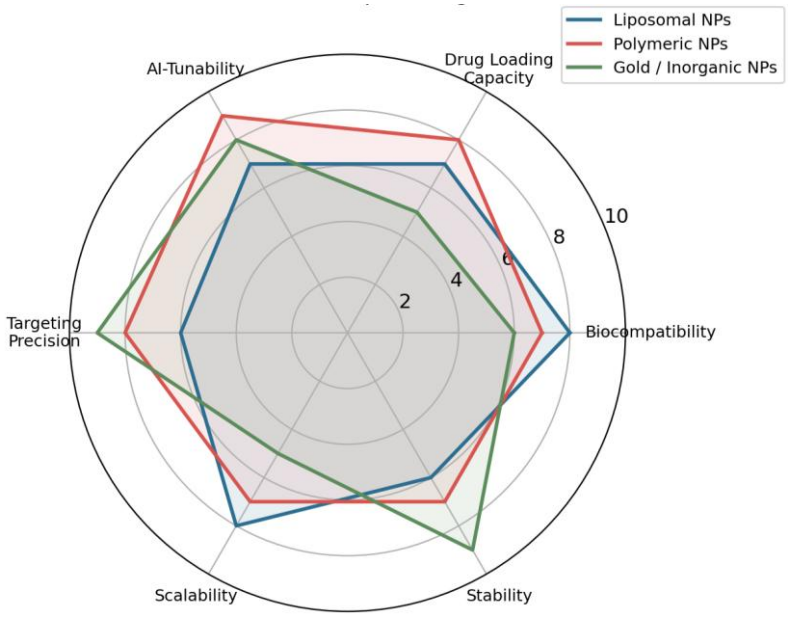


Figure 6. Comparative suitability of nanoparticle platforms for AI-guided personalization.

In this illustrative comparison, lipid-based platforms perform much better regarding AI-tunability; the combination of recent machine learning formulation efforts on lipid nanoparticles, high-throughput combinatorial libraries, well-defined structure-activity relationships between lipid headgroup and tail chemistry and delivery efficiency, and industrially standardized microfluidic manufacturing make lipid nanoparticles an exceptionally data-rich and tractable target for algorithmic optimization (Ding et al., 2023; Witten et al., 2024). In contrast, inorganic platforms may have an advantage in imaging and multimodal theragnostic applications, but only a few tunable parameters that vary continuously over the sample space can be used, potentially reducing the size of the design space for a generative or predictive model.

5. Nanoparticle Platform Comparison

Table 2 compares the main classes of nanoparticles relevant to personalization with AI, listing typical physical properties, parameters and property levels that can be optimized by algorithms, and approximate clinical maturity.

Table 2. Comparison of Nanoparticle Platforms for AI-Guided Personalized Cancer Therapy

Platform	Typical Size Range	Drug Loading Capacity	Key AI-Optimizable Parameters	Clinical Maturity
Liposomes	80–200 nm	Moderate–High	Lipid composition, PEGylation density, surface charge	Multiple approved products
Polymeric Nanoparticles	50–250 nm	High	Polymer ratio, degradation rate, ligand density	Several in clinical trials
Gold / Inorganic Nanoparticles	10–100 nm	Low–Moderate	Core diameter, shape, surface functionalization	Predominantly preclinical/early trials

Dendrimers	5–20 nm	Moderate	Generation number, branching density, terminal groups	Early-stage clinical exploration
Lipid Nanoparticles (mRNA-class)	60–120 nm	High (nucleic acids)	Ionizable lipid ratio, helper lipid selection	Rapidly expanding clinical use

While the decades of manufacturing experience and several approved oncology products that already exist for liposomal carriers make their platform the most clinically ready, the compositional design space, which is largely defined by the lipid identity, PEGylation density, and surface charge, is comparatively low dimensional compared to newer platforms. One of the polymeric nanoparticles that has been the focus of interest is PLGA-based nanoparticles, which have been extensively studied in machine learning structure-property relationships, and predictive models for particle size, encapsulation efficiency, and release kinetics have been reported directly from synthesis parameters (Rezvantalab et al., 2024; Alqarni & Huwaimel, 2025; Noorain et al., 2023). Lipid nanoparticles have carved out a unique niche: They were originally designed to carry a nucleic acid cargo (like short interfering RNA or messenger RNA), but they are now increasingly well understood computationally, and the design principles of these particles (choice of ionizable lipids, ratio of helper lipids, and formulation through microfluidic mixing) are, in our view, the platform class most likely to be scalable to personalized, near-term, AI-guided applications.

