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Review

Quantum and Artificial Intelligence in Drugs and Pharmaceutics

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Abstract

The pharmaceutical industry faces a broken drug development pipeline, characterized by high costs, slow timelines and is prone to high failure rates. The convergence of Artificial Intelligence (AI) and quantum technologies is poised to fundamentally transform this landscape. AI excels in interpreting complex data, optimizing processes and designing drug candidates, while quantum systems enable unprecedented molecular simulation, ultra-sensitive sensing and precise physical control. This convergence establishes an integrated, self-learning ecosystem for the discovery, development, and delivery of therapeutics. This framework co-designs strategies from molecular targeting to formulation stability, compressing timelines and enhancing precision, which may enable safer, faster, and more adaptive medicines.

Keywords: quantum biochemistry; quantum drugs; quantum pharmaceutics; quantum medicine; artificial intelligence; digital twin; Agentic AI

1. Introduction

The traditional pharmaceutical pipeline is widely regarded as inefficient, costly, and suffers from a high failure rate [1,2]. Historically, innovation followed a linear path, progressing from biomarker identification to clinical testing. Today, however, this model struggles to address the complexities of modern biomedicine, including disease heterogeneity, combinatorial biological interactions and the demands of personalized therapeutic [3,4]. Classical computational methods are no longer sufficient to model or optimize these intricate biochemical phenomena [5,6]. Since the 1950s, the cost of developing drugs has increased from tens of millions to billions of dollars, even when adjusted for inflation, underscoring the urgent need for comprehensive methodological improvement in drug development [7]. At its core, pharmaceutical science is biochemistry. Yet, critical biochemical bottlenecks, such as poor solubility, polymorphism, enzyme-mediated metabolism variation and protein aggregation [8–10] are often treated as late-stage hurdles. As a result, these issues are primary drivers of cost, complexity, and attrition. Addressing them requires translational intelligence [11,12], not just acceleration. Targeting these problems early demands models that incorporate atomic-level precision and real-time physical feedback, rather than relying solely on statistical correlation. Furthermore, the COVID-19 pandemic and other global health crises have exposed critical vulnerabilities in global drug supply chains and highlighted the urgent need for nations to achieve health sovereignty [13–15]. In response to these challenges, Artificial Intelligence (AI) and quantum technologies are emerging as essential drivers of pharmaceutical innovation [16,17].

Artificial Intelligence excels at extracting high-dimensional patterns from clinical, omics and structural data [18], while quantum systems offer simulations beyond classical

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Academic Editors: Xueying Zhao and Xue Mi

Received: 31 August 2025
Revised: 6 January 2026
Accepted: 9 January 2026
Published: 14 January 2026

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limits and instruments for interrogating matter at previously inaccessible spatiotemporal scales [17,19,20]. This integration is crucial for compressing the multi-year development timeline and automating the design-test-refine cycle. Together, they enable a shift from static pipelines to dynamic, real-time translational systems [21]. In these systems, drug discovery becomes a continuous loop of inference, simulation, measurement, and design, where AI and quantum tools interact across levels of abstraction, enabling biochemical decisions that are context-aware, data-responsive, and mechanistically grounded. This integration aims to unify computational and experimental workflows, positioning AI and quantum systems as central to molecular ideation, design, and validation [22,23]. This paper proposes a restructured translational architecture that functions as a strategic roadmap for integrating AI and quantum technologies across all stages of the pharmaceutical pipeline, from clinical anchoring and mechanistic modeling to compound synthesis, formulation, and real-time therapeutic monitoring. The proposed system is synthesized through three integrated layers: Computational AI, which handles data and design; Physical Quantum, which provides fundamental simulation, measurement and manipulation capabilities; and Orchestration AI, which manages the self-learning feedback loop. This work argues that AI and quantum technologies are foundational enablers of a new translational logic, offering a blueprint for generating more personalized medicines through the co-design of biology, computation, and physics.

2. Methodology and Synthesis

This integrative narrative review, combining narrative synthesis with structured evidence mapping, was conducted as a strategic synthesis across foundational and applied domains. Its focus was the convergence of Artificial Intelligence (AI) in Drug Development, Applied Quantum Science, and Translational Pharmaceutics, along with associated strategic, ethical, and infrastructural implications. The primary objective was to establish a novel strategic and cognitive framework for a self-learning drug development ecosystem, operationalized as a three-layered architectural model consisting of Computational AI, Physical Quantum and Orchestration AI (Figure 1).

This approach was chosen over systematic meta-analysis due to the nascent state of the technologies. The literature search spanned 2009 to September 2025, selected to align with the translational emergence of Deep Learning in drug discovery and practical solid-state quantum technologies for biomedical applications. The search employed a rigorous two-stage process. First, a Primary Systematic Search queried established databases (PubMed, Web of Science, Google Scholar) and preprint servers (arXiv, ChemRxiv) to mitigate publication bias by including early or null findings. Cross-domain search terms included AI (e.g., Deep Learning, Agentic AI); quantum technologies (e.g., Quantum Computing, NV Centers); and drug development applications (e.g., Drug Discovery, Digital Twin), structured with logical operators for comprehensive coverage. This was followed by a Secondary Non-Systematic Snowballing approach to capture older foundational literature (e.g., core quantum mechanics or early AI principles) predating the systematic search window. Retrieved English-language literature underwent a two-stage screening (Title/Abstract review, then Full-Text assessment) to ensure methodological rigor and minimize selection bias. For inclusion in the core evidence synthesis and model construction, the literature had to explicitly reference both AI/ML and Quantum/QIS concepts in a biomedical or pharmaceutical context, followed by full-text review for methodological robustness and relevance to pharmaceutical R&D. Evidence was synthesized across the drug development pipeline to create comparative tables and an integrated architectural model, illustrating the transformation from a slow, linear pipeline to a dynamic, adaptive system. (see Table 1 for a comparison of classical and quantum AI and physical approaches).

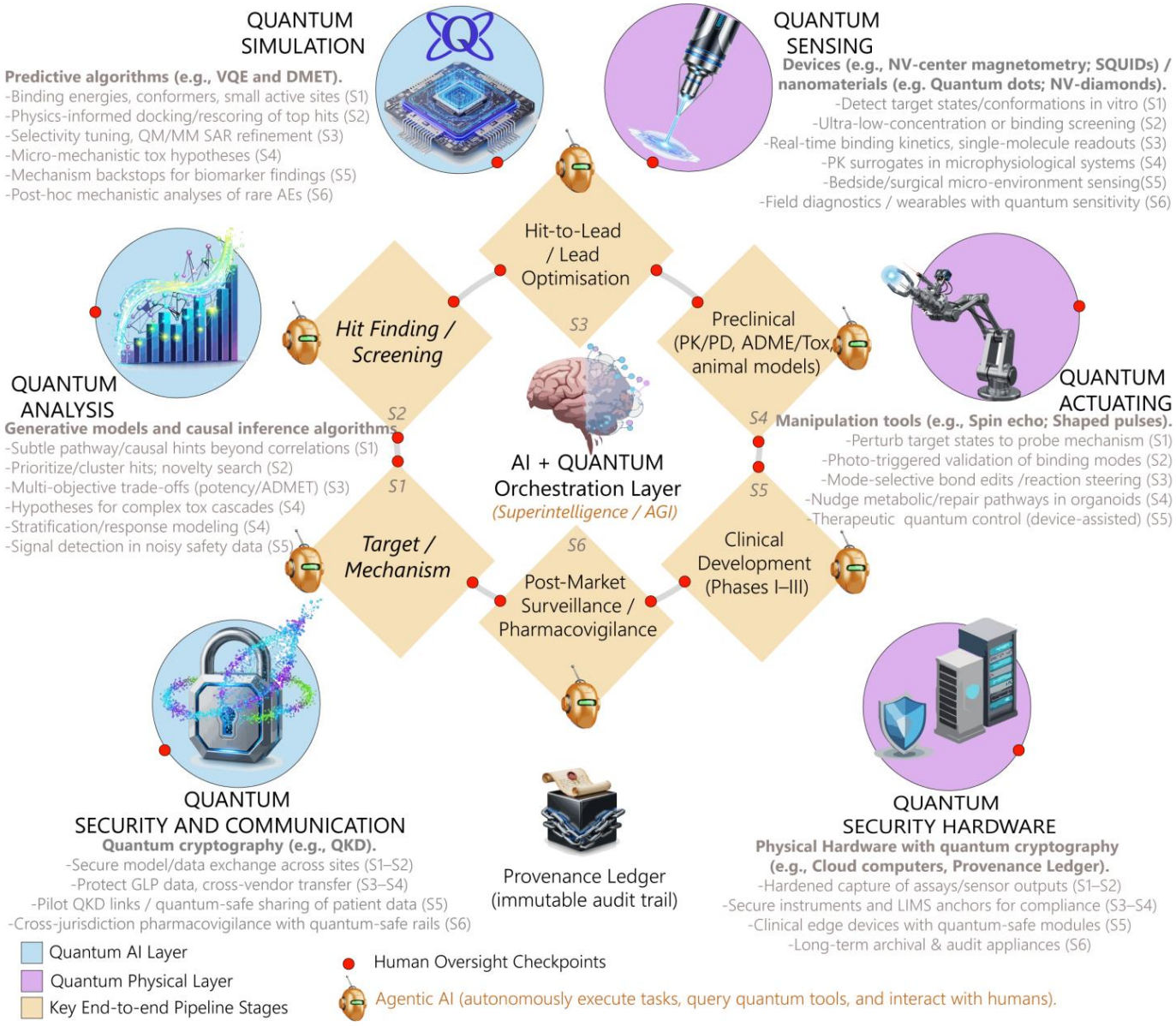


Figure 1. Overview of Quantum–Classical Synergy Across the Pharmaceutical R&D and Artificial Intelligence Pipeline. This schematic illustrates how quantum technologies integrate across six stages of drug discovery and development stages (S1–S6). At the center, an Artificial Intelligence (AI) and Quantum Orchestration Layer coordinates with six quantum modules. The Quantum AI layer (blue circle) includes Quantum Simulation, Quantum Analysis, and Quantum Security & Communication, while the Quantum Physical layer (purple circle) comprises Quantum Sensors, Quantum Actuators, and Quantum Security Hardware. Each module includes representative algorithms and devices (e.g., Variational Quantum Eigensolver (VQE)/Density Matrix Embedding Theory (DMET) for simulation, Nitrogen-Vacancy (NV)-center magnetometry for sensing, spin-based actuators for delivery, quantum key distribution (QKD) for secure communication). The pharmaceutical pipeline (as a gray trace with golden-orange diamond markers), spanning Hit Finding, Target/Mechanism, Preclinical, Clinical Development and Post-Market Surveillance. The Provenance Ledger ensures immutable audit trails, while human oversight checkpoints and Agentic AI governance reinforce safety and accountability.

Table 1. Foundational Dichotomy of Classical vs. Quantum Across AI and Physical Domains.

Aspect	Classical AI/Classical Physical	Quantum-Accelerated AI/ Quantum Physical
Computational Power/ Underlying Principles	**AI:** Relies on binary bits (0 s and 1 s) and classical logic. Exponentially slow and computationally intractable for simulating complex quantum states [24]. **Physical:** Based on classical physics (Newtonian mechanics, electromagnetism, thermodynamics). Measurements of the macroscopic averages of many particles [25].	**AI:** Leverages qubits for superposition and entanglement [26,27]. Can theoretically handle exponentially large computational spaces, making it ideal for simulating quantum-level molecular interactions [28,29]. **Physical:** Based on quantum mechanics (superposition [30,31], entanglement [32–34], quantum tunneling [35,36]. Measurements can be performed at the single-particle or quantum-state level. Quantum states are highly sensitive to decoherence, requiring controlled environments [37].
Typical Instruments/ Methods	**AI:** Widely accessible via cloud computing (AWS, Google Cloud, Azure) [38] and open-source frameworks (Scikit-learn, PyTorch from Linux Foundation) [39]. The entry barriers are relatively low for standard analytical and modeling tasks. **Physical:** Classical Sensing: Mass spectrometers, NMR machines (traditional), optical microscopes, HPLC, calorimetry, fluorescence spectrometers. Classical Control: Automated liquid handling systems, temperature-controlled reaction vessels, robotic arms.	**AI:** Highly specialized and expensive. Access primarily via cloud-based services (IBM Q, IonQ) [40]. Requires expertise in quantum algorithms and hybrid computing. **Physical:** Quantum sensors [41–47] (e.g., NV diamond, quantum dots, SQUID, which extends the sensitivity and resolution of classical instruments. Quantum control [17,48] (e.g., Quantum Rabi Oscillations [49,50], Quantum Shaped Pulses [51–53], Adiabatic Evolution [54,55], Quantum Spin Echo [56]) for manipulating molecular spin states and reaction pathways, which augment conventional control methods.
Ideal Use Cases	**AI:** Pattern recognition [57,58], data-intensive prediction, interpreting large datasets, ADMET prediction [59], biomarker identification from structured data [60,61], high-throughput screening (HTS) [62]. Example: Training a model to identify active compounds from thousands of microscopy images or predicting drug toxicity from vast datasets. **Physical:** High-throughput screening, structural analysis of large molecules (e.g., traditional NMR) [63], bulk sample analysis, measuring macroscopic properties (temperature, concentration). Example: HPLC to separate large compound samples or traditional mass spectrometers to measure protein molecular weight.	**AI:** Simulating molecular dynamics at quantum level, modeling complex protein folding, predicting binding affinities with high accuracy, optimizing chemical reactions intractable for classical computers [29]. Example: Precisely modeling how a new drug binds a specific protein, accounting for quantum effects. **Physical:** High-resolution sensing, single-molecule detection, in vivo sensing, manipulating matter at quantum level [64–67]. Example: NV diamond sensor detecting single electron spin in a living cell or quantum dot as an ultra-sensitive biomarker.

Table 1. *Cont.*

Aspect	Classical AI/Classical Physical	Quantum-Accelerated AI/ Quantum Physical
Limitations	**AI:** Struggles with problems involving quantum phenomena or subtle, high-dimensional molecular interactions (e.g., electronic correlations [29,68]). Provides only an approximation of physical reality. Identifying systems with strong electronic correlations remains difficult with limited indicators. **Physical:** Limited by shot-noise limit (fundamental precision limit in classical measurements). Cannot detect single quantum states or surpass classical optics limits [37,69].	**AI:** Limited by current quantum hardware: noisy, error-prone, and fault tolerant quantum computing for classically challenging molecules (e.g., FeMoco [70]) estimated at ~2000 logical qubits (~4 million physical qubits). Near-term intermediate quantum (NISQ) devices require highly controlled environments [71] and specialized expertise; measurements scale exponentially with circuit depth [72]. Quantum machine learning faces data representation challenges [73], some approaches are subject to de-quantization. **Physical:** Quantum decoherence; quantum states lose properties when interacting with environment [74]. Requires highly controlled conditions; technology not yet mature for robust clinical use.
Future Trajectory and New Possibilities	**AI:** Will excel at data-centric tasks. Focus on larger models Artificial General Intelligence (AGI), better data integration (Multimodal AI), and autonomous action (Agentic AI) [17,48,75,76]. **Physical:** Provides high-quality bulk data but limited to ensemble-averaged results. Cannot capture subtle, real-time molecular dynamics at quantum level.	**AI:** Transition from noisy NISQ to fault tolerant system [70]; true quantum advantage on biochemical problems. Eventually standard tool for computational chemistry alongside classical AI. **Physical:** Potential for sub-nanometer resolution, ultra-high sensitivity (single-molecule), real-time non-invasive in vivo diagnostics, quantum control of reactions, and quantum-enhanced medical imaging.

3. Foundational Technologies: The AI and Quantum Toolkit

3.1. Defining the Dual Nature of Quantum and AI in Pharma

Before exploring applications, it is essential to distinguish the two primary ways quantum technologies impact biochemistry and pharmaceutics. Quantum technologies provide both computational and physical capabilities that are not achievable with classical methods, serving as foundational tools for biochemists (see Table 1) [77,78]. This section provides a foundational overview of these key distinctions. For a more detailed, practical exploration of these concepts in clinical oncology settings, see Matarèse et al. [17].

- The Physical Basis of Quantum Technologies

Quantum mechanics introduces unique behaviors at the atomic and molecular level, enabling capabilities far beyond classical systems by describing a system's fundamental quantum state probabilistically. These include superposition [30,31], where particles exist in multiple states simultaneously, a phenomenon impossible to represent in a classical computer. Another key principle is entanglement [17,32,79], which links particles across space to reduce noise and improve measurement precision (such as two particles that, even

when light-years apart, are generated with opposite spins so that measuring one instantly reveals the other's spin). Quantum tunneling [35,36,79] allows particles to cross energy barriers, playing a critical role in enzymatic catalysis and biosensor sensitivity. Quantum states and spin orientations are central to manipulating molecular synthesis and enabling the function of quantum nanomaterials such as quantum dots (nanoscale semiconductor crystals that emit light in specific colors depending on their size) [50,65,66,80–82] and NV diamond nanoparticles (nanodiamonds with a specific defect that makes them excellent quantum sensors) [41,64,83]. Finally, coherence [30,84,85], the maintenance of quantum behavior, and its loss through decoherence are key challenges. In this context, techniques such as error correction and noise mitigation are essential to maintain stability and reliability in practical applications. Historically, the practical application of quantum mechanics in chemistry dates to the 1950s [86], when pioneers such as the Pullmans began applying quantum chemistry to predict the carcinogenicity of aromatic hydrocarbons, marking a pivotal transition from abstract theory to practical pharmaceutical science.

- The Dual Paradigms: Computational and Physical

Quantum phenomena are not just abstract curiosities, but form the fundamental basis of two distinct paradigms in pharmaceutical science. Computationally, quantum computing and simulation model molecular interactions, predict properties and optimize biochemical processes beyond classical limits [87,88]. A qubit, or quantum bit, is the quantum equivalent of a classical binary bit. While a classical bit can only be a 0 or a 1, a qubit can exist in the superposition of both states simultaneously, offering a massive increase in computational power. The selection between classical AI and quantum-accelerated AI depends on the specific problem being addressed. These two paradigms have distinct strengths, limitations, and ideal use cases, as summarized in Table 1. As a physical paradigm, quantum phenomena are harnessed directly in biochemical systems through sensing, control, and therapeutic delivery [17,48,89]. For example, quantum sensors can detect single-spin states in vivo [90], and ultrafast laser-based quantum control can steer reaction pathways [91], capabilities that Agentic AI can optimize but cannot physically perform on its own. This distinction clarifies how quantum physics expands pharmaceutical capabilities beyond classical instruments, both computationally and in the lab.

- The Role of AI in Orchestrating Quantum Systems

As these systems grow in complexity, Agentic AI and the eventual realization of Artificial General Intelligence (AGI) are projected to play a critical role in enhancing their usability and integration [92–94]. Agentic AI enables autonomous quantum control, learning to shape laser pulses or recalibrate systems in noisy biological environments [17,48,92]. It also interprets the high-fidelity data generated by quantum sensors, extracting insights such as protein conformational shifts or dynamic biomarker fluctuations. In more advanced settings, collective Agentic coordination could allow multiple AI agents to orchestrate distributed quantum systems, detecting anomalies, generating hypotheses, and executing therapeutic interventions autonomously. Equally important, these agentic systems provide provenance tracking, privacy preservation, and secure coordination mechanisms required for regulated biomedical environments, ensuring that quantum-driven decisions remain traceable, verifiable, and compliant with clinical governance. Building on these capabilities, this Quantum–AI synergy, summarized in Figure 2, defines a new class of adaptive, secure, and precision-enabled computational and biochemical systems capable of integration across the pharmaceutical design and clinical translation pipeline.

