

Artificial intelligence-guided nanoparticle design for advanced targeted drug delivery

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Abstract

This editorial aimed to explore the critical role of artificial intelligence (AI) in accurately predicting the structural design of nanoparticles (NPs) during targeted therapy of diseases. Based on experience, it is always surprising that perfect control of NP properties—including size, zeta potential, type, and surface modifications—using smart tools, will be more critical for optimal outcomes than trial and error. It is envisioned that the AI will change the game by predicting NPs' behavior, optimizing formulations, and speeding up clinical trials via the use of supervised learning, deep neural networks, graph neural networks, and generative models. In this context, various AI have led to an increase in drug loading efficiency and mRNA medication delivery. To achieve personalized therapy using NPs, however, issues including data quality, model interpretability, ethical frameworks, and multidisciplinary cooperation should be resolved. To enhance human knowledge and facilitate safer and more precise advancements in healthcare, this editorial urges the proper integration of AI in pharmaceutical/medical nanotechnology.

Keywords: Pharmaceutical nanotechnology, Artificial intelligence, Drug delivery systems, Nanoparticle, Design, Zeta potential, Surface modification, Ethical challenges, Human

After nearly 15 years of experience as a pharmaceutical nanotechnology researcher and journal editor, I have realized that emergent sciences are not accomplished through imagination. The integration of these sciences, in conjunction with the emergence of smart instruments, results in valuable and practical discoveries for researchers. I have always been curious about the potential of pharmaceutical nanotechnology and artificial intelligence (AI) to revolutionize the field of modern science, given the emergence of AI in the past decade. Suppose that smart drug delivery systems, which are based on nanoparticles (NPs) with unique features in terms of shape, size, surface charge, and surface manipulation, are freely roaming inside the body and delivering the drug precisely to the disease site.^{1,2} This not only optimizes the drug dose but also reduces the off-target side effects of the drug in healthy organs. Although the final designed systems have never performed precisely, researchers have consistently tried to construct such a smart system.³ In this editorial, I aim to provide a concise overview of the critical components of NPs design that directly influence their fate in the body. Additionally, I will elucidate the role of AI in the final defect-free design of these drug delivery systems, which is based on the structural properties of NPs. In the interim,

I will explain the current and prospective constraints of this integration.

In nanomedicine, there exist nanoparticles whose physicochemical properties have a large impact on what happens to them biologically.⁴ From the hundreds of papers published each year, one thing is clear: design, not chance, is what makes things work. Think about what kind of particle it is. Gold and other metallic NPs are widely used as contrast agents in magnetic resonance imaging (MRI), but if they are not made properly, they can cause side effects.⁵ Polymeric particles, such as PLGA, on the other hand, cause sustained release, while liposomes have enabled the development of mRNA vaccines.⁶ Hybrid formulations may also include the best parts of each of these groups. The size of the particles is just as essential and has a big effect on biological processes. NPs that are less than 50 nm in size may get

Highlighted Note

Imagine that the next stage of autonomous singularity will happen in nanomedicine, which comprises autonomous labs and places where robotic platforms continually alter NPs designs via AI commands and the use of reinforcement learning on real-time biological input.



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through physiological barriers like the blood-brain barrier. NPs that are more than 200 nm in size are quickly removed from the body by the liver and spleen.⁷ Surface charge and Zeta potential, which describe the electrical charge on the surface of particles, have a big consequence on how stable they are and how they spread throughout the body. Negatively charged particles (between -30 and -50 mV) are less likely to aggregate and therefore greater biological half-life. Positively charged particles (+30 mV), on the other hand, easily attach to cell membranes but cause toxicity and may be detected by the immune system by opsonization and formation of a protein corona.⁸

Functionalization of the surface of NPs with chemical or biological moieties, such as polyethylene glycol (PEG), folic acid, and an antibody, makes it more specialized and decreases opsonization. PEG coats increase the biological half-life of NPs in the body by keeping them from being cleared by the immune system. Targeting ligands, such as anti-HER2 antibodies, help NPs directly target cancer cells. These changes on the surface of the NPs decide whether they can get across the biological barrier (*e.g.*, escaping from the rheological barriers of endothelial cells, crossing to blood-brain barrier, crossing mucosal barriers to go to the lung, or getting out of endosomal entrapment after being taken up by cells).^{1,9} On the other hand, the increased permeability and retention (EPR) effect in the endothelial cells of solid tumors may be utilized for the design of appropriate NPs with optimized size and shape for targeted accumulation of NPs in the site of solid tumors. Therefore, designs that aren't well optimized might cause off-target deposition and side effects.¹⁰