6. Discussion

The vision outlined above, in both the framework and the illustrative analyses, is coherent and, although far from complete, mostly aspirational, for cancer nanomedicine: therapies whose physical and chemical properties are algorithmically optimized to the biology of a tumor from a given patient, and whose dosing is dynamically adjusted based on the degree of treatment response seen. This analysis reveals a number of themes. The idea is that using AI in this area isn't about replacing experimental science, but more about condensing and prioritizing the search space experimentalists have to cover, so that a greater variety of potential formulations could be tested in silico before being synthesized and tested. Second, the layered architecture also clearly establishes the point that the effectiveness of personalization is limited by the weakest link in the chain: the more sparse the patient information that goes upstream into the model, and the less real-time actionable the downstream dosing system, the less useful the model will be. Third, platforms are important, as polymeric and lipid-based platforms continue to have the most extensive array of independently tunable parameters (see Figure 6, Table 2), making them obvious early candidates for algorithmic personalization at scale, but not so easily tunable by algorithm at scale in the case of inorganic platforms, where imaging and targeting properties are good.

Below all, it is essential to be honest about the actual foundation for enthusiasm in this area. The vast majority of published evidence cited to date comes from in vitro and in vivo studies, small early-phase trials, or formulations used in retrospective analyses; the simulated comparisons in Section 4 are meant to represent potential directions of effect that are consistent with the larger body of evidence, but not to necessarily reflect real-world clinical outcomes. Prospective validation of the AI approach, preferably with suitably large, randomized trials of AI-assisted and conventional nanomedicine treatments, is yet to be carried out with a degree of rigor.

Another theme is the extent to which AI has so far demonstrated empirical benefits in the pipeline. Currently, the better established data are concentrated on the design and screening layer (e.g., optimization of lipid nanoparticles and PLGA formulations, where dense and structured data on formulation and outcome exist, and

where formulation variables (e.g., lipid ratios and polymer composition) are relatively easy to model computationally) (Ding et al., 2023; Li et al., 2024; Rezvantalab et al., 2024). The predictive biodistribution layer is accumulating, but with a more diverse mix of tabular organ-level accumulation models (Mahdi et al., 2025) and physiologically-based multiscale simulations. Contrary to this, the adaptive dosing layer has been better developed in the broader field of pharmacometric and hematological applications than in the realm of the specific application of nanoparticles in oncology (Teplytska et al., 2024; De Carlo et al., 2025), implying that this is a near-term research goal rather than a longstanding dream.

Finally, the imaging and radiomics literature, although largely developed outside of the nanomedicine world, provides an excellent proof of concept for the wider personalization thesis presented here: deep learning models trained on pretreatment imaging have repeatedly shown the ability to stratify patients by their predicted response to a particular systemic therapy across tumor types (Zhang et al., 2024; Bao et al., 2024; Ruan et al., 2025; Wu et al., 2025). But if similar predictive precision can be achieved for biodistribution and response to nanoparticles, imaging-based stratification could provide a starting point for AI-personalised nanomedicine without the need for new diagnostic infrastructure, since imaging is already available in the clinic.

7. Challenges and Limitations

Owing to the interrelated technical, regulatory and systemic barriers, achieving the scale-up and implementation of the framework outlined in Section 3 is a realistic challenge. These are arranged below, with detailed comments on each, based on the particular mechanisms that hinder progress.

- Scarcity and fragmentation: quality, standardized nanoparticle formulation-outcome data are limited in size and are often found in individual laboratories with limited generalizability for trained models. In well-studied platforms like PLGA nanoparticles, there are significant differences in the data reported in the literature regarding the physicochemical descriptors and outcome measures, which limit the possibility of aggregating data across studies for training the models on a larger scale.
- Model interpretability: Deep learning models for biodistribution or toxicity prediction can be ‘black box' models, making them difficult to review and trust by regulators. This is especially important for graph neural network and multi-view architectures that have been successful in predicting structure properties but lack the type of rationale usually sought by formulation scientists or regulators at the level of features.
- Reproducibility in manufacturing: Despite an AI system identifying an optimal formulation, batch-to-batch variations in the process of nanoparticle synthesis can arise due to variations in mixing parameters, reagent purity, or changes in scales from lab to production size, which can affect their clinical performance. Additionally, a model developed using laboratory-scale data may not transfer easily to the production-scale manufacturing process.
- Regulatory pathways: Many regulatory pathways were created for the fixed-dose, fixed-formulation products – and are not yet optimized for adaptive, AI-personalized therapeutic systems. The FDA and EMA, among other agencies, have been subjected to classification uncertainty on the regulatory status of a variety of nanoparticle drugs and biologic products, with the inclusion of an AI aspect to drug design or dosing further complicating this question.
- While AI models are generally optimized to predict biodistribution and efficacy, they might not always account for the unique toxicity mechanisms of nanoparticles, such as complement activation, off-target immune stimulation, and organ accumulation with repeated administration, which are not well represented by these endpoints. Long-term safety data is also crucial and not

always included in the datasets used to train AI models (Havelikar et al., 2024).