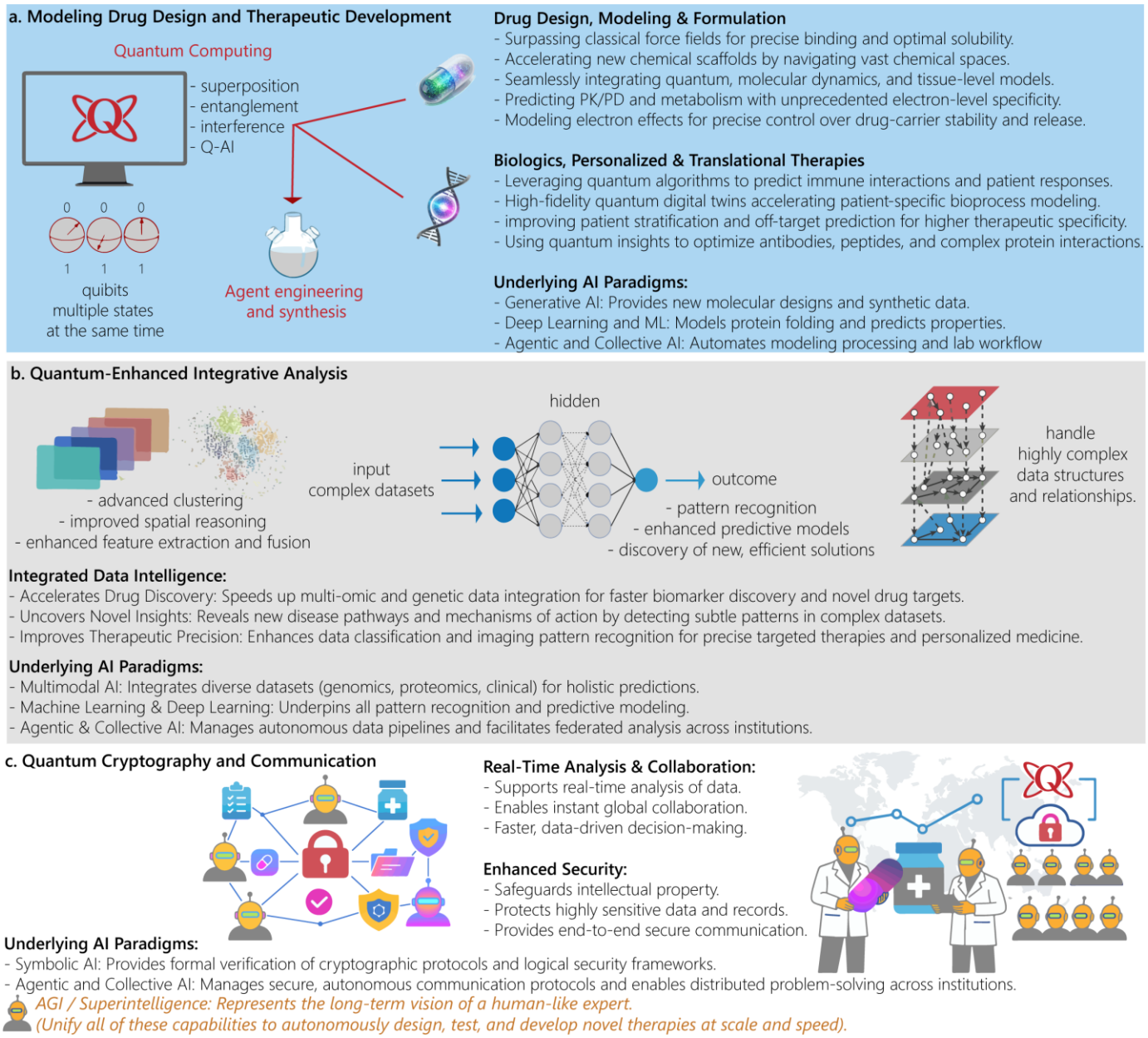


Figure 2. The Computational Layer: A Paradigm Shift with Quantum Computing. (**a**) Modeling Drug Design and Therapeutic Development (using quantum computing principles such as superposition, entanglement, and interference) enables Quantum Artificial Intelligence (Q-AI) to simulate molecular interactions and explore vast chemical spaces with high precision. Quantum Bits (qubits) support Agentic synthesis and multi-scale modeling, enhancing predictions of Pharmacokinetics/Pharmacodynamics (PK/PD), metabolism, and immune responses. AI paradigms such as generative models, deep learning, and Agentic systems automate design, optimize biologics, and stratify patient populations. (**b**) Quantum-Enhanced Integrative Analysis: Quantum machine learning improves clustering, spatial reasoning, and feature fusion across genomic, proteomic, clinical, and pharmacological datasets. This integration uncovers hidden patterns, accelerates biomarker discovery, and enhances therapeutic precision. Multimodal AI and Agentic pipelines enable autonomous data processing and predictive modeling. (**c**) Quantum Cryptography and Communication: Secure, real-time collaboration is enabled through quantum key distribution (QKD) and post-quantum cryptography (PQC), ensuring authentication, data integrity, and privacy. Symbolic AI supports protocol verification, while Agentic AI manages secure data exchange and provenance-aware communication across healthcare systems.

3.2. AI Paradigms and the Biomedical Data Ecosystem

- The Biomedical Data Ecosystem

The comprehensive Biomedical Data Ecosystem is a messy, yet foundational, component for all these technologies [95,96]. It comprises diverse Big Data types critical for drug discovery and development. These include omics data [60,61] for target identification, personalized formulation and biomarker discovery; clinical trial data for efficacy and safety [97]; various imaging and microscopy data (MRI, CT, PET, X-ray, cryo-electron microscopy, histopathology, single-molecule microscopy) for toxicity, biodistribution and structural validation [98–100]; Electronic Health Records (EHRs) for real-world evidence and adverse reaction detection [101,102]; and biomedical literature, research repositories and patent/IP data for hypothesis generation and competitive analysis [103,104]. The ecosystem is defined by high volume, velocity and variety, yet its effective use faces persistent challenges such as a lack of integration standards, incomplete or inconsistent metadata, noise, variability and critical privacy and security concerns. To address these, AI tools are increasingly vital for automating data curation and harmonization (e.g., reducing data cleaning time by 60–80%), by identifying inconsistencies, standardize metadata and semantically integrate heterogeneous data silos, thereby ensuring the quality, usability and "AI-readiness" [105,106]. Emerging solutions such as federated learning and differential privacy enable collaborative model training without compromising sensitive patient data, while frameworks such as the Findable, Accessible, Interoperable, and Reusable (FAIR) data principles and Health Level Seven/Fast Healthcare Interoperability Resources (HL7/FHIR) standards aim to improve interoperability across platforms and institutions [107–109]. This interoperability framework is crucial for achieving health sovereignty, as it allows countries to use local, sovereign datasets to develop treatments for diseases uniquely prevalent in their specific populations. This approach provides a significant advantage over relying on large, external datasets that may not be relevant to a country's unique health needs and regulations. However, a major challenge persists because most available data is based on successful outcomes, a phenomenon known as "survivorship bias" that leaves AI models without critical information about what does not work [110,111]. Although still at an early stage, quantum computing holds significant promise to accelerate data-intensive tasks such as molecular simulation and optimization, if input data is clean, structured, and semantically rich (see Table 2).

Table 2. Next-Gen AI in Life Sciences: From Algorithms to Autonomous Agents.

Paradigm	Definition and Core Features	Pharma/Biomed Applications and Examples	Methodologies/Tools/ Limitation
Symbolic AI (Good Old-Fashioned AI) (Stage 1–3)	Rule-based, logic-driven systems and explicit knowledge representation.	Applied to metabolic pathway mapping [112,113] and early Quantitative Structure-Activity Relationship models [114,115]. Worked in stable, clean contexts but failed in dynamic biological systems due to brittleness. Analogy: brittle "if–then" rules.	Rule-based inference engines and symbolic logic. Failures are due to lack of scalability and inability to handle noisy/ unstructured data.

Table 2. *Cont.*

Paradigm	Definition and Core Features	Pharma/Biomed Applications and Examples	Methodologies/Tools/ Limitation
Machine Learning (ML) (Stage 1–5)	Algorithms that learn from structured data to make predictions/decisions without explicit rules [100,116].	Predictive models for drug discovery, ADME/ADMET, retrosynthesis, multi-omics (e.g., identifying genetic markers linked to drug response), and ethics/interpretability) [18,59,117–120] Analogy: "pattern spotter" uncovering hidden correlations humans miss.	Regression, classification, clustering, dimensionality reduction [58]. Platforms: Scikit-learn, XGBoost, AutoML frameworks (Google AutoML, H_2O.ai) for automated model selection/tuning [39,121]. Dependent on quality/quantity of structured data.
Deep Learning (DL) (Stage 2–5)	Subset of ML using neural networks with multiple deep layers to learn complex hierarchical patterns from raw data.	Protein folding prediction (e.g., AlphaFold) [122–124], structure-based drug design, de novo small-molecule generation [120,125], high-throughput image analysis. Analogy: stacked layers like visual cortex neurons or GNNs learn like networks of interacting proteins.	CNNs (Convolutional Neural Networks), RNNs (Recurrent Neural Networks), Transformers, reinforcement learning and Graph Neural Networks [58,121]. High data/computational requirements and black-box nature are limitations; it excels with unstructured data.
Generative AI (Stage 2–4)	Models creating new data resembling training data (GANs (Generative Adversarial Networks), VAEs (Variational Autoencoders), LLMs (Large Language Models) [120].	Novel molecular design, scaffold optimization, synthetic data for scarce datasets, regulatory document drafting [120,125,126]. Moves drug design from library screening to invention. (e.g., LLMs for summarizing papers or drafting regulatory submissions). Analogy: "two dueling artists" (generator vs. discriminator).	GANs (Generative Adversarial Networks), VAEs (Variational Autoencoders), LLMs (Large Language Models) (GPT-style) [120], diffusion models. Risk of hallucination and need for domain constraints.
Agentic AI (Stage 1–5)	AI with autonomy, planning, and capacity to act in dynamic environments [93,94].	Lab automation, self-optimizing robotic experimental workflows, autonomous design-synthesis-test loops [127–130]. (e.g., Eve, Insilico Medicine labs, LabGenius). Analogy: pneumonia workflow (detect, check history, order labs, notify nurses, update EHR).	Planning algorithms, reinforcement learning and robotics integration [129,131]. Significant regulatory and safety considerations; high complexity.

Table 2. *Cont.*

Paradigm	Definition and Core Features	Pharma/Biomed Applications and Examples	Methodologies/Tools/ Limitation
Collective AI (Stage 1–5)	Multiple specialized AI agents collaborating and sharing intelligence.	Collaborative drug discovery, federated learning for multi-hospital datasets, distributed problem-solving [132]. Analogy: "team of AIs" each with a specialized role.	Federated learning frameworks, agent-based modelling [132]. Coordination overhead and hard to predict emergent behaviors.
Multimodal AI (Stage 2–5)	Integrates diverse data types (omics, imaging, EHR, text) for holistic predictions.	Patient phenotype prediction, drug–disease interaction mapping, precision interventions [58,133,134] (e.g., DeepMind RETFound, IBM Watson Health). Analogy: doctor synthesizing labs + scans + history.	Transformers, multimodal fusion architectures [58,133,134]. Complex integration pipelines. Aligning modalities is challenging but improves understanding of complex biological phenomena.
AGI/ Superintelligence (Stage 1–6)	AI with general reasoning across domains, akin to human cognition (long-term vision).	Governance, complex system optimization, synergy with quantum for pharma R&D. Analogy: "human-like scientist partner," but with unknown risks [75,76,135]	Theoretical models (still aspirational). Ethical, philosophical, and regulatory debates and currently speculative.

- Key AI Methodologies and Quantum Integration

AI methodologies enable early-stage drug repurposing, formulation stability prediction and clinical trial outcome forecasting across various stages of pharmaceutical science [133,136]. These include Symbolic AI, Machine Learning (ML), Deep Learning (DL), Generative AI, Agentic AI, Collective AI, Multimodal AI, and the highly prospective future-focused concepts of AGI, and Superintelligence (explained in Table 2). While Symbolic AI operates on explicit rules, many of these other methodologies fundamentally rely on Machine Learning and Deep Learning, which are applied in a variety of ways. Language Processing (NLP) [137,138] plays a pivotal role in mining scientific literature, detecting adverse drug reactions and extracting drug–drug interactions from patents, while graph mining [139,140] and neural networks facilitate the mapping of protein–protein interaction networks, prediction of allosteric sites and analysis of biochemical pathways. Additionally, Multimodal AI [133,134] integrates heterogeneous data sources to enhance patient phenotype prediction and drug response profiling. Recent advances also highlight the growing use of transformers and large language models (LLMs) [141,142] for biomedical text interpretation and protein structure prediction, alongside generative AI and reinforcement learning for de novo drug design [125]. Building on these AI capabilities, quantum technologies are increasingly integrated to accelerate complex computations and improve data fidelity, enabling tasks such as molecular ground-state energy estimation and combinatorial optimization. For instance, hybrid quantum–classical algorithms, such as Variational Quantum Eigensolver (VQE) and Quantum Approximate Optimization Algorithm (QAOA), are applied to compute molecular ground state energies and solve combinatorial optimization problems [143,144]. Quantum Generative Adversarial Networks (QGANs) and Quantum

Kernel Methods leverage quantum circuits [145] to enhance machine learning for novel molecular design and complex data classification. Algorithms such as Quantum Phase Estimation (QPE) and Quantum Imaginary Time Evolution (QITE) [146] could enable highly accurate molecular simulations, while Quantum Federated Learning (QFL) [147] provides a framework for secure, distributed learning across datasets, combining quantum randomness with differential privacy and fully homomorphic encryption (FHE), which enables computations on encrypted data without ever having to decrypt it, for robust handling of diverse medical data.

4. Computational and Physical Layers

4.1. Computational Design, Analysis and Biochemical Realism

The computational layer serves as the theoretical backbone for drug discovery, leveraging AI and quantum algorithms to model, analyze and predict molecular behavior (Table 3, Figure 2).

Table 3. Synergies Across Physical and AI Layers.

Quantum Aspect	Classical Physical Layer	Quantum Physical Layer	Classical AI Layer	Quantum AI Layer
Quantum Simulation	Scalable modeling via HPC (High-Performance Computing) clusters, NVIDIA DGX, Cryo-EM, X-ray crystallography, SAR (Structure–Activity Relationship), HTS (High-Throughput Screening), MD (Molecular Dynamics), and structure-based design.	High-fidelity quantum modeling with Qiskit Nature, PennyLane, Bloqade, Variational Quantum Eigensolver, Density Matrix Embedding Theory, Quantum Mechanics/Molecular Mechanics, NV centers, and quantum-enhanced spectroscopy—delivering near ab initio accuracy for physical and chemical systems.	AlphaFold for protein folding, generative design, Automated Machine Learning using KNIME and RDKit, multi-omics integration, Quantitative Structure–Activity Relationship, and iterative Design–Make–Test–Analyze cycles.	Hybrid workflows via Chemistry42 and AWS Braket, supporting mechanistic and micro-mechanistic toxicity analyses. Quantum Machine Learning for chemical space exploration, binding affinity prediction, quantum Variational Autoencoders, recursive learning, and multi-objective ADMET optimization.
Quantum Analysis	Fast hit prioritization via docking, HTS, MD, and ligand-based screening with interpretable pathway insights.	Stratification in small cohorts and subtle causal inference via quantum clustering, reverse docking, quantum kernel methods, and signal detection in noisy data. Quantum causal inference enhances pathway modeling.	NLP (Natural Language Processing)-based integration of heterogeneous datasets, anomaly detection, and pathway modeling.	Adaptive chemical space exploration beyond classical reach using hybrid Quantum Generative Adversarial Networks, recursive learning, quantum co-evolution of molecular architectures, and quantum-enhanced feedback loops for stratification.

Table 3. *Cont.*

Quantum Aspect	Classical Physical Layer	Quantum Physical Layer	Classical AI Layer	Quantum AI Layer
Quantum Security (Digital + Physical)	Mature, regulation-ready, cross-jurisdiction compliant. Advanced Encryption Standard/Rivest–Shamir–Adleman encryption, Hardware Security Modules, audit trails, and secure lab infrastructure.	Immutable audit trails and cross-vendor secure exchange. Quantum-safe protocols including Quantum Key Distribution or Post-Quantum Cryptography such as CRYSTALS-Kyber and Dilithium. Quantum-optimized firewalls, and Quantum Random Number Generators.	Explainable AI for compliance, anomaly tracking, secure data exchange, and NLP-based monitoring.	Quantum explainability, provenance-aware Agentic AI, embedded safeguards, and quantum adversarial defense mechanisms with adaptive monitoring beyond classical AI.
Hardware Security	Standardized, robust containment and device-level security: secure instruments, Biosafety Level 3/4 labs, containment protocols, and sequencer safeguards.	Hardened assay/sensor capture appliances, quantum tamper-evident storage, biosensors, edge devices, archival systems, and quantum-safe firmware.	AI-driven monitoring of instruments and compliance systems.	Quantum simulations for pathogen evolution, agentic monitoring, ultra-sensitive hazard detection, and biosurveillance modeling with predictive risk anticipation beyond classical systems.
Quantum Sensors	Reliable, interpretable measurements: high-throughput phenotypic readouts via robotics, AFM, HTS readers, pipetting, and microscopy.	Single-molecule sensitivity and bedside/surgical micro-sensing with wearable diagnostics, enabled by ultra-sensitive detection using NV centers, quantum dots, optical frequency combs, magnetometers, and real-time systems.	High-content phenotypic screening using Convolutional Neural Networks, Long Short-Term Memory networks, and Vision Transformers for imaging, feedback, and anomaly detection.	Quantum-assisted interpretation, control optimization, and adaptive diagnostics using quantum algorithms and sensor fusion—enabling real-time adaptive experimentation.
Quantum Actuators	Mature and scalable robotic and optical manipulation for precise, reproducible perturbations.	Mode-selective bond editing, photo-triggered validation, metabolic/repair pathway nudging, and reflexive control via quantum-level photonic actuators, optogenetics, and therapeutic modulation—for precise molecular actuation and quantum-scale physico-chemical manipulation.	Reinforcement learning for multi-objective design, self-tuning optimization, and lead prioritization for fast, interpretable refinement.	AI-optimized quantum control for co-evolving molecular architectures and self-optimizing therapeutic interventions via hybrid quantum-classical systems—enabling interventions beyond classical capability.

- Bridging the Gap: From Statistical Models to Physical Reality

Effective computational drug design requires strategies that go beyond the simple application of AI or quantum algorithms (Table 3, Figure 2). A major challenge that leads to inaccurate predictions is the lack of biochemical realism [148,149], which is the degree to which models faithfully reflect underlying physical, chemical, and biological principles. While AlphaFold [122–124] excels in protein folding due to its implicit learning of physical constraints, predicting polymorphs [150] (e.g., capturing a drug molecule's alternative crystal structures) remains difficult. This difficulty arises from sparse datasets, subtle free-energy differences and complex environmental interactions [151–153]. These challenges underscore the need for models that more faithfully integrate fundamental physicochemical principles. A core challenge in late-stage development is polymorph failure, where a potent compound unexpectedly forms a crystal structure with poor solubility [8–10]. For example, consider a potent lead molecule that failed standard dissolution tests (e.g., those following United States Pharmacopeia [USP] protocols), resulting in costly setback or even series abandonment. This failure often stems from the inability of classical computational models to accurately capture subtle free-energy differences. To resolve this bottleneck, the integrated quantum framework utilizes either high-fidelity Quantum Machine Learning (QML) models or hybrid Quantum Mechanics/Molecular Mechanics (QM/MM) simulations [152,154,155], depending on the complexity and nature of the molecular system. These methods allow precise calculation of free energy surfaces [156,157] for the crystal forms, capturing subtle energy differences that classical methods cannot reliably detect. For instance, a simulation may reveals a subtle 0.8 kcal/mol energy difference between the desired kinetic form and the stable, non-viable thermodynamic polymorph [158], which is below the threshold of reliable classical force fields and critical for quantifying stability. The quantum-validated energy value provides a clear go/no-go decision for formulation [159,160], allowing the R&D team to pivot immediately to a stable derivative.

- Classical AI as foundational pillar

As a mature and widely deployed technology, classical AI models, such as quantitative structure-activity relationship (QSAR) [115] and ligand-based screening [119], provide rapid statistical predictions of molecular behavior. These methods are widely deployable and efficient with large datasets but lack the ability to capture electron-level phenomena, subtle free-energy differences, or non-classical energy surfaces requiring quantum mechanical calculations. Classical AI remains a mature, cost-effective technology, capable of handling large, complex biomedical datasets [161]. Its well-understood error correction and fault tolerance make classical AI reliable for high-throughput screening, where broad accuracy across millions of compounds outweighs the need for quantum-level precision on individual molecules. However, limitations include non-physical predictions for novel molecular classes or reduced extrapolation beyond their training data, as pre-trained models may fail to generalize to out-of-distribution patient populations. Despite these, classical AI supports de novo drug design [125] using generative models (e.g., Generative Adversarial Networks, Variational Autoencoders), predictive toxicology, patient stratification, NLP on safety reports and mining real-world evidence from EHRs and claims data.