Experimental works, both *in vitro* and *in vivo*, are significant components of the conventional method for the formulation of NPs. In most cases, these procedures are both time-consuming and costly, and the outcomes often remain uncertain.¹¹ Even minute alterations in the zeta potential or surface chemistry of NPs may have a significant influence on the biological functioning of the prepared NPs. This is where AI comes in as a useful tool. AI is capable of analyzing vast databases of laboratory findings, simulations, and clinical trials to make highly accurate predictions about the performance of NPs. This is in contrast to the traditional method of using AI as a simple trick. The process of bench-to-bed may be accelerated while simultaneously reducing the time and investment required for final formulation development. Generally, the use of AI in the process of NPs formulation has the potential to enhance efficiency, decrease side effects associated with conventional trials, and speed up innovation in the sector.

Adaptability is one of the most important aspects of AI strength. Supervised learning techniques, such as random forest models, can recognize patterns in many types of data sets that are rather complicated. For example,

these algorithms are capable of making very accurate predictions about the formation of a protein corona on the surface of silver NPs. These models are helpful in the preparation of NPs that can avoid being detected by immune systems, in large part because of their balanced factors of size and surface charge.¹²

The links between protein corona composition/amount, tissue distribution, and potential toxicity of NPs are crucial for overcoming biological barriers in nanomedicine. Advanced algorithms like as XGBoost further clarify these interactions, which are essential for overcoming biological barriers.¹³ Besides, deep learning algorithms are very useful when applied to nonlinear and high-dimensional data sets. Utilizing deep neural networks alongside quantitative structure-activity relationship (QSAR) models enables predictions regarding the effectiveness of NP penetration into the tumor microenvironment, with a primary focus on the chemical structure of the surface, size, and shape of the particles.¹⁴

Importantly, graph neural networks (GNNs), which are used in AI-Guided Ionizable Lipid Engineering (AGILE), can be utilized to optimize lipid NP formulations by adjusting the pKa and chain length of phospholipids to enhance endosomal escape characteristics.¹⁵ Besides, scientists from Massachusetts Institute of Technology (MIT) tried to enhance mRNA delivery for colorectal cancer treatment using a COMET platform recently. This platform makes use of transformer-based designs to find successful lipid molecules from over 3,000 trial formulations.¹⁶ These advancements shed light on the significant role that AI plays an important role in enhancing the design and performance of NPs for use in medical/clinical applications.

This frontier has now been expanded to include generative learning as well as reinforcement learning. The use of generative adversarial networks (GANs) may lead to the development of innovative NP surface designs that enhance systemic delivery. Furthermore, reinforcement learning facilitates the gradual refinement of formulations to achieve deeper tumor penetration.¹⁷

NanoSafari is an AI Copilot for Biomedical Nanoengineering that utilizes large language models and data from over 20,000 articles to provide recommendations for delivery systems that outperform traditional approaches.¹⁸ Similarly, TuNa-AI uses different machine learning paradigms to optimize over 1,200 NP formulations. As a result, it was able to achieve a 43% increase in loading efficiency for a different drug delivery system, such as Ventoclast.¹⁹

When these models are paired with neural ordinary differential equations (neural ODEs) to predict drug release, they may dramatically advance the discovery process and get the researcher closer to optimized/customized nanomedicine. This includes anything from gene-guided cancer therapy to mRNA vaccinations.

In light of these developments, I would like to remind the reasons why I set such a high importance on the goal of this journal: *BioImpacts* (BI) offers a unique platform for the concepts that will define the subsequent period of medical practice.

In spite of the above-mentioned developments, significant complications still exist. The area has to address concerns such as the quality of the data, reusing the existing data, the ethical use of AI, and the need for cooperation across different disciplines. Most importantly, the goal of investments in this field should be to enable human creativity via AI rather than to replace it.