- Cost and equity: Personalized nanomedicine workflows, which include genomic profiling, custom formulation, and continual monitoring, can be resource-intensive, and there is a concern for equitable access. If these do not intentionally shape their cost and infrastructure needs, then there is a real danger that the AI-p personalised nanomedicine becomes more accessible to patients at large, well-resourced academic centres.
- Validation gap: as mentioned above, substantial preclinical or early phase supporting evidence still exists, and there is a need for prospective comparative trials before definitive conclusions about efficacy can be drawn. Retrospective and simulation-based demonstrations (summarized in Section 4) are helpful for hypothesis building, but are not sufficient to replace appropriate powered, prospectively registered clinical comparison.

8. Future Directions

A coordinated effort on many fronts will likely be needed to move forward with the field. Potential federated learning approaches include the ability of multiple institutions to collectively train predictive models without having to share sensitive patient data or proprietary formulation information, which may help overcome data scarcity without compromising privacy or intellectual property, and which has been proposed for precision-oncology dosing applications as early as 2020 in a federated learning architecture that integrates graph neural networks with multi-omic data. Early federated learning architectures that integrate graph neural networks and multi-omic data integration have been proposed specifically for precision-oncology dosing applications, providing a template for nanomedicine-focused consortia to adapt. AI approaches that are designed to be explainable in nanomedicine, including approaches that link predictions of biodistribution or toxicity to specific formulation characteristics that are easily understood by formulation scientists and regulators, could help address the interpretability gap described in Section 7.

Characterisation protocols and common benchmark datasets that have helped progress in other applied machine learning fields would help to enable comparability between studies, which are early steps that can be achieved with the nanomaterial data repositories that have been made available but not yet widely adopted or harmonised across laboratories. From the generative modeling standpoint, additional progress in de novo formulation design in the vein of generative molecular and protein design will likely increase the space of candidates accessible to screening-based approaches beyond what purely predictive modeling techniques can cover, ultimately enabling the discovery of nanoparticles via diffusion models, variational autoencoders, or reinforcement learning-guided generators (Rahman et al., 2025).

Enforcing more strict coupling between generative design and automated/robotic synthesis and characterization platforms, known as self-driving laboratories, could further shorten design-make-test-analyze cycles for nanoparticle formulations, especially early in the process, as was first demonstrated in closely related areas like protein engineering (Rapp et al., 2024). Adaptive regulatory frameworks, similar to those being developed for software-driven and AI-enabled medical devices, may be required to keep up with the formulation or dosing of AI-therapies that are intended to change over time due to real-world patient data; risk-based, case-by-case regulatory review, which has already been proposed for nanomedicine products broadly, may be a logical first step in the extension of that review to AI-therapies. Lastly, prospective, properly powered clinical trials directly comparing the effect of AI-optimized nanomedicine formulations with conventional formulations would help establish a strong evidence basis for the broader clinical use of AI, particularly in cases where the layer of AI design is most developed, such as mRNA-LNP therapeutics or PLGA drug-eluting systems.

9. Conclusion

AI-based personalized nanomedicine is a promising and technically coherent approach to overcome two common drawbacks of cancer treatments: poor and non-uniform drug delivery and high inter-patient drug response and toxicity variability. The four-layer framework proposed in this paper outlines a structured approach to envisioning how these tools can be applied throughout the therapeutic journey — from multi-omic data integration to AI-driven formulation design, predictive biodistribution modeling, and closed-loop adaptive dosing. A literature review of the existing literature for this model reveals some disparities but real progress: the formulation design layer, especially lipid and polymeric nanoparticles, has some meaningful empirical support; the predictive biodistribution layer is developing fairly quickly; and the adaptive dosing layer is the least developed in the context of nanoparticle carriers directly.

At the same time, the field remains at an early stage of clinical maturity, and substantial technical, regulatory, and equity-related challenges must be addressed before AI-personalized nanomedicine can be routinely deployed. Data fragmentation, model interpretability, manufacturing reproducibility, unsettled regulatory classification, and the risk of unequal access are genuine obstacles rather than incidental details, and none of them will be resolved by algorithmic progress alone. Continued interdisciplinary collaboration among computational scientists, nanomedicine chemists, clinicians, regulators, and patients themselves will be essential to translating this conceptual promise into consistent, equitably distributed clinical benefit — and to ensuring that the considerable recent enthusiasm for AI in this space is matched by correspondingly rigorous prospective evidence.

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