- Quantum-Enhanced AI to bridge the Gap

By contrast, Quantum-enhanced classical AI, including hybrid models that incorporate variational quantum algorithms (e.g., Variational Quantum Eigensolver, QAOA) [154,162], bridges classical workflow accessibility and enhanced mechanistic insight. Currently, these models are limited to small systems due to hardware noise and scaling constraints [163], these models improve energy landscape precision and conformational sampling. They support quantum refinement of binding energies [164], hybrid retrosynthesis [165], quantum

corrections for metabolism [87] and detection of rare patient subgroups [166]. Such hybrid approaches serve as a stepping stone toward more physics-informed workflows [167]. However, these models remain tethered to classical data, and QPU access is limited by encoding bottlenecks and classical-quantum communication overhead [72]. Beyond hybrid models, quantum-native AI directly simulates or learns from molecular and electronic states [168]. Examples include quantum circuit Born machines (QCBM) [169] and electron-level generative chemistry models. These methods simulate distributions over molecular and electronic scales, capturing complex phenomena like electron correlation and mode-selective properties without performing full electronic structure calculations [170]. They enable quantum generative chemistry [168], quantum causal networks [171], fully quantum retrosynthesis planning [118], quantum enhanced high-resolution ADME modeling [117,172] and individual-level prediction via quantum state encoding [173]. Currently, high-fidelity representations are demonstrated mostly on very small molecules due to limited qubit counts, decoherence and resource-intensive execution [74]. While its strength lies in accurately reflecting fundamental physical and chemical realities, regulatory validation remains challenging because non-classical outputs lack direct classical comparators.

- Advancing the Computational Workflow

Recent strategies for computational drug design integrate mechanistic and network-based simulations with hybrid AI frameworks that incorporate physics-informed constraints (Figure 2). This enhances predictability by grounding models in biochemical principles and addressing overfitting challenges. For example, Explainable AI (XAI) methods [174,175], including SHAP and Local Interpretable Model-agnostic Explanations (LIME), improve interpretability and regulatory trust by helping align model decisions with underlying science. The computational layer integrates multi-omics data and employs federated learning to securely support the full digital workflow [176]. This tightly coupled framework links prediction with experimental control through closed-loop feedback systems and self-driving labs [177,178]. In this unified system, classical, quantum-enhanced and quantum-native workflows perform complementary roles, from statistical modeling to uncertainty quantification and direct molecular state encoding [179]. This integration ensures each layer benefits from mechanistic insight and real-time feedback [180], forming a robust, predictive backbone for drug discovery. In addition to these workflow integration, the probabilistic data from quantum simulations can capture nuanced physical realities of molecular behavior [181,182] (e.g., electron correlation and non-classical energy surfaces) enhancing predictive robustness.

4.2. Real-Time Control, Sensing, and Automation

The physical layer translates computational predictions into actionable experimental workflows, highlighting stark differences between classical and quantum-enabled approaches across sensing, characterization, manipulation, and control (Table 3, Figure 3).

- The Promise of Quantum Sensing

  In classical workflows, biochemists often face a fundamental trade-off between the speed of a tool and the detail of its data. For example, techniques such as High-Performance Liquid Chromatography (HPLC) [183] for separating components in a mixture, and Gas Chromatography–Mass Spectrometry (GC-MS) for identifying different substances within a test sample, are reliable and reproducible, but their data are batch-based with limited temporal resolution. Furthermore, signal amplification in assays such as Polymerase Chain Reaction (PCR) and immunoassays can introduce errors or biases [184,185]. Additionally, live-cell fluorescence microscopy is constrained by photobleaching and short observation windows [186,187]. Despite these limitations, classical physical sensing and control methods remain mature, reliable, and widely

accessible, though less precise than specialized quantum-enabled approaches [188,189]. They are also widely accepted by regulatory bodies such as the FDA, offering a significant compliance advantage.

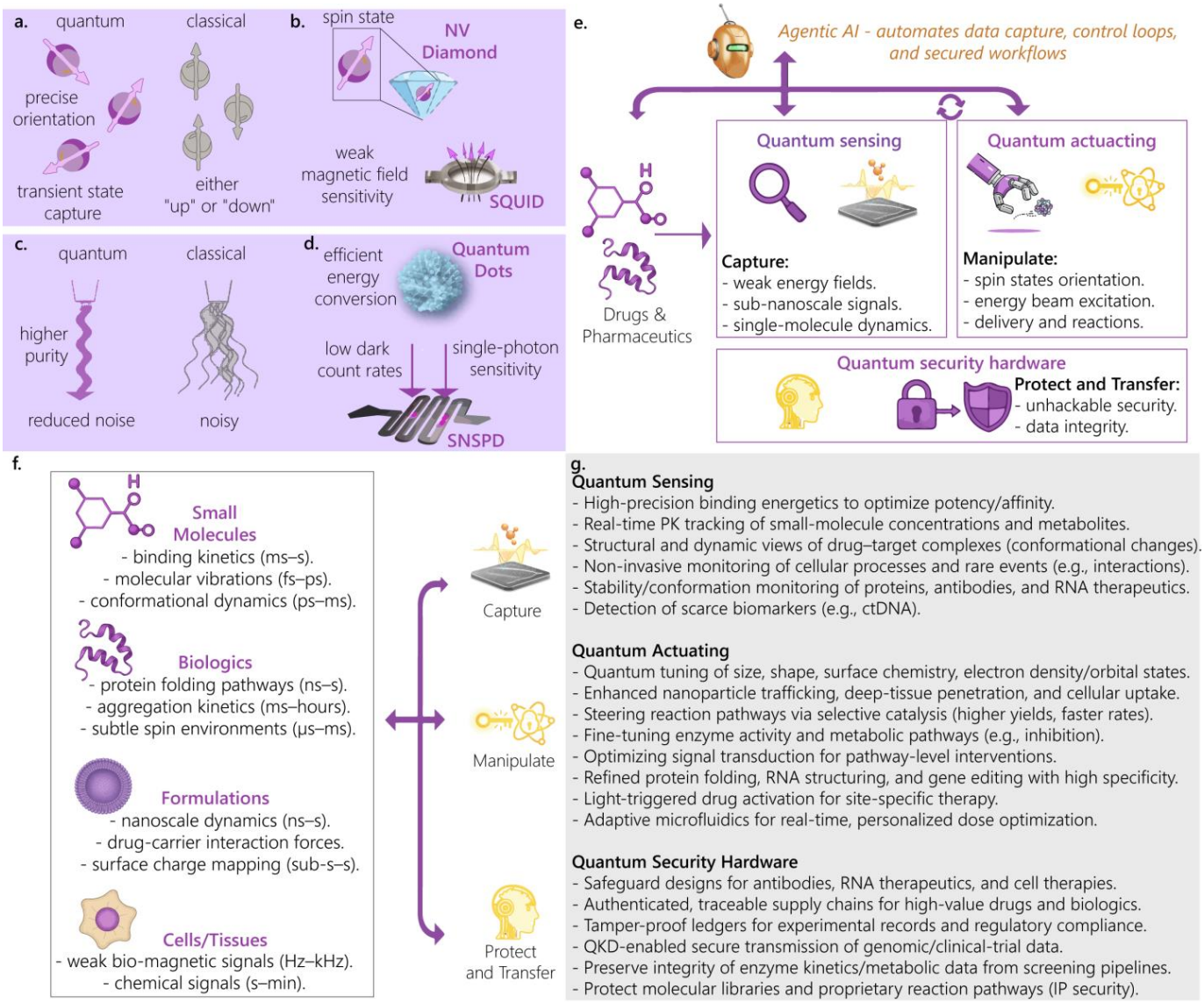


Figure 3. The Physical Layer: Bridging Computational Design with Experimental Reality. This schematic illustrates the integration of quantum systems with physical materials and highlights quantum control and sensing mechanisms across multiple domains: (**a**) Quantum Spin-State Control: Comparison of classical spins (binary "up" or "down") with quantum spins capable of precise orientation and simultaneous multi-state control. (**b**) Quantum Sensors: Nitrogen-Vacancy (NV) diamonds and Superconducting Quantum Interference Devices SQUIDs detect spin states directly or via magnetic field fluctuations. (**c**) Quantum Energy Beams: Classical noisy beams are contrasted with focused, low-noise quantum beams (e.g., laser-based). (**d**) Energy Beam Detection: Superconducting Nanowire Single-Photon Detectors SNSPDs and quantum dot (QD)-based sensors enhance detection, Quantum Dots (QDs) and Nitrogen-Vacancy (NV) diamonds also serve as functional nanoparticles. (**e**) A high-level diagram outlining the functional and interactive relationships between the core quantum physical technologies. (**f**) Physical materials, including small molecules, biologics, formulations, and cells/tissues, which are interfaced with the quantum systems. (**g**) The specific impact of each physical layer on sensing, actuating, and security hardware.

In contrast, quantum sensing enables real-time, intelligent intervention at molecular and sub-molecular scales (Figure 3). For instance, ultra-sensitive quantum sensors such as NV (nitrogen-vacancy) diamonds [17,83,190], SQUIDs (Superconducting Quantum Interference Devices) [17,47,191,192] and Superconducting Nanowire Single-Photon Detectors (SNSPDs) [17], provide extraordinary sensitivity, capable of detecting subtle protein folding changes in nanoliter samples. They enable real-time tracking of single molecules, overcoming photobleaching and supporting long-term biodistribution studies in vivo, currently limited to specialized laboratory settings.

This limitation is often due to stringent device requirements, such as cryogenic cooling (required for SQUIDs and SNSPDs, which are superconducting devices capable of detecting minute magnetic fields and single photons, respectively), or dedicated excitation optics (needed for NV diamonds, which operate at room temperature and detect nanoscale magnetic and electric fields). These sensors facilitate real-time monitoring of protein folding dynamics, quantification of low-abundance biomarkers, and nanoscale imaging of molecular interactions. Notably, NV centers in diamonds enable in vivo nanoscale sensing, unlike SQUIDs and SNSPDs, which require cryogenic conditions and are restricted to external use. Beyond these cryogenic systems, quantum dots (QDs) and nitrogen-vacancy (NV) nanodiamonds are used in vivo as nanometric materials to act as both quantum sensors and energy-responsive functional platforms [17,48], and are engineered to react to internal or external energy stimulus such as photonic or magnetic fields—enabling advanced applications in imaging, sensing, and targeted therapeutic activation. Quantum dots offer tunable fluorescence and high photostability but pose significant chemical toxicity risks due to heavy metal ion release. These risks can be mitigated through surface coatings (e.g., PEGylation [193]), by using non-toxic alternatives (e.g., carbon-based quantum dots), or by incorporating additional strategies inspired by photothermal or photosensitizing organic nanostructures that protect against reactive species and enhance cellular membrane interactions [194]. In contrast, NV nanodiamonds, being carbon-based, are highly biocompatible and photostable, allowing real-time detection of magnetic and electric fields [17,195]. However, both QDs and NV nanodiamonds, as nanoscale materials, share the long-term challenges of organ accumulation and poor biodegradability, which must be addressed through surface engineering and biodegradable designs.

These quantum capabilities also significantly augment analytical techniques in drug development. For example, quantum sensors can enhance nuclear magnetic resonance (NMR) by detecting sub-atomic signals from individual nuclei [45,67], revealing subtle protein folding dynamics and molecular interactions critical for drug design. In mass spectrometry, quantum ion trap sensors leverage quantum coherence for ultra-precise frequency measurements. These sensors enable single-ion mass resolution [196,197], improving metabolite profiling and impurity detection. Integrated into microfluidic assays, they support high-resolution droplet generation for encapsulating individual cells or nanoparticles [198,199], advancing metabolite profiling and drug response analysis. Additionally, squeezed-light Raman and IR spectroscopy use quantum-correlated photons to boost vibrational signal-to-noise ratios, enabling molecular detection at lower light powers and guiding selective reaction pathways control, especially to minimize photo-damage during live-cell or trace compound analysis [200–202].

- The Promise of Quantum Actuation

Reaction control typically adjusts bulk conditions such as temperature or solvent, which can produce unintended side reactions. While catalysis is an inherently molecular-level process, conventional catalysts cannot dynamically achieve single-molecule selectivity [203,204]. In contrast, quantum actuation (see Figure 3) introduces techniques such as quantum optical tweezers to manipulate single molecules with sub-atomic precision,

modulate metabolic QSAR, or regulate protein-protein and RNA folding interactions [115]. This precision is also used to shape radiation beams, synthesize nanomaterials, and manipulate drug activation with external stimuli such as light [17,48]. Forexample, ultrafast Coherent Control (using precise laser pulses to manipulate chemical reactions) allows selective bond manipulation [205], guiding reactions to produce target enantiomers [206] and mimicking enzyme-like selectivity in microfluidic systems [89,207]. Innovative approaches, such as synthesizing Carbon Quantum Dots (CQDs), nanoscale semiconductor crystals with quantum properties, directly from Active Pharmaceutical Ingredients (APIs) to create "Quantum Drugs" have been shown to enhance photoluminescence, bioavailability, and even mechanisms of action [208].

- From Lab Automation to Self-Driving Labs

The self-driving lab framework provides a critical link between computational predictions and physical interventions, as shown in Figures 2 and 3. Lab automation improves reproducibility, yet robots execute predefined protocols without adaptive feedback, limiting dynamic optimization. The integration of AI and quantum technologies transforms conventional laboratory automation into adaptive "self-driving labs" (Figures 2 and 3) [127,128]. In these systems, real-time data from quantum sensors feeds computational models, which detect deviations in reaction pathways and autonomously recalibrate experimental conditions. These closed-loop systems enable dramatic acceleration of the design, build and test cycle at a pilot scale. Within this framework, AI generates experimental protocol (e.g., specifying new compounds or reaction parameters), robots execute these protocols, and data flows back into AI for continuous refinement. Classical experimental approaches provide robust, accessible, and reproducible measurements but are limited in temporal resolution, molecular precision, and adaptive feedback. By contrast, quantum-enabled approaches [92], offer technical potential for single-molecule resolution and real-time feedback, although they remain specialized, costly, and technically demanding.

4.3. Optimizing Clinical Trials and Operations

The integration of computational and physical layers extends into the clinical domain, establishing a patient-centric framework that links molecular insights with therapeutic strategies and optimizes trial design and execution. AI, quantum sensing and autonomous systems collectively generate patient-enriched datasets that inform disease modeling, trial simulations and personalized therapies (Table 4) [17,48].

Table 4. Key Translational Objectives in Pharmaceutical Design.

Stage	Classical Physical Layer	Quantum Physical Layer	Classical AI Layer	Quantum AI Layer
Stage 1: Target Discovery/Patient Stratification	Immunoassays, blood tests, traditional imaging (Magnetic Resonance Imaging, Computed Tomography), bulk sample analysis, flow cytometry, Enzyme-Linked Immunosorbent Assay (ELISA) panels for known biomarkers.	Quantum sensors (e.g., Superconducting Quantum Interference Devices (SQUIDs) [47,191,192,209,210], Nitrogen-Vacancy center [37,41,45,64]; and Quantum Dots [211]), allow high-resolution, real-time biomarker detection, continuous monitoring, and multiplexed sensing	Integrates multi-omics [57,58], Electronic Health Records, and wearable data for subtyping, digital twin modelling [212–214], and patient risk stratification.	Simulates mutation effects on protein function, metabolism, and signaling pathways at atomic resolution; quantum-enhanced biomarker discovery in high-dimensional combinatorial space [71].

Table 4. *Cont.*

Stage	Classical Physical Layer	Quantum Physical Layer	Classical AI Layer	Quantum AI Layer
Stage 2: Lead Identification/Mechanism of Action Clarity	Traditional spectroscopy (Circular Dichroism, Fourier Transform Infrared Spectroscopy), bulk kinetics assays (Surface Plasmon Resonance), gel electrophoresis; fluorescence and absorbance assays for enzymatic activity; NMR for secondary structure.	Quantum spectroscopy (e.g., Quantum Cascade Lasers [42], SPR, interferometry), tracks conformational changes, reaction fingerprints, electron tunneling, and excited state dynamics [114].	Uses graph neural networks (GNNs), causal inference, and network analysis to model drug actions [139,140], allosteric modulation, and off-target interactions.	Models binding, tunneling, and excited states ab initio; simulates electron density changes, transition states, and quantum-induced allosteric effects invisible to classical methods [114,164,215,216].
Stage 3: Lead Optimization/Molecular Specificity	Rational drug design using classical molecular mechanics and docking [71,217]; traditional synthetic chemistry; high-throughput screening; chromatography and NMR for structure confirmation.	Coherent control (laser shaping, pulse sequences) enables enantioselective synthesis, bond activation, and monitoring of transient reactive intermediates [41–45,67]	Generative Adversarial Networks, Variational Autoencoders and Large Language Models [120], explore chemical space, predict synthesis routes, optimize ADMET properties [59,120,218,219], and design selective ligands or bifunctional molecules.	Simulates stereoselective pathways, electron-level interactions, reaction energetics, and molecular dynamics for stable, targeted designs; evaluates quantum tunneling in catalytic reactions [215,220–222].
Stage 4: Preclinical Development/Manufacturability and Stability	High-Performance Liquid Chromatography for purity, rheometers for viscosity, stability chambers, traditional machine vision for Quality Control, spectrophotometry for degradation monitoring; thermal analysis (DSC, TGA).	Quantum sensors [200,201,223], detect nanoscale stability shifts, polymorph transitions, and excipient interactions; quantum electrodynamics could support light-activated carriers and precision-controlled reactions.	Predicts formulation compatibility, degradation kinetics, excipient selection, and process parameters; uses classical ML to anticipate stability issues under multiple conditions [59,224,225].	Models' polymorph transitions, solubility, chemical degradation pathways, and metabolism with quantum precision; simulates quantum-controlled excipient interactions for improved stability [114,222].
Stage 5: Clinical Trials/ Toxicity and Safety Profiling	Traditional toxicology assays (MTT, LDH), animal models, clinical observations, ECG/biomarker monitoring; imaging for organ toxicity; hematology and biochemistry panels.	Quantum sensors detect early toxicity biomarkers, metabolic perturbations, and reactive intermediates, enabling closed-loop adaptive safety testing in preclinical and clinical phases.	Uses toxicogenomic, pharmacovigilance, and population health data to forecast adverse events; AI models predict dose–response relationships and rare events [100,111,226].	Simulates reactive intermediates, metabolic byproducts, enzyme interactions, and off-target effects at quantum resolution; could enable atomic-level modeling of toxicity pathways. [6,117].
Stage 6: Post-Market and Trial Optimization	Manual data collection, fixed trial designs, EHRs, patient registries; traditional remote monitoring; periodic lab tests and imaging.	Quantum sensors enable dynamic endpoint adjustment, decentralized trial monitoring, real-time physiological tracking, and high-resolution wearable integration [227].	Designs adaptive trials, stratifies patients using real-world and longitudinal data, and predicts adherence and long-term outcomes [111,228].	Models' patient-drug interactions under uncertainty, evaluates population-level responses, predicts rare adverse events, and improves trial robustness with quantum-enhanced simulations [71,111].

Across this spectrum, AI has the capacity to provide robust predictive modeling, patient stratification, the development of digital twins for potential personalized treatment [212,229], pharmacovigilance, generative compound design [230], regulatory drafting and decentralized monitoring via digital biomarkers. Quantum methods enhance chemical calculations [156,157], optimize portfolio and site selection, and enable high-dimensional cohort identification, including rare diseases (Table 4). Rather than operating in isolation, these technologies function as complementary layers of an adaptive, data-driven pipeline that connects molecular discovery directly to clinical delivery. Effective translation of clinical insights into therapies still requires a mechanistic understanding linking patient heterogeneity to molecular causality. While AI and quantum approach substantially enhance trial design, patient stratification and real-world monitoring, ultimate therapeutic precision depends on understanding the biomarkers, targets and pathways that drive disease and response [17]. To illustrate this duality, Tables 4 and 5 comparing classical and quantum methods across a range of biochemical objectives and across clinical development stages (Supplementary Table S1).