Although the integration of AI and nanomedicine is seeing a fast transformation in the design of drug delivery systems, there are still a great deal of difficulties that hinder this field from making complete progress. The quality of the data and the standardization of the data are two of the most significant issues. There is a significant amount of data on NPs in drug delivery systems that is either insufficient, irregular, or the product of experimental techniques that are inconsistent. One of the most common reasons why direct comparison or transfer of models is not possible is because of the variability in particle manufacturing processes, experimental settings, and biological models. As a consequence, even very complex algorithms are capable of producing findings that are condition-dependent or biased. Therefore, to guarantee repeatability and efficient training of AI, it is necessary to establish data repositories that are available to the public, of high quality, and that adhere to the principles of FAIR (Findable, Accessible, Interoperable, and Reusable).

The interpretability and generalizability of models are the other drawbacks that must be overcome. It is common practice to refer to deep learning and transformer-based systems as "black boxes," despite the fact that they are capable of providing quite precise predictions. In the absence of a comprehensive comprehension of the fundamental dynamics, it continues to be challenging to integrate the insights acquired from AI into sensible design principles. Therefore, it will be essential to make efforts to build explainable AI (XAI) and modeling that is based on physics to close this gap and acquire confidence in clinics and regulatory settings.

In comparison to the development of new technology, ethical and regulatory frameworks have not evolved as much. Questions that remain unsolved include the responsible use of formulations developed by AI, openness in data sources, and the administration of intellectual property for nanomaterials designed by machine learning. Scientists, physicians, ethicists, politicians, and stockholders must engage in interdisciplinary conversation and work together in order to build governance models that not only encourage innovation but also guarantee safety and justice.

It is envisioned that the nanomedicine industry

is critically dependent on the integration of human knowledge with technological advancements, rather than on the replacement of human expertise. AI should not be used to replace human skills but rather as a tool to complement such skills. Increasing the speed at which discoveries are made while preserving the integrity of scientific research may be accomplished by combining algorithmic predictions with empirical confirmation via practical experiments. Imagine that the next stage of autonomous singularity will happen in nanomedicine, which comprises autonomous labs and places where robotic platforms continually alter NPs designs via AI commands and the use of reinforcement learning on real-time biological input.

Furthermore, a new age in personalized nanomedicine will be accompanied by the introduction of digital twins, patient-specific modeling, and multi-omics data. Nanoparticles that are customized to a person's genetic and metabolic profile may be produced using AI-driven optimization. Therefore, it is envisioned that the therapy would become safer and more successful as a result. We must continue to invest, collaborate transparently, and embrace open science if we are to achieve this aim.

The researcher, therefore, should focus more on this aspect of science, and policymakers as well as regulators should continue to invest, collaborate transparently with researchers, and embrace open science if they are to achieve this aim.

In conclusion, there are both positive and negative aspects to the integration between AI and nanomedicine. While it has the potential to revolutionize health, it requires rigorous ethical and scientific oversight. The researchers must address this revolution's current drawbacks with responsibility and planning if they are to see whether it can deliver on its promise of safer, more intelligent, and more inclusive healthcare.

We extend this offer to our readers, who are innovators, scientists, and physicians. Tell us what you learned and what you think, please. Together, we can transform the potential of AI and nanomedicine into practical solutions for the healthcare sector. These disciplines' convergence is significant in addition to being fascinating. The future of nanomedicine will be created one intelligent/optimized/personalized nanoparticle at a time.

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Study Highlights

What is the current knowledge?

- Nanoparticle behavior in the body is strongly influenced by physicochemical properties such as size, zeta potential, surface modifications, and material type.
- Conventional NP formulation relies heavily on trial-and-error experimentation, which is time-consuming, costly, and often yields inconsistent outcomes.
- AI tools are increasingly used in healthcare and drug delivery research, with applications ranging from data analysis and prediction to optimization of complex biological systems.

What is new here?

- This editorial integrates core nanoparticle design determinants with modern AI capabilities to illustrate how predictive modeling can guide formulation decisions.
- It highlights how advanced algorithms—such as GNNs, generative models, and transformer-based platforms—are now being applied to optimize NP structure, stability, targeting, and drug release.
- It provides a balanced perspective by outlining the practical limitations, ethical considerations, and translational barriers that must be addressed for AI-guided nanomedicine to advance safely.

Competing Interests

The author declares that there are no competing interests or conflicts of interest related to this editorial. The views expressed in this article are solely those of the author and do not necessarily reflect the opinions of the journal or its affiliated organizations.

Consent for Publication

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