5. Mechanistic Layer: Biomarkers, Targets, and Pathways

5.1. The Role of Classical Physics and AI in Mechanistic Discovery

At the cutting edge of computational science, classical mechanics and artificial intelligence in mechanistic discovery form a powerful synergy that leverages the efficiency of classical models within an AI framework. This approach begins with using Newtonian mechanics, specifically molecular dynamics simulations [181,182], to generate the vast datasets required to train robust AI models. This combined approach provides a physically informed framework for AI; by building classical principles (e.g., Newton's Second Law or the conservation of energy) directly into the models, AI systems are guided to learn meaningful physical laws rather than spurious correlations. This integration is often achieved through techniques such as symbolic regression [231], where the AI searches for explicit mathematical equations, or by designing neural network architectures that respect the symmetries and invariances of physical systems. For instance, graph neural networks (GNNs) and causal inference can construct complex biological interaction maps, identifying subtle allosteric sites and drug effects that classical methods often miss [232]. Such strategy also enables large-scale, long-timescale simulations, as AI-enhanced classical molecular dynamics [181,182] can model millions of atoms over microseconds, a feat impossible with quantum simulations alone, making them highly relevant for processes such as protein folding, polymer dynamics and self-assembly. Additionally, AI plays a central role in a data-driven form of mechanistic discovery by applying advanced pattern recognition to multi-omics data [57], thereby identifying and functionally clustering biomarkers and targets such as dysregulated receptors, ion channels, and transporters. These models, known as machine-learned interatomic potentials (MLIPs) [224,233], learn to predict atomic forces, effectively creating a computationally efficient, "quantum-like" field that bridges the gap between quantum mechanics and classical methods. Quantitatively, MLIP frameworks have demonstrated the ability to achieve sub-chemical accuracy (error < 1 kcal/mol) for pharmaceutical solids using as few as ~200 reference data structures [234], representing an order of magnitude increase in data efficiency over previous state-of-the-art methods. Active learning loops that couple classical molecular dynamics with AI uncertainty estimates focus simulation effort on mechanistically informative regimes (e.g., transition states and rare events), accelerating the discovery of rate-limiting steps and allosteric routes. This is complemented by generative AI [125,126,168,230], which learns from chemical databases to structural data, and enhances drug discovery by designing entirely new molecules and predicting novel binding poses. These combined approaches illustrate how classical mechanics,

AI, and generative models accelerate mechanistic insights in drug discovery. Rather than simply expanding chemical space, the integration of classical physics and AI fundamentally enhances mechanistic discovery by uncovering causal relationships, identifying emergent behaviors, and predicting reaction pathways with physical interpretability. This shift from correlation-driven models to physics-informed AI ensures that mechanistic hypotheses are not only computationally efficient but also experimentally actionable, reinforcing the central role of classical principles in guiding AI-driven discovery (see Table 5).

Table 5. Quantum-AI Applications in Drug Discovery.

System/Application	Machines and Hardware	Classical Physical Capabilities	Quantum Machines and Hardware	Classical-AI Solutions	Quantum-AI Solutions
Target Discovery and Interaction (Stage 1–2)	High-Performance Computing clusters, Cryogenic Electron Microscopy; Quantum chemistry platforms	Traditional spectroscopy (Circular Dichroism, Fourier Transform Infrared Spectroscopy) [235], bulk kinetics assays (Surface Plasmon Resonance).	Quantum-enhanced spectroscopy enables high-resolution structural analysis [236,237].	Target prioritization using network biology and causal inference [238].	Atomic-level simulations for binding energy and drugability [114,163,216]
Generative Drug Design (Stage 2–4)	NVIDIA DGX systems, generative platforms; Quantum annealers.	Molecular docking [71,217,239,240], HTS, MD simulations; Structure-based drug design [241,242]; Rational drug design; Traditional synthetic chemistry.	Quantum spectroscopy and coherent control techniques (e.g., laser pulse shaping) enable high-resolution structural analysis and enantioselective synthesis [243].	Graph Neural Networks, Generative Adversarial Networks, Variational Autoencoders and Large Language Models [244] for molecule design; AlphaFold predicts protein folding [122–124]	Quantum generative models (e.g., quantum Generative Adversarial Networks, quantum Variational Autoencoders) for chemical space exploration and optimize molecular generation [222,245]
Molecular Design and Optimization (Stage 2–4)	High-Performance Computing robotics, Mass Spectrometry, NMR, Cryo-EM; Quantum simulators.	Traditional spectroscopy (Circular Dichroism, Fourier Transform Infrared Spectroscopy), bulk kinetics assays (Surface Plasmon Resonance).	Quantum-enhanced spectroscopy [17,48,71,217]	Property prediction and hypothesis generation (e.g., Graph Neural Networks, AlphaFold) [122–124];	Quantum deep learning for property prediction and chemical space navigation [17, 48,92,245,246]

Table 5. *Cont.*

System/Application	Machines and Hardware	Classical Physical Capabilities	Quantum Machines and Hardware	Classical-AI Solutions	Quantum-AI Solutions
Protein-Ligand Binding (Stage 2–4)	Docking platforms; MD engines.	Bulk kinetics assays (SPR), gel electrophoresis [247].	Quantum-enhanced spectroscopy for detailed binding dynamics [17]	ML scoring functions and absorption models for binding prediction [59,119,248].	Hybrid quantum neural networks for FCI-level binding affinity prediction [245,249].
Chirality and IDP Dynamics (Stage 2–4)	Circular Dichroism spectrometers, Vibrational Circular Dichroism systems; Quantum simulators.	Circular Dichroism and Vibrational Circular Dichroism spectroscopy.	Quantum-enhanced spectroscopy resolves chirality with precision [250,251].	Docking, chirality, and protein dynamics modeling [71,217,252].	Quantum simulations for tunneling and stereoselectivity; generative AI for Intrinsically Disordered Proteins conformations [253].
Toxicity and Safety Profiling (Stage 3–5)	Toxicology assays (MTT), animal models	MTT assays; clinical observations	Quantum sensors detect early toxicity biomarkers, while closed-loop systems enable adaptive safety testing [254].	Prediction of ADMET properties and adverse events [59,120,218].	Quantum simulations for metabolic reactions and toxicity validation [255,256].
Biosecurity and Dual-Use Risk (Stage 1–6)	Pathogen surveillance, genomic profiling.	Genomic profiling, traditional toxicology.	Ultra-sensitive detection of biohazards with quantum biosensors [254,257].	NLP prediction of outbreak signals and dual-use risks [258]	Quantum models for protein-pathogen interactions and risk forecasting [22].

5.2. The Complementary Contributions of Quantum in Mechanistic Discovery

- Quantum Mechanics Provides Access to Electronic-Level Phenomena

Classical methods treat atoms as point masses and describe their interactions with predefined potentials (force fields). While effective for structural and dynamic properties, these models do not capture electron behavior. By explicitly considering electrons and their wave functions, quantum mechanics provides the only rigorous framework for modeling bond formation and breaking [259,260], where classical force fields with fixed connectivity fail. This quantum mechanical framework is essential for calculating transition-state energies and activation barriers, and for modeling purely electronic phenomena such as fluorescence, phosphorescence, and charge transfer. Quantum methods further enable the calculation of molecular charge distributions, critical for understanding electron transfer in oxidation–reduction reactions or the conductivity of materials. Ab initio simulations [261,262], based on first principles, extend these insights to drug–target binding dynamics, proton tunneling in enzyme active sites and excited-state transitions in chromophores. These phenomena are central to catalytic efficiency and the design of light-activated therapies [79,263].

- Quantum Mechanics For Accurate Description of Potential Energy Surfaces

The Potential Energy Surfaces is the "map" that governs a molecular system's behavior. Classical methods rely on empirical force fields [264,265] that are limited in scope (often parameterized for a specific class of molecules), non-predictive for novel chemistry and lack polarization effects. In contrast, Quantum mechanics, by solving the Schrödinger equation from first principles [266,267], naturally accounts for the redistribution of electron density as a molecule interacts with its environment. This provides a much more accurate and predictive description of a system's energetics, particularly for bond lengths, angles and reaction barriers [268,269].

- Quantum Mechanics Accounts for Unique Physical Phenomena

Beyond purely electronic aspects, quantum mechanics also captures effects that are not present in classical physics. This includes quantum tunneling [17,79], which can significantly affect reaction rates, especially with light atoms such as hydrogen. It also accounts for zero-point energy [270,271], the minimum vibrational energy of a system even at absolute zero, which is important for calculating accurate reaction thermochemistry and kinetic isotope effects [272,273].

To provide a consolidated view, Table 6 summarizes how classical and quantum approaches complement each other in biochemistry, outlining their advantages, and mechanistic insights across structure, dynamics, kinetics and catalytic processes.

Table 6. Classical vs. Quantum in Biochemistry.

Objective	Classical Methods	Benefits and Limitations	Quantum Methods	Benefits and Limitations
Molecular Structure and Dynamics (Stage 1–4)	NMR, X-ray Crystallography, Cryo-Electron Microscopy, Atomic Force Microscopy, Circular Dichroism (CD).	**Benefits:** High-resolution 3D structures (X-ray, Cryo-EM), non-destructive analysis (NMR), conformational insights (CD). **Limitations**: Requires large sample sizes (NMR), static snapshots (X-ray), complex image processing (Cryo-EM), limited spatial resolution (NMR), bulk averaging (CD).	Quantum-enhanced NMR [209,210]; Quantum tunneling Microscopy [274]; Nitrogen-Vacancy center (NV-center) nanoscopy [41,45,64]; Quantum embedding and hybrid QM/MM	**Benefits**: Enhanced sensitivity and resolution, nanoscale imaging of electronic and spin properties, single-molecule kinetics, label-free detection. QM/MM and Fragment Molecular Orbital (FMO) methods enable scalable modeling of large biomolecules. **Limitations**: Early-stage technologies, specialized instrumentation, potential imaging artifacts (QTM), complex data interpretation.

Table 6. *Cont.*

Objective	Classical Methods	Benefits and Limitations	Quantum Methods	Benefits and Limitations
Reaction Kinetics (Stage 1–4)	Spectroscopy, Plate Readers, Liquid Chromatography-Mass Spectrometry/Mass Spectrometry	**Benefits**: Established protocols, high-throughput screening, detailed mass and concentration analysis. **Limitations**: Bulk measurements, limited temporal resolution, indirect detection, potential invasiveness.	Quantum-enhanced Spectroscopy [202,243], Pulse-shaped ultrafast lasers [275], Quantum Causal Reasoning [276]; Quantum optimal control	**Benefits**: Femtosecond-scale time resolution, sub-diffraction imaging, mechanistic inference, single-molecule sensitivity. Quantum optimal control enables steering of reaction pathways and lowering of activation barriers. **Limitations**: Technically demanding, high cost, limited accessibility, early-stage development.
Photophysical Properties (Stage 1–4)	Fluorescence/ Absorbance Spectroscopy	**Benefits**: Cost-effective, widely used for quantum yield and absorption spectra. **Limitations**: Bulk averaging, indirect measurements, limited specificity, diffraction-limited resolution.	Quantum-enhanced Spectroscopy [243], Quantum plasmonic biosensing, entangled-photon Fluorescence Lifetime Imaging Microscopy (FLIM) [201,277].	**Benefits**: Shot-noise-limited sensitivity, sub-diffraction resolution, enhanced lifetime and energy transfer measurements. Quantum plasmonics enables real-time monitoring of photophysical changes. **Limitations**: Requires stable squeezed light sources, homodyne detection, and specialized equipment.
Cellular and in vivo Imaging (Stage 2–5)	Confocal/Fluorescence Microscopy, Cryo-EM	**Benefits**: High-resolution imaging, applicable to live-cell studies. **Limitations**: Limited depth penetration, photo-toxicity, static imaging (Cryo-EM), diffraction-limited resolution.	NV-center nanoscopy [41,45,64]; Quantum Dot Microscopy [278]; Hyperpolarized quantum MRI/NMR [279].	**Benefits**: Nanoscale resolution, single-molecule sensitivity, non-invasive imaging, deeper tissue penetration, metabolic imaging. **Limitations**: Requires specialized setups, susceptible to noise, quantum dot toxicity varies with coating and size.

Table 6. *Cont.*

Objective	Classical Methods	Benefits and Limitations	Quantum Methods	Benefits and Limitations
Binding, Stability and Thermodynamics (Stage 2–5)	Surface Plasmon Resonance/Biolayer Interferometry, Dynamic Light Scattering, Differential Scanning Calorimetry.	**Benefits**: Real-time kinetics, label-free detection, particle sizing, thermal stability profiling. **Limitations**: Bulk measurements, low spatial resolution, slow acquisition, sensitivity to non-specific interactions.	Vibrational Strong Coupling [280,281], Quantum diamond magnetometry [282].	**Benefits**: High sensitivity to subtle molecular changes, single-molecule binding detection, sub-Hz resolution of interactions. **Limitations**: Requires precise cavity design, strong coupling conditions, and specialized setups (still in early experimental stages).
Reaction Rates and Pathways (Stage 2–4)	Temperature/Pressure Controllers, Chiral Catalysts	**Benefits**: Scalable, well-established for bulk synthesis and control. **Limitations**: Non-specific control, thermally driven reactions, catalyst design constraints.	Pulse-shaped ultrafast lasers [275], Vibrational Strong Coupling [280,283], Radiofrequency (RF)/B-field Spin Control [284]; Quantum control via photonic reagents	**Benefits**: Selective bond excitation, manipulation of energy landscapes, spin-selective reactions, precise control over reaction outcomes. Photonic reagents enable targeted reaction control. **Limitations**: Complex setups, early-stage development, sensitive to environmental noise.
Catalysis and Selectivity (Stage 2–4)	Traditional Catalysts, Photochemistry	**Benefits**: Broad applicability, diverse reaction conditions. **Limitations**: Non-specific catalysis, bulk-level control, often requires harsh conditions.	Quantum-enhanced Catalysis [283,285], Vibrational Strong Coupling	**Benefits**: Enhanced reaction rates via quantum tunneling, energy landscape modulation, electrocatalysis via heteroatom doping and defect engineering. **Limitations**: Theoretical and early experimental stages, conductivity limitations in CQDs, scalability challenges.
Synthesis and Automation (Stage 2–4)	Microfluidics, Robotics	**Benefits**: Precise fluid handling, small sample volumes, automated workflows. **Limitations**: Limited scalability, specialized fabrication required.	Quantum-assisted Microfluidics or Robotics Synthesis [286]; Quantum-enhanced process optimization	**Benefits**: Potential for quantum-level precision in synthesis, optimization of synthetic routes using hybrid quantum-classical algorithms. **Limitations**: Largely conceptual, limited experimental validation, high complexity.

- Solving Complex Biological Challenges with Quantum Computing

In many areas of disease etiology, classical models often cannot fully capture fundamental molecular unknowns such as protein aggregation, misfolding, and subtle molecular

interactions [287,288]. For example, a biochemist developing a biologic drug (Table 6), such as a monoclonal antibody prone to aggregation, often confronts challenges that classical simulations cannot fully address, as subtle, early misfolding events that trigger aggregation and immunogenicity are frequently missed [289]. To overcome this, quantum-enhanced simulations can model electron-level interactions and conformational entropy with high precision [290] to identify structural weak points and predict specific amino acid modifications [291], substantially reducing trial-and-error experimentation and formulation failures. This precision is also critical for modeling drug-protein interactions in conditions such as asthma and enhancing gene-editing techniques such as CRISPR [292], improving accuracy and minimizing off-target effects. Furthermore, quantum-immune algorithms identify cryptic pockets that form via electronic reorganization and quantum simulations can be used to model protein aggregation in neurodegenerative diseases [293]. Beyond current applications, large-scale quantum computers will allow direct simulation of molecular wavefunctions [181,182], describing the probability of electrons, further expanding the frontier of drug discovery. For example, hybrid quantum-classical algorithms, such as the Variational Quantum Eigensolver (VQE), have successfully calculated electronic ground state energies of small pharmaceutical-relevant molecules (e.g., LiH, BeH_2) to chemical accuracy (error < 1 kcal/mol), necessary for predicting molecular stability and binding affinities [294]. Quantum-mechanical calculations in drug design would benefit most from speed-ups to Density Functional Theory (DFT) and coupled-cluster methods [222,295,296]. Additionally, quantum computing, through Hamiltonian formulations, enables precise characterization of protein binding sites and pocket engineering, capturing subtle electronic changes that traditional force fields approximate only roughly. It also offers highly granular simulations of disease-specific metabolic spaces, valuable in conditions such as inborn errors of metabolism, Type 2 Diabetes and rare genetic diseases where quantum-level interactions govern biochemical function [297,298]. This approach also extends to nutrition-related diseases (especially those with a genetic component) fall under this umbrella, as improper nutrient metabolism can lead to health issues requiring specific dietary management or interventions.

- Ultra-Sensitive Quantum Sensing in Mechanistic Discovery

Complementing computational advances, quantum sensing technologies (e.g., Nitrogen-Vacancy (NV) diamond centers [17,41,83,190], Quantum Cascade Lasers [42], and SQUIDs [17,47,191,192]) offer ultra-sensitive capabilities enabling precise detection of molecular states, vibrational fingerprinting, and real-time monitoring of binding kinetics (Figure 3; Table 3). These sensors achieve sub-picomolar detection limits, with sensitivity thousands of times greater than the nanogram per milliliter (ng/mL) thresholds typical of classical assays, as demonstrated in specialized pharmaceutical biomarker and stability testing [80,299]. Such precision allows detection of misfolded proteins at the single-molecule level and observation of subtle metabolic shifts in individual cells, critical for understanding drug mechanisms and disease progression. [80,299]. Quantum sensors also have the capability to deliver signal-to-noise ratios up to 100,000 times higher than classical methods under optimized conditions (e.g., quantum-amplified global-phase spectroscopy [300], spin squeezing [301], and entanglement-enhanced optical transitions [302]). They operate without requiring bulk or averaged samples, enabling resolution of rare molecular events that would otherwise be lost in background noise. This ultra-sensitive capability is especially valuable for in vivo drug tracking, providing fine-grained pharmacodynamic monitoring in real time. Moreover, integrating AI with quantum sensor data unlocks mechanistic insights inaccessible to classical methods. AI models trained on high-fidelity quantum measurements [223] can uncover hidden molecular patterns, predict binding affinities, and support precision dosing and cohort selection in clinical trials.

6. Molecule and Modality Design Layer

6.1. Modality as Strategic Constraint and Design

The entire process of creating molecules with specific desired properties is underpinned by the fundamental principle of molecular design, which relies on computational and theoretical methods. At its core is the concept of structure-property relationships, which states that a molecule's function and behavior are directly determined by its chemical structure [303]. This principle involves a deep understanding of chemical bonding and geometry [304,305], which explains how atoms connect and arrange in three-dimensional space to form a molecule; of intermolecular forces [303], which are the non-covalent interactions critical for how molecules interact and form materials; and of electronic properties [306], which refer to the distribution and behavior of electrons within a molecule that determine its ability to absorb and emit light, its electrical conductivity and its reactivity. Pharmaceutical companies are increasingly adopting platform-first strategies, focusing on therapeutic modalities such as mRNA and DNA vaccines, monoclonal antibodies, recombinant and fusion proteins, cell and gene therapies, and synthetic peptides (Table 7).

Table 7. Biomarker Challenges and Solutions.

Biomarker	Challenges	Classical AI Layer	Quantum AI Layer	Quantum Physical Layer
Antigen	Subtle changes; specificity vs. similar proteins [307].	Predict antigenicity, epitopes; Natural Language Processing (NLP) for associations [308,309].	Quantum algorithms simulate antigen–antibody binding and explore conformational spaces for epitope prediction [114,213].	Quantum-enhanced plasmonic spectroscopy, including Surface Plasmon Resonance [237,310] and NV centers [41,311], could enable ultra-sensitive detection of antigen–antibody kinetics; and conformational changes; quantum photonic sensors support real-time epitope mapping [82,312].
Protein & Peptides	Folding diversity; Post-Translational Modifications (PTMs) hard to detect [307].	Deep learning for 3D structure; aggregation motif prediction.	Quantum algorithms model protein folding and PTMs [114,213,245] outperform classical methods in conformational sampling [313].	Quantum Chemical Mass Spectrometry (QC-MS) [196,197], quantum dots [65,66], and hyperpolarized NMR with magnetometry enable PTM detection and folding state analysis. [209,210].
Enzyme	Complex reaction pathways; inhibitor design [307].	Docking for inhibitors; generative AI for active sites.	Quantum simulations model transition states and reaction pathways; quantum annealing accelerates inhibitor design [114,118,264,314].	Quantum Cascade Lasers [42] and quantum dot nanosensors detect enzymatic activity [17,81,315]; NV centers monitor catalytic sites with high spatial resolution [316].

Table 7. *Cont.*

Biomarker	Challenges	Classical AI Layer	Quantum AI Layer	Quantum Physical Layer
Gene, Nucleic Acids	Regulatory complexity; off-target edits; epigenetic modulation [307].	Network analysis; multimodal AI for mutations and methylation [18,57,134].	Quantum neural networks discover genetic biomarkers in large search spaces; classical machine learning struggles with multi-omics [79,317].	Quantum microscopy and quantum-enhanced fluorescence enable visualization of gene expression [318] and DNA damage [319,320].
Ion Channels	Rapid conformational changes; subtype specificity [307].	Time-series gating prediction; allosteric site screening.	Quantum simulations model gating dynamics and ion transport with higher fidelity than classical Molecular Dynamics [79,245].	Quantum sensors detect weak electric fields [321,322], NV centers [41,45,64] and quantum dots [83,323,324] track gating and conformational changes, or ion channel gating.
Transporter	Drug binding/release; drug–drug interactions [307].	Substrate prediction; Graph Neural Networks for transporter networks.	Quantum simulations model dynamic drug-transporter interactions and substrate flux [17,79].	Quantum-enhanced microscopy and tunneling sensors detect substrate flux and pH gradients in transporter dynamics [17,79,325].
Receptor	Allosteric modulation complexity [307].	Predictive AI for allosteric sites; generative molecule design.	Quantum simulations [17,79]. Capture allosteric modulation effects and ligand-induced conformational shifts.	Quantum-enhanced SPR and single-molecule FRET detect binding kinetics and ligand-induced shifts; quantum field sensors monitor conformational changes [17,79].
Chemical Biomarkers	Trace levels; oxidation state; metabolite profiling [307].	Predictive analytics for disease correlation [18,134].	Quantum simulations detect redox states and trace metabolites with high sensitivity [326].	Quantum sensors (e.g., SQUIDs [47,191,192], NV centers [195,311], Quantum Cascade Lasers [42]) detect trace metabolites and redox states with ultra-sensitivity [196,197].
Toxin	High potency; rapid detection in mixtures [307].	Toxicity prediction [59,218]; symptom correlation via multimodal AI.	Quantum simulations [114,117] resolve toxin binding mechanisms and enable sorting in complex mixtures.	Quantum biosensors [65,66,211], and quantum microfluidics [17] enable rapid screening and sorting of toxins. [327,328]; Quantum Mass Spectrometry [196,197].
Cell & Organelle	Heterogeneity; system-level modeling; imaging complexity [307].	Image analysis; signaling network mapping [18,134].	Quantum simulations build digital twins of cells and model electron transport across organelles [17,166,329].	Quantum dots and microscopy enable organelle imaging [65,66,211]; hyperpolarized MRI/NMR and magnetometry map metabolic flux [209,210].

Table 7. *Cont.*

Biomarker	Challenges	Classical AI Layer	Quantum AI Layer	Quantum Physical Layer
Biological Factor	Broad category (hormones, cytokines, microbiome); feedback loops [307].	Predict downstream effects; correlate with disease [18,134].	Quantum computing models nonlinear feedback loops and high-dimensional biological networks [317].	Quantum-enhanced sensors and interferometry detect hormones, cytokines, and microbial metabolites [17].
Digital Biomarkers	Noise, artifacts, variability; linking signals to clinical outcomes [307].	Signal processing; predictive modeling from wearables/apps.	Quantum ML [17,166,329] improves pattern recognition in noisy wearable data; classical ML struggles with real-time inference.	Quantum sensors in wearables; quantum encryption for secure data transmission; quantum accelerometers and magnetometers for physiological signal fidelity [17].

These modalities act not only as delivery mechanisms but also as strategic constraints that shape the scope and direction of drug development. AI plays a central role in optimizing these strategies by predicting the most suitable targets for a given modality, enabling more efficient platform deployment and reducing attrition rates. In addition, AI supports proteochemometric modeling, which integrates information about a molecule's structure with its biological activity, and generative design approaches that simultaneously evaluate ligand-target interactions [125,126,168,230]. These methods accelerate the identification of novel molecular entities and expand the therapeutic potential of underexplored target classes. Quantum computing complements these efforts by simulating complex folding patterns, degradation pathways and molecular reactivity under diverse cellular conditions [181,182], which is critical for ensuring stability and efficacy in vivo. Crucially, quantum-enhanced algorithms enable precise modeling of pharmacokinetics and drug-receptor binding affinities [182], particularly for biologics, such as monoclonal antibodies and cytokines [330], as well as cell-based therapies such as engineered T cells [331,332], where classical simulations often fall short. Equally, nucleic-acid therapeutics (ASOs, siRNA, mRNA) impose unique delivery and tissue-PK constraints that AI now optimizes, with FDA guidance underscoring their maturity.

6.2. Molecule Synthesis and Retrosynthesis

Synthesis of complex drug molecules, ranging from small molecules to synthetic peptides and biologics, remains a central challenge in pharmaceutical development. The drug discovery process typically begins with target protein identification and involves optimizing millions of initial compounds, screened from a vast chemical space library containing approximately 10^{60} potential molecules [333]. The process often spans several years during hit-to-lead and lead-optimization programs.

- Advancing Retrosynthesis with AI and Quantum Computing

AI has transformed retrosynthetic prediction through deep learning, graph neural networks [334,335], and reinforcement learning [336], enabling automated reaction planning, optimal route selection, and generation of novel molecules with desired pharmacological profiles [221,337,338]. These models learn from extensive reaction databases [339], moving beyond rule-based systems to propose efficient, scalable, and sometimes unconventional synthesis pathways [113], while accounting for thermodynamic and kinetic feasibility. Importantly, recent frameworks address scalability by leveraging distributed architectures and cloud-based platforms to handle large compound libraries and industrial-scale synthesis

planning. Integration with cheminformatics tools and robotic lab systems further bridges computational predictions with automated experimental workflows, accelerating translation from in silico to bench. Quantum computing complements AI by modeling reaction energetics and transition states with high precision [340], capturing subtle electronic effects and non-classical tunneling behaviors that classical models often miss [79,267]. (See Table 8 for examples of therapeutic molecule challenges and AI/quantum solutions).

Table 8. Therapeutic Molecule Challenges and Solutions.

Molecule Type	Challenges	Classical AI Layer	Quantum AI Layer	Quantum Physical Layer
RNA-Based Therapeutics (Antisense, siRNA, miRNA, mRNA)	Degradation; off-target binding; intracellular delivery.	Predictive modeling for degradation/off targets; generative AI for sequence/mRNA vaccine design.	Quantum simulation of RNA folding and hybridization; quantum annealing for guide optimization [17,341].	SQUID [47] or NV center-based electric field sensing [41,316] enable degradation profiling and RNA folding analysis; quantum dots [65,66] support intracellular tracking and Quantum Mass Spectrometry [196,197].
Antibody-Based Therapeutics (Monoclonal, ADCs)	Immunogenicity; binding specificity; payload delivery; manufacturing.	Generative AI for low-immunogenicity design; predictive analytics for affinity and conjugation [117,213].	Quantum chemistry models binding energy and simulates mutation and linker behavior in antibody-drug conjugates [114,245].	Quantum-enhanced plasmonic spectroscopy, including Surface Plasmon Resonance [237,310], biosensing improve binding kinetics and specificity; NV centers could detect conformational changes [17,41,311].
Small Molecule Therapeutics (includes PROTACs)	ADMET prediction [59,218]; polymorphism; synthesis; targeted degradation.	Generative AI for ADMET and PROT40AC design; GNNs for interaction modeling [59,218].	Quantum simulation of metabolism, polymorph prediction, and degrader dynamics [245].	Quantum Cascade Lasers [42] and quantum-enhanced NMR [45,67] enable vibrational fingerprinting and purity analysis; quantum hydration mapping supports ligand binding.
Synthetic Peptides	Rapid degradation; folding complexity; delivery.	Deep learning for 3D structure (e.g., AlphaFold); predictive AI for stability [122–124].	Quantum simulation of folding and peptide-membrane interactions [245,342].	Quantum-enhanced microscopy and quantum dot sensors [65,66] visualize folding and track degradation; single-photon detection reveals conformational states.

Table 8. *Cont.*

Molecule Type	Challenges	Classical AI Layer	Quantum AI Layer	Quantum Physical Layer
Polysaccharides	Branching complexity; immunogenicity.	Predictive analytics for immune response; generative AI for novel structures.	Quantum simulation of branching and delivery optimization.	Raman spectroscopies analyze branching and immune profiles, NV centers map charge distribution. Quantum Mass Spectrometry [196,197].
Vaccines (including mRNA)	Immunogenicity; degradation; targeted delivery.	Generative AI for mRNA/epitope design; deep learning for immunogenicity.	Quantum simulation of vaccine-receptor interactions; adjuvant design [343].	Quantum dot [65,66] tracking and NV center-based sensing monitor payload distribution and immune activation; quantum-enhanced cytokine assays improve profiling [17].
Cell Therapy	Batch variability; targeting; patient-specific efficacy.	Multimodal AI for response prediction [134,344]; image analysis for QC.	Quantum digital twins [345] simulate cell behavior and optimize manufacturing.	Quantum microscopy and sensors monitor cell tracking and metabolic states; molecular quantum sensors assess membrane protein dynamics [17].
Gene Therapy and Editing (CRISPR, TALENs)	Off-target integration; vector safety; immunogenicity.	Predictive AI for vector design; deep learning for off-target prediction.	Quantum annealing [17] for CRISPR guide optimization; simulation of editing mechanics.	Quantum-enhanced microscopy (e.g., NV centers and Quantum dot) detects gene expression and vector delivery [17].
Fusion/Recombinant Proteins	Folding accuracy; aggregation; immunogenicity.	Deep learning for structure; predictive analytics for aggregation [59,124].	Quantum simulation of folding and aggregation; quantum chemistry for binding energy [114,245].	NV centers [41,316] and quantum fluorescence probe [65,66] assess folding states. Quantum Mass Spectrometry [196,197] detects aggregation.
Allergenics	Allergen identification; desensitization; batch consistency.	Predictive AI for epitope identification; multimodal AI for patient correlation.	Quantum simulation of allergen-receptor interactions and mixture modeling.	Quantum-enhanced assays [346] and Quantum-enhanced NMR [45,67] ensure batch consistency; biosensors detect hypersensitivity responses.

Table 8. *Cont.*

Molecule Type	Challenges	Classical AI Layer	Quantum AI Layer	Quantum Physical Layer
Biologics (proteins, antibodies, enzymes)	Structural complexity; stability; immunogenicity; scalability.	Generative AI for novel biologics; predictive analytics for stability or sequence [17,59,213].	Quantum simulation [114,213,245] of folding, catalysis, and manufacturing optimization.	Quantum mass spectrometry and molecular sensors assess purity and stability; Quantum Cascade Lasers [42] and NV centers [41,316] and Quantum Dots [81,315]; monitor enzymatic activity and conformational dynamics.

This synergy reduces false positives, predicts off-target effects, and shortens R&D cycles. For example, hybrid quantum-classical pipelines recovered key molecular properties for covalent drug interactions in the KRAS–Sotorasib scenario, completing quantum kernel calculations in under a minute compared to hours with classical methods [167]. Quantum machine learning enhances retrosynthesis by integrating quantum-derived features into hybrid AI models, improving accuracy and guiding synthesis decisions. In de novo ligand generation, algorithms such as the Quantum Approximate Optimization Algorithm [347] efficiently explore conformational space, while quantum generative models evaluate multiple configurations simultaneously. To ensure reliability, modern systems incorporate uncertainty quantification and interpretability layers, enabling chemists to assess confidence in predictions and understand underlying decision logic. Computational outputs are iteratively validated through experimental synthesis and in vitro/in vivo assays, refining models and ensuring chemical feasibility and biological activity.

- The Computational Challenges for Accurate Molecular Prediction

To achieve high accuracy in binding strength (within 1.0 kcal mol^{-1} of experimental results) is critical, as a deviation of just 1.5 kcal mol^{-1} at physiological temperatures results in a dose estimation error of one order of magnitude [114,220,348]. Quantum simulations offer <0.5 kcal mol^{-1} precision for polymorph free-energy differences [349,350], which is critical for ensuring drug stability and avoiding batch failures. This is a significant improvement over most classical approaches, where the typical mean absolute error is on the order of 1 to 2 kcal mol^{-1}, often failing to reach sub-chemical accuracy. The pursuit of sub-chemical accuracy necessitates careful consideration of the computational error budget when achieving targets below 1.0 kcal·mol^{-1} in complex systems, which typically requires trade-offs involving computationally expensive, high-level basis sets (e.g., Triple-Zeta quality such as cc-pVTZ or def2-TZVP) [351,352], implicit solvent models (e.g., COSMO or PCM) over explicit solvation [353] and constrained molecular sampling lengths (often <1 ns) to maintain feasibility [182,354]. Using quantum mechanical methods such as Density Functional Theory (DFT) [222,295] or higher-accuracy coupled-cluster techniques [222,295,296] increases computational cost dramatically, restricting full free-energy calculations to small systems [355,356], since cost grows exponentially with system size (often O(N7), where N is the number of atoms). While these methods approach experimental accuracy, their practical application is limited, which motivates the development of alternative approaches such as machine learning corrections. Recent developments in machine learning, such as Δ-learning approaches that correct DFT-calculated energies

toward coupled-cluster accuracy [222,357,358], offer promising solutions for achieving sub-chemical accuracy in gas-phase simulations, though they still require careful validation and integration with physics-based models to ensure reliability across diverse pharmaceutical targets [225,298,299].

- Applicability to High-Accuracy Methods

Currently, these approaches offer good accuracy for most relevant systems but remain too slow for widespread application in drug development. This is primarily because most oral drugs are small closed-shell organic molecules that need to pass through the gut wall to be absorbed [160]. Such molecules generally lack strong correlation and can be treated with lower-accuracy methods due to their general elemental compositions. However, there are a few examples of drug molecules with metal centers [359] that could show some strong correlation in their electronic structure, for example, drugs developed for cancer treatments or contrast-enhanced imaging of tissues. An open question is whether the scarcity of potentially strongly correlated, metal-bearing drugs reflects intrinsic chemical limitations or results from challenges in computational optimization that quantum computers could help overcome.

- Advanced Synthesis and Optimization

In practice, a biochemist attempting to synthesize a complex chiral molecule, one with non-superimposable mirror-image forms, where only one is biologically active, may produce a non-functional mirror image (Table 6). A quantum-enhanced retrosynthesis system can model the transition state of a key stereoselective step with sufficient precision that it predicts the exact conditions, including pressure and catalyst geometry, required to achieve near-perfect enantioselectivity (preferential production of the biologically active mirror image) [215,360], saving months of experimental trial-and-error. Alchemical perturbation methods provide a faster approach when screening many structurally similar compounds, as they directly compute differences in binding affinity by gradually morphing a known compound into a new one [361,362]. Quantum electronic-structure calculations further guide synthesis by providing a quantum-level understanding of reaction conditions and calculating molecular spectra (NMR, IR, or VCD) for precise structural identification [156,157].

6.3. Formulation and Stability

AI-driven predictive modeling has become foundational in pharmaceutical formulation [225], using machine learning and deep learning algorithms [58,121] to forecast drug degradation, optimize excipient combinations and predict shelf-life under varying environmental conditions. These models analyze extensive preclinical datasets to identify patterns in drug-excipient interactions, enabling the design of formulations that enhance solubility, stability and bioavailability while reducing experimental workload and development costs. Quantum computing complements these capabilities by providing detailed insights into reaction energetics and molecular behavior [181,182], particularly in polymorph prediction, predicting different crystal structures of a drug molecule where subtle free energy differences and crystallization dynamics critically influence drug performance (Table 6). In addition, quantum electrodynamics is increasingly applied in drug delivery systems [211,363], enabling light-activated carriers, fluorescence imaging and photonic control using quantum dots and entangled light sources for spatiotemporal drug release [17]. Quantum-enhanced NMR [45,67] and mass spectrometry [47,196,197], particularly using diamond-based NV centers and SQUID detectors, allow ultra-sensitive detection of molecular changes, supporting trace-level quality assurance and dynamic monitoring of drug stability [45,67]. For example, a biochemist developing a monoclonal antibody may face protein aggregation, a major cause of failure during manufacturing (Supplementary Table S2).

Classical methods can measure aggregation [364] but often struggle to predict it. Quantum simulations model subtle changes in the protein's electron cloud and the weak intermolecular forces [290,365,366] that initiate aggregation, providing high-resolution data. AI can then identify the exact excipient molecules that stabilize the protein and prevent aggregation, producing a more robust and effective formulation from the outset.

7. Feedback Loops: From Broken Pipelines to a Learning System

The most profound shift in modern drug development is the move from a linear, fragmented pipeline to a living, learning system. This shift represents the underlying "why" that makes other technical advances matter [367]. In the traditional model, candidates march from discovery to preclinical to clinical [368]. A Phase II failure typically returns only low resolution, hard-to-interpret signals, such as an unexpected off-target effect, an unforeseen toxicity. This lack of actionable data offers no clear redesign path and forces teams to start over by creating an expensive, time-wasting dead end. The emerging paradigm replaces this "shoot and forget" sequence with an intelligent, self-correcting loop in which each stage informs the next with AI anchoring discovery by learning from extensive datasets of prior clinical failures and real-world evidence to propose molecules explicitly designed to avoid known pitfalls (hypotheses grounded in multimodal chemical, biological, and clinical information [369,370], not speculative guesses). Before wet-lab work, candidates could pass through quantum-validated simulations that could model interactions with targets and off-targets at high resolution [163]. Predictive modeling act as a virtual filter, removing consistently over 90% of suboptimal candidates efficiently, and in some case studies, exceeding 99.9%, narrowing over a million molecules to just a few for targets like KRAS and SARS-CoV-2 [167,371], dramatically accelerating discovery before costly physical experimentation [372,373]. Those that pass may be synthesized in automated labs [129,130,374], where quantum sensors [17,46] stream real-time data on purity, yield, and structural fidelity, while an AI agent continuously monitors for issues such as unwanted isomers or incorrect stereochemistry, triggering immediate corrections [127,128]. If a molecule ultimately fails in the clinic, the system converts that outcome into structured, high-resolution learning, comprising patient biomarkers, pharmacodynamics, and therapeutic responses, which flow back to retrain the AI and refine the next generation of quantum simulations [16], steadily improving predictive power. In turning failures into high-value data points and wiring discovery, validation and execution into a seamless feedback loop [214], the pipeline evolves intoa dynamic ecosystem of continuous improvement.

8. Functional Landscape

8.1. Emerging AI Contributions

In the realm of discovery and mechanistic understanding, biotech and pharmaceutical companies are increasingly deploying AI platforms that integrate multimodal biological data to automate hypothesis generation, accelerate target identification and optimize experimental design. Leading examples include Exscientia, which applies patient-centric AI design [375] by combining viable patient tissue data with generative algorithms and robotic automation to enhance drug discovery; Recursion Pharmaceuticals [376], which leverages high-dimensional cellular imaging and vast proprietary datasets to train machine learning models that uncover novel drug candidates; and Insilico Medicine, whose generative AI platform has successfully designed de novo molecules, including INS018_055 (the first AI-discovered and AI-designed drug to enter Phase II clinical trials for idiopathic pulmonary fibrosis) [125,126,168,230]. Advances in protein structure prediction, such as those enabled by AlphaFold [122–124] for global protein folds, are now being combined with AI-driven lead optimization, while specialized peptide-design companies are pushing

the boundaries of molecular design. Peptide-focused firms such as Peptone [377], which uses AI and experimental physics to model intrinsically disordered proteins that AlphaFold cannot predict; and Pepticom [248], which applies reinforcement learning and generative AI to explore vast peptide chemical spaces and design novel oral IL-17 inhibitors for psoriasis, are advancing scaffold design with optimized ADMET properties [59,120,218]. In molecular design and lead optimization, companies like XtalPi, Pfizer, and Schrödinger integrate physics-informed and quantum-inspired algorithms for predicting crystal structures and polymorph stability, dramatically reducing timelines for solid-state screening [226]. Laboratory automation and workflow transformation are being driven by platforms like Arctoris [378], Synthace [62], and Emerald Cloud Lab [379], which combine robotics, cloud orchestration and AI to scale experimental throughput and reproducibility. Disease modeling and genetic design are also advancing, with NovoHeart offering bioengineered human mini-heart models for realistic cardiac screening and drug testing [380], and Desktop Genetics providing AI-powered CRISPR library design tools for precision genetic engineering [381]. However, despite these innovations across discovery and clinical operations, formulation and delivery remain comparatively underexplored, with XtalPi among the few applying AI to polymorph behavior and shelf-life prediction [226], highlighting a critical opportunity for AI-driven formulation science. At the clinical and operational level, large pharmaceutical companies such as Janssen [382] and AstraZeneca [383] are piloting AI platforms for trial optimization, patient matching and real-world evidence integration, potentially increasing recruitment efficiency and reducing time-to-insight.

8.2. Emerging Quantum Contributions

- Quantum Computing landscape

Quantum computing and quantum-enhanced methods are increasingly applied across several pharmaceutical problem classes. Specialized vendors and research institutions are developing hybrid quantum-classical algorithms for targeted tasks such as quantum-assisted generative design, small-region electronic structure calculations, and sampling for hard optimization problems. For example, D-Wave's quantum annealing systems have been used in drug discovery collaborations with companies like Japan Tobacco and Menten AI, demonstrating improved performance in generating valid, drug-like molecules compared to classical methods [384]. The Cleveland Clinic and IBM have jointly developed a quantum-classical framework for protein structure prediction, successfully modeling the folding of Zika virus protein fragments using quantum algorithms that outperformed classical approaches [385]. IBM has also demonstrated quantum workflows for protein–ligand problems (e.g., docking-site identification and hybrid QML modules) using superconducting quantum devices [40]. Startups such as Qubit Pharmaceuticals [386] are applying quantum-informed models to predict toxicity and simulate molecular behavior with high precision, while aiDA Technologies use transcriptomic data and machine-optimized algorithms to personalize cancer therapies, particularly in oncology. Emerging quantum hardware platforms, such as Gaussian boson sampling devices like Abacus, are being investigated for niche applications in molecular docking (e.g., PARP-CQ and TACE-TS) and RNA-folding prediction using graph-based quantum sampling techniques [71].While these advances are promising, it is crucial to maintain an objective perspective regarding vendor claims of quantum advantage; increasingly, algorithmic dequantization and the optimization of classical baselines have shown that the purported performance gaps can be narrowed or even closed, necessitating rigorous comparative testing to validate true quantum superiority.

- Quantum Sensing and Quantum Control Landscape

On the sensing and experimental front, quantum technologies like nitrogen-vacancy (NV) diamond sensors and quantum dots are being investigated for ultra-sensitive biochemical assays, biodistribution monitoring, and precision control in synthesis. Companies such as Quantum Diamond Technologies Inc. (QDTI) and Sumitomo Electric Industries are developing NV-diamond-based biosensors for applications ranging from magnetocardiography to cytosensing because they leverage their high spin coherence and biocompatibility. Quantum dots, with their tunable optical properties and long fluorescence lifetimes, are being used in pharmaceutical analysis and drug delivery systems by companies like Thermo Fisher Scientific and Sigma-Aldrich, enabling real-time tracking and targeted biodistribution. Complementing these computational and sensing advances, quantum control techniques are being developed to enhance biochemical reaction selectivity. Research groups such as Johns Hopkins Institute for NanoBioTechnology are engineering quantum-enabled dial proteins (QEDs) that use spin-correlated radical pairs to actuate biological functions, demonstrating programmable control over enzymatic reactions using magnetosensitive quantum effects. However, quantum control is nascent but critical [17,48], requiring substantial research to enable clinical applications such as targeted therapy and programmable biochemical modulation.

- Emerging Hybrid Quantum-AI Clinical Trials

Meanwhile, the clinical trial landscape for quantum healthcare remains nascent but expanding. Institutions like Cleveland Clinic, in collaboration with IBM, are conducting pilot studies that combine quantum computing and AI to optimize diagnostics and therapeutic strategies in oncology, including early lung cancer detection and antibiotic resistance prediction. Similar efforts are being pursued by startups such as Algorithmiq, which is developing quantum algorithms for photon-drug interactions; Picture Health, which applies quantum-enhanced AI to histopathology; and Qradle, which builds quantum software for drug discovery. Between 2021 and 2024, approximately 27% of quantum-related trials incorporated AI, reflecting a growing trend toward personalized medicine and enhanced diagnostics. AI-quantum convergence blurs traditional boundaries, enabling hybrid ecosystems for drug discovery and clinical innovation.

8.3. Hybrid Quantum–AI Ecosystems

The emerging hybrid quantum–AI ecosystem rests on a core principle, which leverages high-fidelity, quantum-derived data to ground AI models, thereby directly addressing the "black box" opacity of deep learning [387]. This principle aligns with regulatory requirements, as agencies such as the FDA require mechanistic transparency before committing resources to costly synthesis and clinical trials; quantum-derived interpretability is a crucial enabler of scientific trust and regulatory approval. Importantly, the first impactful applications of fault tolerant (error-corrected) quantum computers are expected not in purely AI-driven predictions, but in chemical calculations where quantum methods produce interpretable molecular and mechanistic data that train AI systems. In turn, AI optimizes the control of complex quantum workflows [388], creating a feedback loop that improves patient stratification and supports regulatory-grade evidence [144]. Consequently, this synergy enables emerging simulation frameworks for biological systems that inform adaptive trial design and regulatory decision-making. Fully quantum simulations of large systems remain computationally prohibitive [24]. To overcome this limitation, hybrid architectures integrate Quantum Mechanics/Molecular Mechanics (QM/MM) approaches [29,87], with the classical MM portion often enhanced by AI. Reactive regions are treated quantum-mechanically while surrounding environments remain classical, with AI orchestrating simulation parameters, interpreting outputs, and managing large-scale data integration.

Additionally, Ab initio methods such as Density Functional Theory (DFT) and coupled-cluster techniques [222,295,296] already deliver near-quantum accuracy at classical speeds, providing tractable inputs for complex drug discovery problems, including kinase–inhibitor binding and enzyme–substrate kinetics. Furthermore, distributed quantum computing enables collaborative simulations while preserving confidentiality [389]. Secure protocols [227,390] (including quantum-secure key exchange and federated learning with local quantum processors) allow sensitive datasets to be processed in place before aggregated insights are combined. Finally, modern chemical language models and quantum-enhanced embeddings complement these secure architectures by strengthening predictions of binding affinities and accelerate lead optimization, forming the foundation of emerging functional ecosystems in pharmaceuticals.

8.4. The Hybrid Future Quantum-AI Convergence in Pharmaceuticals

Looking ahead, integrated quantum–AI ecosystems are expected to define the future platform for pharmaceutical innovation. Fusing quantum-derived measurements and simulations with advanced AI is anticipated to enable quantum digital twins [212,213]. These computational representations can simulate molecular and physiological behavior in quasi-real time to support personalized therapies and adaptive manufacturing. In the near term, Agentic AI, autonomous, goal-directed systems, will orchestrate complex R&D workflows [92–94], dynamically adapting experiment design, resource allocation and screening strategies in response to streaming data. Coupled with quantum-enhanced subroutines [92,329], these systems will compress cycle times and enable more adaptive precision-medicine interventions. Over the medium term, the potential development of Artificial General Intelligence (AGI) [76,212] could potentially achieve a cross-scale understanding of biological systems, design integrative experiments, and predict emergent phenomena such as multi-factorial resistance or lifestyle–drug synergies. Quantum computing might also augment AGI by providing probabilistic reasoning frameworks and novel physical insights from quantum datasets [391], theoretically opening pathways to programmable biology (synthetic circuits and gene therapies with quantum-controlled dynamics). In the long term, and in a highly speculative scenario, the prospect of superintelligent AI, if successfully realized and combined with mature quantum technologies, is projected to potentially reshape molecular architectures, therapeutic microenvironments and potentially manipulate quantum biological states. [75,135]. These possibilities raise profound ethical, alignment, and governance challenges that must be addressed alongside technical advances.

9. Operationalizing and Governing Pharmaceutical Innovation

9.1. Operational Complexities and Adoption Hurdles

- Infrastructure, Financial, and Logistical Hurdles

Operationalizing decentralized networks requires more than theoretical predictions; it demands rigorous wet-lab validation and a continuous feedback loop. Socio-economic adoption is challenging, as these models require local technical capacity and sustainable maintenance infrastructure, often scarce in low-resource contexts [392–394]. Major obstacles include the absence of clean, structured data and the foundational infrastructure required to train sophisticated AI models, even when hardware is low-cost. Ongoing maintenance, repair and replacement supply chains present massive logistical challenges, particularly in remote or geopolitically complex regions. The technical complexity of preparing initial quantum states, managing Hilbert space scaling, and implementing hybrid quantum–AI algorithms adds operational burdens [73,395,396]. Beyond logistics, a shift to an AI/quantum-driven process requires immense investment in software, data

infrastructure and interdisciplinary workforce training [397]. Utility-scale quantum computers require dedicated rooms with controlled cryogenic environments and specialized shielding, often costing tens of millions of dollars [398]. Even theoretically deployable systems face algorithmic and hardware constraints, translating into financial and logistical barriers. Finally, AI systems face persistent challenges [399], including the need for high-quality, harmonized datasets, limited interpretability, and generalizability across novel biological contexts. Even with these technologies, drug costs are often driven more by failed optimization programs and clinical trials than synthesis; lower-accuracy methods such as DFT [222,295] can predict NMR spectra adequately, highlighting the need to balance computational cost and practical accuracy [2].

- Human Capital and Procedural Challenges

A steep learning curve is another barrier; quantum-enhanced sensors may produce entirely new forms of data (e.g., single-spin state changes) [37,400] requiring extensive interdisciplinary training. This presents challenges for a "sovereign kit" vision, as advanced technologies require specialized expertise in computational biology, quantum physics and data science, which is difficult to develop and retain in under-resourced settings. Automation cannot fully replace human expertise [401]; skilled local chemists remain indispensable for troubleshooting failed syntheses, interpreting ambiguous assay results, and providing the tacit knowledge needed for synthetic route optimization. Some validation steps are inherently non-decentralizable and require the physical co-location of specialized equipment such as NMR or mass spectrometry [63,402]. Even with advanced AI, nascent quantum technologies (still constrained by near-term hardware fragility and error-correction limitations) and robotics, human expertise remains essential. To be sure, machines can replicate technical tasks using sensor fusion for wet-lab judgment, multimodal models for biological variability and generative AI for creative design [125,126,168,230]; however, their capabilities are bounded by both technical and social limits. Compounding these barriers, the lack of standardized protocols and user-friendly interfaces further complicates adoption, often requiring quantum specialists to code experiments manually. The process still relies heavily on human "scientific taste" for anomaly triage and tacit knowledge (key components of serendipity and improvisation) [403,404]. To mitigate these challenges, hybrid quantum-classical systems and cloud-based quantum access offer practical near-term solutions, while strategic investment in infrastructure, workforce development, and cross-sector partnerships will be critical for safe, effective and equitable integration of these technologies.

9.2. Socioethical, Regulatory, and Commercial Dynamics

- Ethical and Regulatory Challenges

Beyond operational hurdle, the rapid advancement of AI and quantum technologies introduces a complex array of ethical and regulatory challenges, including implications for drug pricing as R&D becomes faster and more efficient. To begin with, a central concern is AI interpretability, as "black box" deep learning models hinder trust and complicate both regulatory validation and clinical accountability [387]. Equally important, data governance presents major obstacles, since patient-derived datasets and proprietary chemical libraries raise questions of ownership, licensing and reproducibility [132,228,405,406] especially in cross-border collaborations where laws such as GDPR and HIPAA may conflict. In parallel, the urgent need for quantum-safe cryptography to protect sensitive biomedical data represents a major threat that current infrastructures are ill-prepared to address. Although regulatory bodies such as the FDA and EMA are beginning to respond to these challenges, their frameworks remain largely reactive and fragmented, with guidance documents often lacking specificity for quantum-involved pipelines. Beyond regulatory gaps, the deploy-

ment of quantum technologies introduces novel ethical concerns, including the potential to redefine biological identity through quantum-level interventions, implications for informed consent in quantum-enhanced diagnostics and the speculative creation of highly theoretical quantum-modulated psychoactive compounds that may alter consciousness [17,79] at a fundamental neurochemical level. Furthermore, highly autonomous AI systems and the prospective development of AGI raise profound accountability and biosecurity risks, from proposing molecules with unknown systemic effects to designing novel pathogens [17]. If access remains restricted, such advances could also exacerbate existing health inequalities. Therefore, governance frameworks must address not only safety and efficacy but also equity, transparency and long-term societal impact, through horizon-scanning, public oversight, ethical audits and human-in-the-loop safeguards to ensure alignment with clinical values and public trust.

- Commercialization Dynamics and Ethical Governance

The role of commercialization is pivotal in shaping pharmaceutical innovation, often prioritizing early-stage platforms that promise rapid intellectual property (IP) generation while underfunding critical but less IP-attractive areas, such as polymorph stability prediction or formulation science [407]. In addition, funding structures and geographic clustering strongly influence company maturity and risk tolerance, thereby constraining what is developed and ultimately transferred into practice. Beyond funding structures, decentralized computing and AI models that rely on data from regions facing political and economic inequities raise pressing concerns about power asymmetries, data sovereignty, algorithmic bias and equitable access [408,409]. Open-source initiatives can counterbalance proprietary systems to improve equity. Another central issue is the accountability of machines versus humans, since machines cannot assume legal or moral liability or build the rapport and trust with patients and the public that are essential for societal acceptance. This underscores an irreducible gap between a model's prediction of a subjective state and the first-person experience of it [410,411], thereby preserving the need for human empathy and highlighting fundamental limits in both technical capability and social legitimacy. Moreover, the dual-use potential of quantum technologies, in both therapeutic and biosecurity contexts, demands anticipatory governance and global coordination. This will require institutional frameworks that integrate ethical risk scoring, regulatory sandboxes, and public advisory boards. Similarly, the commercialization of quantum-enhanced therapeutics, including drugs that operate at sub-cellular levels, promote human enhancement; or even target consciousness recovery in extreme, future scenarios, raises profound ethical questions about human autonomy [412,413]. Taken together, these considerations points toward a powerful synergy where humans provide strategic direction and conceptual oversight, while machines contribute speed and analytical power, ensuring that technological progress serves public health equitably and transparently.

9.3. Decentralizing and Democratizing Innovation for Global Health

- The Foundational Data Sovereignty Kit

At the core of this strategic model is a modular, scalable approach to sovereign drug discovery. This model begins with the deployment of a low-cost, foundational Sovereign Data Kit at each local research site. This kit, built from cost-effective, off-the-shelf components and open-source software [414–416], is designed to integrate with existing low-resource capabilities rather than impose new infrastructure costs. Equipped with frugal, open-source hardware (e.g., 3D-printed microscopes and simple electrochemical biosensors) and AI agents, the kit autonomously monitors experiments, predicts outcomes, and optimizes protocols [417,418]. As a result, a newly established sovereign hub can function independently even under intermittent connectivity, thereby securing data sovereignty for the entire

region. The system's first and most critical function is to provide a secure environment for on-device consent management and data tokenization, protecting patient privacy at the source. In doing so, it ensures that data are captured and safeguarded with a verifiable audit trail. This kit serves as the entry point to a broader federated infrastructure, enabling participation without requiring full-scale infrastructure upfront (see Figure 4).

- Building a Distributed Network

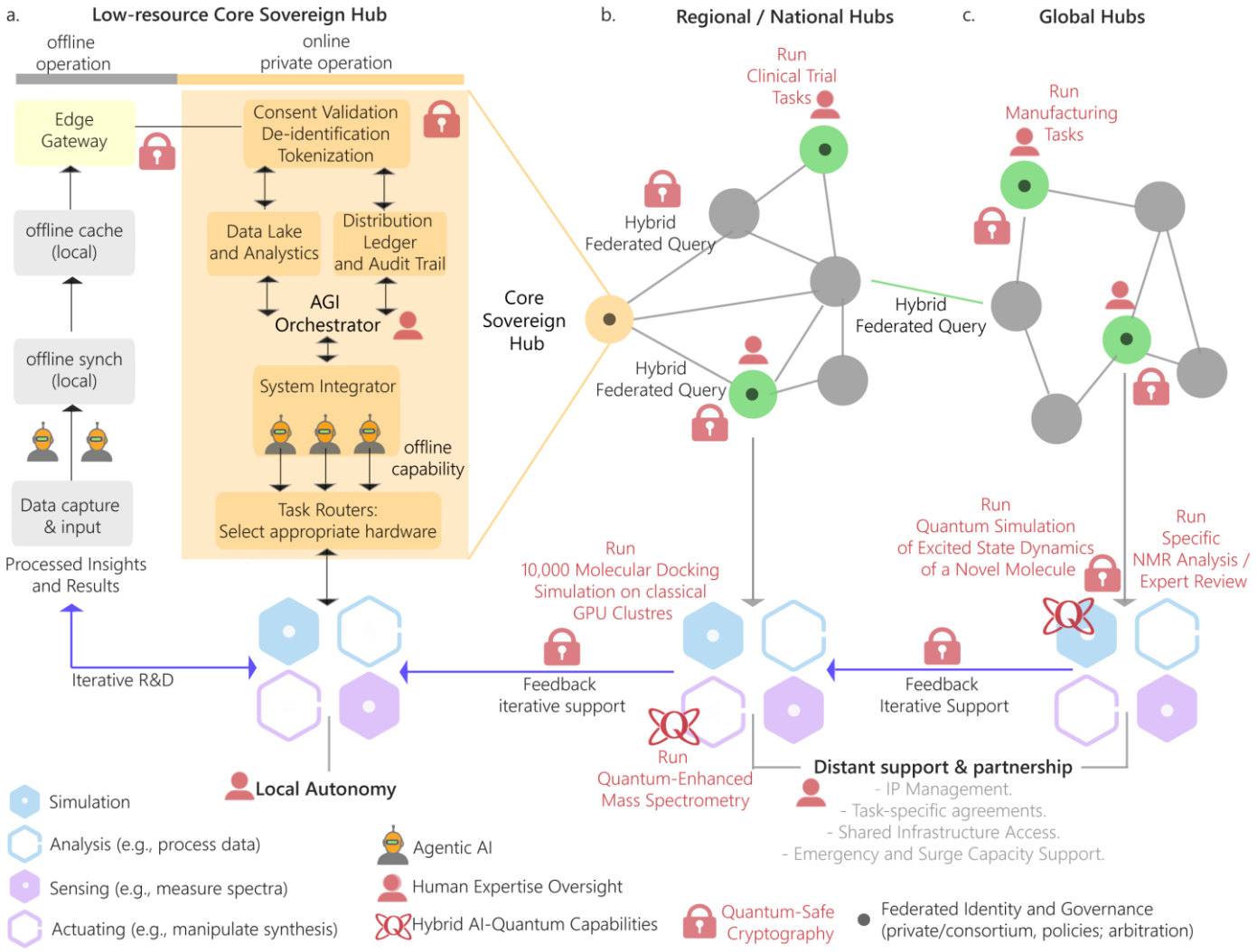


Figure 4. Forward-Looking Federated Artificial Intelligence AI Infrastructure for Sovereign Biomedical Innovation. This schematic illustrates a tiered federated AI system designed to support decentralized drug discovery and development across low-resource, regional, and global contexts. (**a**) Low-Resource Core Sovereign Hub: Built on frugal hardware and open-source tools, this hub operates autonomously with edge gateways, offline caches, and local synchronization. It supports secure data capture, consent management, tokenization, and iterative Research and Development (R&D), enabling full data sovereignty even in intermittent connectivity environments. (**b**) Regional/National Hubs: Facilitate hybrid federated queries for tasks such as clinical trials, while preserving local control over sensitive data. (**c**) Global Hubs: Handle large-scale simulations and manufacturing tasks, including quantum-enhanced mass spectrometry and molecular docking. The infrastructure supports quantum-safe cryptography, federated identity and governance, and external partnerships for advanced capabilities such as Nuclear Magnetic Resonance (NMR) and High-Performance Computing (HPC). Multi-agent AI systems coordinate tasks under strict human-in-the-loop oversight, ensuring accountability and ethical decision-making. Together, the system enables scalable, secure, and equitable participation in global biomedical innovation.

After establishing local data integrity, each sovereign hub functions as a secure gateway to a distributed network of regional and global partners [419]. The initial focus is on establishing regional and national partnerships. This enables the hub to retain full control over its own sensitive data while participating in a broader ecosystem that shares de-identified, tokenized datasets under agreed-upon protocols. For complex tasks such as high-performance computing (HPC) simulations [420], the hub can securely transmit tokenized data to remote labs, which then return the results. In this way, the local site gains the benefits of HPC without the burden of acquiring or maintaining costly infrastructure. These hubs coordinate tasks such as clinical trials, molecular simulations and manufacturing, as illustrated in Figure 4. Crucially, this model also addresses the "garbage in, garbage out" problem through a continuous feedback loop between the hub's physical sensors and AI-generated drug candidates. At the same time, it pragmatically acknowledges that more sophisticated technologies such as NMR or mass spectrometry would be accessed through external partnerships rather than on-site.

- Advanced Integration and Governance

Over time, the system can gradually incorporate more advanced technologies, including phased blockchain implementation to provide a verifiable audit trail for intellectual property and ownership across multiple partners [421]. Coordination is managed by multi-agent AI systems (referred to here as Collective Agentics) within a strict human-in-the-loop governance framework. This framework records all agent actions in a local logbook, which can be used to establish a formal trade-off structure for multi-objective optimization, presenting conflicting evidence to human experts. All agent actions are logged locally, supporting the provenance and arbitration mechanisms depicted in the federated infrastructure. Importantly, this ensures that human sign-off is required on final decisions, preventing the system from "oscillating" between priorities and ensuring that machines cannot assume legal or moral accountability. Taken together, this tiered, pragmatic approach enables low-resource areas to protect their data and build capacity at their own pace, engaging in global partnerships only when they are ready. Figure 4 shows how these components come together in a federated architecture that supports secure, scalable, and equitable biomedical innovation.

While this federated architecture offers a secure and scalable foundation for biomedical innovation, making this vision a reality requires direct confrontation with its significant limitations. The core challenge lies in grounding these technologies in the high-stakes requirements of biopharma, including regulatory compliance, patient safety, and integration with existing clinical and industrial workflows. These technical and institutional hurdles naturally lead into the need for strategic roadmaps and policy solutions, which are discussed in the following section.

10. Strategic Roadmaps and Policy Solutions

10.1. Strategic and Institutional Hurdles

On the economic side, while a token-based incentive model could support the sustainability of on-site research activities, it risks creating perverse incentives unless a strong, on-chain verification mechanism, such as zero-knowledge proofs (ZKP) [422], is in place, making transparent data governance a near-term feasibility requirement. Institutionally, challenges are equally significant. These include interoperability problems when quantum-enhanced diagnostic devices produce data that hospital EHRs cannot read, and regulatory hurdles since agencies such as the FDA have no established guidelines for quantum-simulated drug validation. Addressing these data and regulatory gaps is a critical prerequisite for industry adoption. From a legal perspective, the question of who or what holds the patent for a drug discovered by an AI remains an ongoing debate. Until clear

precedents are set, companies risk losing patents on multi-billion-dollar drugs, which may limit AI-first adoption. Cybersecurity concerns further compound these risks. Protecting sensitive clinical data requires quantum-safe cryptography such as Post-Quantum Cryptography (PQC), blind quantum computing and quantum kernel methods. These platforms also depend on robust support ecosystems, including real-time error correction, hardware redundancy and AI-assisted control systems. Although quantum-safe cryptographic standards are under development, their widespread implementation remains incomplete, creating ongoing vulnerabilities that necessitate immediate PQC deployment.

10.2. Policy Solutions and Roadmaps

To address these hurdles, the success of the model depends on a strategic approach that prioritizes practical feasibility by first proving efficacy in a controlled, modular setting, such as drug repurposing [423], before attempting a full-scale, end-to-end pipeline aligned with established regulatory standards such as Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP) and Good Clinical Practice (GCP) [424]. Beyond technical compliance, ethical AI frameworks, equitable access to quantum resources and mitigation of environmental footprints must be carefully considered. These safeguards will ensure that accelerated R&D translates into affordable, globally accessible treatments. Concrete policy precedents already exist. India's quantum mission, Brazil's genomic equity initiatives and the WHO's push for open genomic data illustrate how national and global policies can connect technological innovation with intellectual property regimes. Similar efforts could include incentives for "public AI chemistry models" and the establishment of global biochemical observatories to harmonize data [425]. Regulatory evolution must provide clear guidelines for data privacy, security and accessibility. Parallel to this, educational programs will be essential to equip healthcare professionals with the skills required to work effectively with quantum-secured systems. Finally, any roadmap must also acknowledge practical challenges such as cost, operational complexity and the environmental footprint of large-scale computation, while outlining pathways to advance quantum control methods and devices.

10.3. Roadmap by Timeline

- Immediate and Near-Term (0–3 years)

AI will become standard for ADMET prediction, generative chemistry, and clinical trial optimization. Early adoption of quantum-accelerated classical simulations will improve binding affinity predictions. At the same time, quantum sensing will be immediately deployed in vitro for high-precision diagnostics and manufacturing quality control. The immediate focus must be on Hybrid Quantum–Classical algorithms (e.g., VQE and QAOA) and Quantum-Enhanced Sensors (e.g., NV-centers) rather than awaiting fully fault-tolerant quantum computers. These near-term intermediate quantum (NISQ) devices offer the most practical value today. Hybrid quantum–classical systems will dominate, accelerating drug discovery with faster molecular models. Key technical challenges during this phase will include maintaining quantum coherence in noisy biological environments and ensuring biocompatibility for in vivo devices.

- Mid-Term (3–7 years)

Broader integration of hybrid AI–quantum workflows are anticipated to emerge, tackling complex problems such as protein aggregation and drug–target interactions. During this stage, more robust quantum algorithms for de novo design may allow creation of entirely new molecular scaffolds. Quantum sensing will expand into early in vivo applications, while quantum digital twins [212,213] are expected to enable patient-specific simulations and predictive manufacturing. Regulatory bodies, therefore, must establish

validation guidelines for both digital twin models and the quantum-enhanced datasets they generate.

- Long-Term (7–10+ years)

Quantum advantage in de novo design and complex simulations is expected to yield novel therapeutic modalities. Widespread deployment of quantum-enhanced diagnostics and real-time therapeutic monitoring are anticipated, culminating in fully autonomous, AI-driven laboratories guided by quantum insights. This will usher in a "simulation-first" paradigm where drugs are iteratively designed and tested virtually before physical synthesis. Looking further ahead, quantum-mechanical calculations (e.g., DFT and coupled-cluster methods [222,295,296]) will benefit most from these speed-ups, enabling applications to highly complex systems. Yet, despite computational progress, physical wet-lab validation will remain the ultimate bottleneck. A hybrid architecture, balancing local autonomy with selective access to centralized facilities, represents the most realistic path for scaling decentralized pharma innovation.

- Grand Outlook Challenge: Energy and Computational Scale

The next frontier in pharmaceutical innovation—particularly quantum-enabled drug discovery at planetary scale—will likely demand unprecedented computational capacity. This trajectory suggests that the most advanced modeling and simulation workloads will remain anchored in centralized, high-performance data centers. However, the energy demands of such systems could extend well beyond traditional R&D considerations, prompting strategic reflection on the supporting infrastructure. Emerging energy technologies, such as small modular reactors (SMRs), offer potentially promising solutions, yet their integration must be carefully evaluated considering longstanding societal, regulatory and technological concerns surrounding nuclear power [426]. Navigating these far-reaching implications will require a coordinated, cross-sectoral effort—uniting pharma, energy and policy stakeholders to ensure sustainable innovation at scale.

11. Conclusions

The pharmaceutical pipeline remains slow, costly and poorly suited to modern, personalized medicine. This review demonstrates that a fundamental transformation is achievable through the convergence of Artificial Intelligence (AI) and quantum technologies, which together create a dynamic, self-learning ecosystem for drug discovery and development. The proposed three-layer framework—Computational (AI and quantum simulation), Physical (quantum sensing and control), and Orchestration (Agentic AI coordination)—integrates molecular modeling, real-time experimentation, and continuous feedback into a unified translational architecture. This system promises faster, safer, and more adaptive therapeutics grounded in molecular-level precision. Successful implementation, however, is a matter of practical feasibility that demands a clear, immediate strategic focus. The most productive near-term research priority must be the adoption of Hybrid Quantum–Classical algorithms (VQE, QAOA) and Quantum-Enhanced Sensors (NV-centers), as these intermediate, available technologies offer the most immediate, realizable value over waiting for fully fault-tolerant quantum computers. Achieving success also requires a concerted effort to overcome non-technical barriers, including establishing clear regulatory guidelines and addressing cybersecurity risks (e.g., PQC deployment) that currently impede industry commitment. Successful implementation will depend on proactive strategies for regulation, cybersecurity, ethical oversight, and equitable access, alongside sustained investment in infrastructure and workforce training. Embracing this integrated model offers both a scientific and strategic advantage—accelerating innovation, enhancing health sovereignty, and addressing the deep structural inefficiencies of today's pharmaceutical model.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/biochem6010002/s1, Table S1: Clinical Development and Patient Care; Table S2: Manufacturing and Supply Chain.

Funding: This research received no external funding.

Data Availability Statement: All the data and information relevant to the review are present within the review itself.

Conflicts of Interest: The author declares no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

VQE	Variational Quantum Eigensolver
QAOA	Quantum Approximate Optimization Algorithm
QITE	Quantum Imaginary Time Evolution
QKD	Quantum Key Distribution
FAIR	Findable, Accessible, Interoperable, and Reusable
FHE	Fully Homomorphic Encryption
NV	Nitrogen-Vacancy
SNSPD	Superconducting Nanowire Single-Photon Detector
QC-MS	Quantum Computing Mass Spectrometry

References

1. Khanna, I. Drug discovery in pharmaceutical industry: Productivity challenges and trends. *Drug Discov. Today* **2012**, *17*, 1088–1102. [CrossRef]
2. Sun, D.; Gao, W.; Hu, H.; Zhou, S. Why 90% of clinical drug development fails and how to improve it? *Acta Pharm. Sin. B* **2022**, *12*, 3049–3062. [CrossRef]
3. Villoutreix, B.O. Post-Pandemic Drug Discovery and Development: Facing Present and Future Challenges. *Front. Drug Discov.* **2021**, *1*, 728469. [CrossRef]
4. Ioannidis, J.P.A.; Bossuyt, P.M.M. Waste, leaks, and failures in the biomarker pipeline. *Clin. Chem.* **2017**, *63*, 963–972. [CrossRef] [PubMed]
5. Hassan Baig, M.; Ahmad, K.; Roy, S.; Ashraf, J.M.; Adil, M.; Siddiqui, M.H.; Khan, S.; Kamal, M.A.; Provazník, I.; Choi, I. Computer Aided Drug Design: Success and Limitations. *Curr. Pharm. Des.* **2016**, *22*, 572–581. [CrossRef]
6. von Korff, M.; Sander, T. Limits of Prediction for Machine Learning in Drug Discovery. *Front. Pharmacol.* **2022**, *13*, 832120. [CrossRef]
7. Simoens, S.; Huys, I. R&D Costs of New Medicines: A Landscape Analysis. *Front. Med.* **2021**, *8*, 760762. [CrossRef] [PubMed]
8. Kalepu, S.; Nekkanti, V. Insoluble drug delivery strategies: Review of recent advances and business prospects. *Acta Pharm. Sin. B* **2015**, *5*, 442–453. [CrossRef]
9. Censi, R.; Di Martino, P. Polymorph impact on the bioavailability and stability of poorly soluble drugs. *Molecules* **2015**, *20*, 18759–18776. [CrossRef] [PubMed]
10. Rahban, M.; Ahmad, F.; Piatyszek, M.A.; Haertlé, T.; Saso, L.; Saboury, A.A. Stabilization challenges and aggregation in protein-based therapeutics in the pharmaceutical industry. *RSC Adv.* **2023**, *13*, 35947–35963. [CrossRef] [PubMed]
11. Pushkaran, A.C.; Arabi, A.A. From understanding diseases to drug design: Can artificial intelligence bridge the gap? *Artif. Intell. Rev.* **2024**, *57*, 86. [CrossRef]
12. Paul, D.; Sanap, G.; Shenoy, S.; Kalyane, D.; Kalia, K.; Tekade, R.K. Artificial intelligence in drug discovery and development. *Drug Discov. Today* **2021**, *26*, 80–93. [CrossRef]
13. Miller, F.A.; Young, S.B.; Dobrow, M.; Shojania, K.G. Vulnerability of the medical product supply chain: The wake-up call of COVID-19. *BMJ Qual. Saf.* **2021**, *30*, 331–335. [CrossRef]
14. Mulumba, M.; Oga, J.; Koomson, N.; Kara, T.A.; Cynthia, A.N.; Forman, L. Decolonizing global health: Africa's pursuit of pharmaceutical sovereignty. *BMC Health Serv. Res.* **2025**, *25*, 1015. [CrossRef]
15. Fadojutimi, B. Exploring the critical factors in pharmaceutical supply chains revealed during COVID-19 and addressing missing links. *World J. Adv. Res. Rev.* **2024**, *24*, 2407–2425. [CrossRef]
16. Cova, T.; Vitorino, C.; Ferreira, M.; Nunes, S.; Rondon-Villarreal, P.; Pais, A. Artificial Intelligence and Quantum Computing as the Next Pharma Disruptors. In *Methods in Molecular Biology*; Humana: New York, NY, USA, 2022.

17. Matarèse, B.F.E.; Purushotham, A. Quantum Oncology. *Quantum Rep.* **2025**, *7*, 9. [CrossRef]
18. Narayanan, R.; Peker, E.; DeGroat, W.; Mendhe, D.; Zeeshan, S.; Ahmed, Z. 3D IntelliGenes: AI/ML application using multi-omics data for biomarker discovery and disease prediction with multi-dimensional visualization. *BMC Med. Res. Methodol.* **2025**, *25*, 193. [CrossRef]
19. Maskara, N.; Ostermann, S.; Shee, J.; Kalinowski, M.; Gomez, A.M.; Bravo, R.A.; Wang, D.S.; Krylov, A.I.; Yao, N.Y.; Head-Gordon, M.; et al. Programmable simulations of molecules and materials with reconfigurable quantum processors. *Nat. Phys.* **2025**, *21*, 289–297. [CrossRef]
20. Clinton, L.; Cubitt, T.; Flynn, B.; Gambetta, F.M.; Klassen, J.; Montanaro, A.; Piddock, S.; Santos, R.A.; Sheridan, E. Towards near-term quantum simulation of materials. *Nat. Commun.* **2024**, *15*, 211. [CrossRef] [PubMed]
21. Kadowaki, T. Quantum Computing and AI: Perspectives on Advanced Automation in Science and Engineering. *arXiv* **2025**, arXiv:2505.10012. [CrossRef]
22. Braga, D.M.; Rawal, B. Harnessing AI and Quantum Computing for Revolutionizing Drug Discovery and Approval Processes: Case Example for Collagen Toxicity. *JMIR Bioinform. Biotechnol.* **2025**, *6*, e69800. [CrossRef] [PubMed]
23. Plé, T.; Adjoua, O.; Benali, A.; Posenitskiy, E.; Villot, C.; Lagardère, L.; Piquemal, J.-P. A Foundation Model for Accurate Atomistic Simulations in Drug Design. *ChemRxiv* **2025**. [CrossRef]
24. Zhou, Y.; Stoudenmire, E.M.; Waintal, X. What Limits the Simulation of Quantum Computers? *Phys. Rev. X* **2020**, *10*, 041038. [CrossRef]
25. Strocchi, F. Microscopic and macroscopic quantities in statistical mechanics. *Il Nuovo C. B Ser. 10* **1970**, *65*, 239–265. [CrossRef]
26. Chae, E.; Choi, J.; Kim, J. An elementary review on basic principles and developments of qubits for quantum computing. *Nano Converg.* **2024**, *11*, 11. [CrossRef]
27. Zhang, H. Quantum Entanglement and Qubit Interactions: The Key to Quantum Supremacy. *Theor. Nat. Sci.* **2024**, *41*, 112–118. [CrossRef]
28. Shen, L.; Yang, W. Molecular Dynamics Simulations with Quantum Mechanics/Molecular Mechanics and Adaptive Neural Networks. *J. Chem. Theory Comput.* **2018**, *14*, 1442–1455. [CrossRef]
29. Kulkarni, P.U.; Shah, H.; Vyas, V.K. Hybrid Quantum Mechanics/Molecular Mechanics (QM/MM) Simulation: A Tool for Structure-Based Drug Design and Discovery. *Mini Rev. Med. Chem.* **2021**, *22*, 1096–1107. [CrossRef] [PubMed]
30. Schrödinger, E. Quantisierung als Eigenwertproblem. *Ann. Phys.* **1926**, *384*, 361–376. [CrossRef]
31. Oszmaniec, M.; Grudka, A.; Horodecki, M.; Wójcik, A. Creating a Superposition of Unknown Quantum States. *Phys. Rev. Lett.* **2016**, *116*, 110403. [CrossRef]
32. Freedman, S.J.; Clauser, J.F. Experimental test of local hidden-variable theories. *Phys. Rev. Lett.* **1972**, *28*, 938–941. [CrossRef]
33. Aspect, A.; Dalibard, J.; Roger, G. Experimental test of Bell's inequalities using time- varying analyzers. *Phys. Rev. Lett.* **1982**, *49*, 1804–1807. [CrossRef]
34. Pan, J.W.; Bouwmeester, D.; Weinfurter, H.; Zeilinger, A. Experimental entanglement swapping: Entangling photons that never interacted. *Phys. Rev. Lett.* **1998**, *80*, 3891–3894. [CrossRef]
35. Gamow, G. Zur Quantentheorie des Atomkernes. *Z. Phys.* **1928**, *51*, 204–212. [CrossRef]
36. Gurney, R.W.; Condon, E.U. Quantum mechanics and radioactive disintegration. *Phys. Rev.* **1929**, *33*, 127–140. [CrossRef]
37. Wrachtrup, J.; Finkler, A. Single spin magnetic resonance. *J. Magn. Reson.* **2016**, *269*, 225–236. [CrossRef]
38. Kaushik, P.; Rao, A.M.; Singh, D.P.; Vashisht, S.; Gupta, S. Cloud Computing and Comparison based on Service and Performance between Amazon AWS, Microsoft Azure, and Google Cloud. In Proceedings of the 2021 International Conference on Technological Advancements and Innovations (ICTAI), Tashkent, Uzbekistan, 10–12 November 2021; IEEE: Piscataway, NJ, USA, 2021; pp. 268–273.
39. Pajankar, A.; Joshi, A. *Hands-on Machine Learning with Python: Implement Neural Network Solutions with Scikit-Learn and PyTorch*; Apress: New York, NY, USA, 2022.
40. Liliopoulos, I.; Varsamis, G.D.; Karamanidou, T.; Papalitsas, C.; Koulouras, G.; Pantazopoulos, V.; Stavropoulos, T.G.; Karafyllidis, I.G. Quantum algorithm for protein-ligand docking sites identification in the interaction space. *J. Comput. Aided Mol. Des.* **2025**, *39*, 40. [CrossRef]
41. Du, J.; Shi, F.; Kong, X.; Jelezko, F.; Wrachtrup, J. Single-molecule scale magnetic resonance spectroscopy using quantum diamond sensors. *Rev. Mod. Phys.* **2024**, *96*, 025001. [CrossRef]
42. Bird, B.; Baker, M.J. Quantum Cascade Lasers in Biomedical Infrared Imaging. *Trends Biotechnol.* **2015**, *33*, 557–558. [CrossRef]
43. Chemla, Y.R.; Grossman, H.L.; Poon, Y.; McDermott, R.; Stevens, R.; Alper, M.D.; Clarke, J. Ultrasensitive magnetic biosensor for homogeneous immunoassay. *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 14268–14272. [CrossRef]
44. Meinel, J.; Kwon, M.; Maier, R.; Dasari, D.; Sumiya, H.; Onoda, S.; Isoya, J.; Vorobyov, V.; Wrachtrup, J. High-resolution nanoscale NMR for arbitrary magnetic fields. *Commun. Phys.* **2023**, *6*, 302. [CrossRef]
45. Bucher, D.B.; Aude Craik, D.P.L.; Backlund, M.P.; Turner, M.J.; Dor, O.B.; Glenn, D.R.; Walsworth, R.L. Quantum diamond spectrometer for nanoscale NMR and ESR spectroscopy. *Nat. Protoc.* **2019**, *14*, 2707–2747. [CrossRef]

46. Zwick, A.; Álvarez, G.A. Quantum sensing tools to characterize physical, chemical and biological processes with magnetic resonance. *J. Magn. Reson. Open* **2023**, *16–17*, 100113. [CrossRef]
47. Wu, S.; Gong, C.; Li, S.; Ni, R.; Zhu, J. Weak Radio Frequency Signal Reception Sensitivity Based on DC Superconducting Quantum Interference Devices. *IEEE Trans. Appl. Supercond.* **2023**, *33*, 1–8. [CrossRef]
48. Matarèse, B.F.E.; Purushotham, A. Unlocking clinical quantum oncology through quantum control. *Eur. J. Cancer* **2025**, *226*, 115632. [CrossRef]
49. Chang, B.Y.; Sola, I.R.; Malinovsky, V.S. Anomalous Rabi Oscillations in Multilevel Quantum Systems. *Phys. Rev. Lett.* **2018**, *120*, 133201. [CrossRef] [PubMed]
50. Wigger, D.; Schneider, C.; Gerhardt, S.; Kamp, M.; Höfling, S.; Kuhn, T.; Kasprzak, J. Rabi oscillations of a quantum dot exciton coupled to acoustic phonons: Coherence and population readout. *Optica* **2018**, *5*, 1442–1450. [CrossRef]
51. Daems, D.; Ruschhaupt, A.; Sugny, D.; Guérin, S. Robust quantum control by a single-shot shaped pulse. *Phys. Rev. Lett.* **2013**, *111*, 050404. [CrossRef] [PubMed]
52. Torosov, B.T.; Vitanov, N.V. Smooth composite pulses for high-fidelity quantum information processing. *Phys. Rev. A* **2011**, *83*, 053420. [CrossRef]
53. Ndong, M.; Djotyan, G.; Ruschhaupt, A.; Guérin, S. Robust coherent superposition of states by single-shot shaped pulse. *J. Phys. B At. Mol. Opt. Phys.* **2015**, *48*, 174007. [CrossRef]
54. Yin, Z.; Li, C.; Allcock, J.; Zheng, Y.; Gu, X.; Dai, M.; Zhang, S.; An, S. Shortcuts to adiabaticity for open systems in circuit quantum electrodynamics. *Nat. Commun.* **2022**, *13*, 188. [CrossRef]
55. Rangelov, A.A.; Vitanov, N.V.; Yatsenko, L.P.; Shore, B.W.; Halfmann, T.; Bergmann, K. Stark-shift-chirped rapid-adiabatic-passage technique among three states. *Phys. Rev. A* **2005**, *72*, 053403. [CrossRef]
56. Gregefalk, A.; Sjöqvist, E. Transitionless Quantum Driving in Spin Echo. *Phys. Rev. Appl.* **2022**, *17*, 024012. [CrossRef]
57. Lin, M.; Guo, J.; Gu, Z.; Tang, W.; Tao, H.; You, S.; Jia, D.; Sun, Y.; Jia, P. Machine learning and multi-omics integration: Advancing cardiovascular translational research and clinical practice. *J. Transl. Med.* **2025**, *23*, 388. [CrossRef] [PubMed]
58. Chandra, A.; Tünnermann, L.; Löfstedt, T.; Gratz, R. Transformer-based deep learning for predicting protein properties in the life sciences. *eLife* **2023**, *12*, e82819. [CrossRef]
59. de Sá, A.G.C.; Ascher, D.B. Auto-ADMET: An Effective and Interpretable AutoML Method for Chemical ADMET Property Prediction. *arXiv* **2025**, arXiv:2502.16378.
60. Thiele, M.; Villesen, I.F.; Niu, L.; Johansen, S.; Sulek, K.; Nishijima, S.; Espen, L.V.; Keller, M.; Israelsen, M.; Suvitaival, T.; et al. Opportunities and barriers in omics-based biomarker discovery for steatotic liver diseases. *J. Hepatol.* **2024**, *81*, 345–359. [CrossRef] [PubMed]
61. Paananen, J.; Fortino, V. An omics perspective on drug target discovery platforms. *Brief. Bioinform.* **2020**, *21*, 1937–1953. [CrossRef] [PubMed]
62. Raniga, K.; Stebbeds, W.; Shivalingam, A.; Pembertond, M.; Denning, C. Design of experiments for the automated development of a multicellular cardiac model for high-throughput screening. *SLAS Discov.* **2023**, *28*, 410–417. [CrossRef]
63. Yang, Z.; Ren, Z.; Cheng, Y.; Sun, W.; Xi, Z.; Jia, W.; Li, G.; Wang, Y.; Guo, M.; Li, D. Review and prospect on portable mass spectrometer for recent applications. *Vacuum* **2022**, *199*, 110889. [CrossRef]
64. Leung, H.M.; Chu, H.C.; Mao, Z.W.; Lo, P.K. Versatile nanodiamond-based tools for therapeutics and bioimaging. *Chem. Commun.* **2023**, *59*, 2039–2055. [CrossRef]
65. Truskewycz, A.; Yin, H.; Halberg, N.; Lai, D.T.H.; Ball, A.S.; Truong, V.K.; Rybicka, A.M.; Cole, I. Carbon Dot Therapeutic Platforms: Administration, Distribution, Metabolism, Excretion, Toxicity, and Therapeutic Potential. *Small* **2022**, *18*, 2106342. [CrossRef] [PubMed]
66. Zrazhevskiy, P.; Sena, M.; Gao, X. Designing multifunctional quantum dots for bioimaging, detection, and drug delivery. *Chem. Soc. Rev.* **2010**, *39*, 4326–4354. [CrossRef]
67. Liu, K.S.; Henning, A.; Heindl, M.W.; Bucher, D.B. Surface NMR using quantum sensors in diamond. *Proc. Natl. Acad. Sci. USA* **2022**, *119*, e2111607119. [CrossRef]
68. Zhou, C.; Hermes, M.R.; Wu, D.; Bao, J.J.; Pandharkar, R.; King, D.S.; Zhang, D.; Scott, T.R.; Lykhin, A.O.; Gagliardi, L.; et al. Electronic structure of strongly correlated systems: Recent developments in multiconfiguration pair-density functional theory and multiconfiguration nonclassical-energy functional theory. *Chem. Sci.* **2022**, *13*, 7685–7706. [CrossRef]
69. Schmidt-Böcking, H.; Eckart, S.; Lüdde, H.J.; Gruber, G.; Jahnke, T. The Precision Limits in a Single-Event Quantum Measurement of Electron Momentum and Position. In *Molecular Beams in Physics and Chemistry: From Otto Stern's Pioneering Exploits to Present-Day Feat*; Springer: Berlin/Heidelberg, Germany, 2021.
70. Lee, J.; Berry, D.W.; Gidney, C.; Huggins, W.J.; McClean, J.R.; Wiebe, N.; Babbush, R.B. Even More Efficient Quantum Computations of Chemistry through Tensor Hypercontraction. *PRX Quantum* **2021**, *2*, 030305. [CrossRef]
71. Yu, S.; Zhong, Z.-P.; Fang, Y.; Patel, R.B.; Li, Q.-P.; Liu, W.; Li, Z.; Xu, L.; Sagona-Stophel, S.; Mer, E.; et al. A universal programmable Gaussian boson sampler for drug discovery. *Nat. Comput. Sci.* **2023**, *3*, 839–848. [CrossRef]

72. Lau, J.W.Z.; Lim, K.H.; Shrotriya, H.; Kwek, L.C. NISQ computing: Where are we and where do we go? *AAPPS Bull.* **2022**, *32*, 27. [CrossRef]
73. Schuld, M.; Killoran, N. Quantum Machine Learning in Feature Hilbert Spaces. *Phys. Rev. Lett.* **2019**, *122*, 040504. [CrossRef] [PubMed]
74. Fellous-Asiani, M.; Chai, J.H.; Whitney, R.S.; Auffèves, A.; Ng, H.K. Limitations in Quantum Computing from Resource Constraints. *PRX Quantum* **2021**, *2*, 040335. [CrossRef]
75. Westerberg, H. *The Superintelligence That Cares About Us*; GitHub: San Francisco, CA, USA, 2025.
76. Talati, D. Quantum Minds: Merging Quantum Computing with Next-Gen AI. *SSRN* **2025**. [CrossRef]
77. Holdgate, G.; Embrey, K.; Milbradt, A.; Davies, G. Biophysical methods in early drug discovery. *ADMET DMPK* **2019**, *7*, 222–241. [CrossRef]
78. Iyengar, R. Computational biochemistry: Systems biology minireview series. *J. Biol. Chem.* **2009**, *284*, 5425–5426. [CrossRef]
79. Matarèse, B.F.E.; Rusin, A.; Seymour, C.; Mothersill, C. Quantum Biology and the Potential Role of Entanglement and Tunneling in Non-Targeted Effects of Ionizing Radiation: A Review and Proposed Model. *Int. J. Mol. Sci.* **2023**, *24*, 16464. [CrossRef] [PubMed]
80. Iyer, G.; Michalet, X.; Chang, Y.P.; Weiss, S. Tracking Single Proteins in Live Cells Using Single-Chain Antibody Fragment-Fluorescent Quantum Dot Affinity Pair. *Methods Enzymol.* **2010**, *475*, 61–79.
81. Knudsen, B.R.; Jepsen, M.L.; Ho, Y.P. Quantum dot-based nanosensors for diagnosis via enzyme activity measurement. *Expert Rev. Mol. Diagn.* **2013**, *13*, 367–375. [CrossRef] [PubMed]
82. Mousavi, S.M.; Hashemi, S.A.; Yari Kalashgrani, M.; Omidifar, N.; Lai, C.W.; Vijayakameswara Rao, N.; Gholami, A.; Chiang, W.H. The Pivotal Role of Quantum Dots-Based Biomarkers Integrated with Ultra-Sensitive Probes for Multiplex Detection of Human Viral Infections. *Pharmaceuticals* **2022**, *15*, 880. [CrossRef] [PubMed]
83. Sotoma, S.; Okita, H.; Chuma, S.; Harada, Y. Quantum nanodiamonds for sensing of biological quantities: Angle, temperature, and thermal conductivity. *Biophys. Physicobiol.* **2022**, *19*, e190034. [CrossRef]
84. Luo, S.; Sun, Y. Quantum coherence versus quantum uncertainty. *Phys. Rev. A* **2017**, *96*, 022130. [CrossRef]
85. Bischof, F.; Kampermann, H.; Bru, D. Quantifying coherence with respect to general quantum measurements. *Phys. Rev. A* **2021**, *103*, 032429. [CrossRef]
86. Pullman, A.; Pullman, B. Electronic Structure and Carcinogenic Activity of Aromatic Molecules New Developments. *Adv. Cancer Res.* **1955**, *3*, 117–169. [CrossRef]
87. Kar, R.K. Benefits of hybrid QM/MM over traditional classical mechanics in pharmaceutical systems. *Drug Discov. Today* **2023**, *28*, 103374.
88. Cheng, H.P.; Deumens, E.; Freericks, J.K.; Li, C.; Sanders, B.A. Application of Quantum Computing to Biochemical Systems: A Look to the Future. *Front. Chem.* **2020**, *8*, 587143. [CrossRef]
89. Rice, S.A.; Tannor, D.J.; Kosloff, R. Coherent pulse sequence induced control of selectivity of reactions. Exact quantum-mechanical calculations. *J. Chem. Soc. Faraday Trans. 2* **1986**, *82*, 2423. [CrossRef]
90. Wang, J.; Li, D.; Betzholz, R.; Cai, J. Real-Time Adaptive Sensing of Nuclear Spins by a Single-Spin Quantum Sensor. *Phys. Rev. Appl.* **2022**, *18*, 024040. [CrossRef]
91. Li, H.; Gong, X.; Ni, H.; Lu, P.; Luo, X.; Wen, J.; Yang, Y.; Qian, X.; Sun, Z.; Wu, J. Light-Induced Ultrafast Molecular Dynamics: From Photochemistry to Optochemistry. *J. Phys. Chem. Lett.* **2022**, *13*, 5881–5893. [CrossRef] [PubMed]
92. Sultanow, E.; Tehrani, M.; Dutta, S.; Buchanan, W.J.; Khan, M.S. Quantum Agents. *arXiv* **2025**, arXiv:2506.01536. [PubMed]
93. Mione, F.M.; Kaspersetz, L.; Luna, M.F.; Aizpuru, J.; Scholz, R.; Borisyak, M.; Kemmer, A.; Schermeyer, M.T.; Martinez, E.C.; Neubauer, P.; et al. A workflow management system for reproducible and interoperable high-throughput self-driving experiments. *Comput. Chem. Eng.* **2024**, *187*, 108720. [CrossRef]
94. Shahin, M.H.; Goswami, S.; Lobentanzer, S.; Corrigan, B.W. Agents for Change: Artificial Intelligent Workflows for Quantitative Clinical Pharmacology and Translational Sciences. *Clin. Transl. Sci.* **2025**, *18*, e70188. [CrossRef] [PubMed]
95. Yang, X.; Huang, K.; Yang, D.; Zhao, W.; Zhou, X. Biomedical Big Data Technologies, Applications, and Challenges for Precision Medicine: A Review. *Glob. Chall.* **2024**, *8*, 2300163.
96. Swift, B.; Jain, L.; White, C.; Chandrasekaran, V.; Bhandari, A.; Hughes, D.A.; Jadhav, P.R. Innovation at the Intersection of Clinical Trials and Real-World Data Science to Advance Patient Care. *Clin. Transl. Sci.* **2018**, *11*, 450–460. [CrossRef] [PubMed]
97. Chen, K.Y.; Borglund, E.M.; Postema, E.C.; Dunn, A.G.; Bourgeois, F.T. Reporting of clinical trial safety results in ClinicalTrials.gov for FDA-approved drugs: A cross-sectional analysis. *Clin. Trials* **2022**, *19*, 442–451. [CrossRef]
98. Ding, H.; Wu, F. Image guided biodistribution and pharmacokinetic studies of theranostics. *Theranostics* **2012**, *2*, 1040–1053. [CrossRef] [PubMed]
99. Khan, S.; Anwar, S.; Choudhury, A.; Mohammad, T.; Hassan, M.I. Validation of Drug Targets Using Molecular Methodologies and Enzymatic Activity Assays for Validation of Inhibitory Potential. In *Bacterial Enzymes as Targets for Drug Discovery*; Elsevier: Amsterdam, The Netherlands, 2025; pp. 91–112.

100. Wilson, L.J.; Kiffer, F.C.; Berrios, D.C.; Bryce-Atkinson, A.; Costes, S.V.; Gevaert, O.; Matarèse, B.F.E.; Miller, J.; Mukherjee, P.; Peach, K.; et al. Machine intelligence for radiation science: Summary of the Radiation Research Society 67th annual meeting symposium. *Int. J. Radiat. Biol.* **2023**, *99*, 1291–1300. [CrossRef]
101. Lavertu, A.; Vora, B.; Giacomini, K.M.; Altman, R.; Rensi, S. A New Era in Pharmacovigilance: Toward Real-World Data and Digital Monitoring. *Clin. Pharmacol. Ther.* **2021**, *109*, 1197–1202. [CrossRef]
102. Ng, D.Q.; Dang, E.; Chen, L.; Nguyen, M.T.; Nguyen, M.K.N.; Samman, S.; Nguyen, T.M.T.; Cadiz, C.L.; Nguyen, L.; Chan, A. Current and recommended practices for evaluating adverse drug events using electronic health records: A systematic review. *JACCP J. Am. Coll. Clin. Pharm.* **2021**, *4*, 1457–1468. [CrossRef]
103. Agarwal, P.; Searls, D.B. Can literature analysis identify innovation drivers in drug discovery? *Nat. Rev. Drug Discov.* **2009**, *8*, 865–878. [CrossRef]
104. Gadiya, Y.; Gribbon, P.; Hofmann-Apitius, M.; Zaliani, A. Pharmaceutical patent landscaping: A novel approach to understand patents from the drug discovery perspective. *Artif. Intell. Life Sci.* **2023**, *3*, 100069. [CrossRef]
105. Long, R.A.; Ballard, S.; Shah, S.; Bianchi, O.; Jones, L.; Koretsky, M.J.; Kuznetsov, N.; Marsan, E.; Jen, B.; Chiang, P.; et al. A new AI-assisted data standard accelerates interoperability in biomedical research. *medRxiv* **2024**. [CrossRef] [PubMed]
106. Tabari, P.; Costagliola, G.; De Rosa, M.; Boeker, M. State-of-the-Art Fast Healthcare Interoperability Resources (FHIR)-Based Data Model and Structure Implementations: Systematic Scoping Review. *JMIR Med. Inform.* **2024**, *12*, e58445. [CrossRef]
107. Babuc, D.; Fortiş, T.-F. *Federated Learning Platforms for Privacy-Preserving Histopathological Image Classification*; Springer: Cham, Switzerland, 2025; pp. 317–328.
108. Sinaci, A.A.; Gencturk, M.; Teoman, H.A.; Laleci Erturkmen, G.B.; Alvarez-Romero, C.; Martinez-Garcia, A.; Poblador-Plou, B.; Carmona-Pírez, J.; Löbe, M.; Parra-Calderon, C.L. A Data Transformation Methodology to Create Findable, Accessible, Interoperable, and Reusable Health Data: Software Design, Development, and Evaluation Study. *J. Med. Internet Res.* **2023**, *25*, e42822. [CrossRef] [PubMed]
109. Zheng, L.; Cao, Y.; Yoshikawa, M.; Shen, Y.; Rashed, E.A.; Taura, K.; Hanaoka, S.; Zhang, T. Sensitivity-Aware Differential Privacy for Federated Medical Imaging. *Sensors* **2025**, *25*, 2847. [CrossRef] [PubMed]
110. Cross, J.L.; Choma, M.A.; Onofrey, J.A. Bias in medical AI: Implications for clinical decision-making. *PLoS Digit. Health* **2024**, *3*, e0000651. [CrossRef]
111. Hanna, M.G.; Pantanowitz, L.; Jackson, B.; Palmer, O.; Visweswaran, S.; Pantanowitz, J.; Deebajah, M.; Rashidi, H.H. Ethical and Bias Considerations in Artificial Intelligence/Machine Learning. *Mod. Pathol.* **2025**, *38*, 100686. [CrossRef]
112. Shah, H.A.; Liu, J.; Yang, Z.; Feng, J. Review of Machine Learning Methods for the Prediction and Reconstruction of Metabolic Pathways. *Front. Mol. Biosci.* **2021**, *8*, 634141. [CrossRef]
113. Cit, A.; Elly, B.; Alam, D. AI-Driven Optimization of Drug Synthesis Pathways. *Preprints* **2025**, 2025020911. [CrossRef]
114. Molani, F.; Cho, A.E. Accurate protein-ligand binding free energy estimation using QM/MM on multi-conformers predicted from classical mining minima. *Commun. Chem.* **2024**, *7*, 247. [CrossRef]
115. Neves, B.J.; Braga, R.C.; Melo-Filho, C.C.; Moreira-Filho, J.T.; Muratov, E.N.; Andrade, C.H. QSAR-Based Virtual Screening: Advances and Applications in Drug Discovery. *Front. Pharmacol.* **2018**, *9*, 1275. [CrossRef]
116. Brnabic, A.; Hess, L.M. Systematic literature review of machine learning methods used in the analysis of real-world data for patient-provider decision making. *BMC Med. Inform. Decis. Mak.* **2021**, *21*, 54. [CrossRef]
117. Bhatia, A.S.; Saggi, M.K.; Kais, S. Quantum Machine Learning Predicting ADME-Tox Properties in Drug Discovery. *J. Chem. Inf. Model.* **2023**, *63*, 6476–6486. [CrossRef]
118. Wei, Y.; Shan, L.; Qiu, T.; Lu, D.; Liu, Z. Machine learning-assisted retrosynthesis planning: Current status and future prospects. *Chin. J. Chem. Eng.* **2025**, *77*, 273–292. [CrossRef]
119. Raschka, S.; Kaufman, B. Machine learning and AI-based approaches for bioactive ligand discovery and GPCR-ligand recognition. *Methods* **2020**, *180*, 89–110. [CrossRef] [PubMed]
120. Das, U. Generative AI for drug discovery and protein design: The next frontier in AI-driven molecular science. *Med. Drug Discov.* **2025**, *27*, 100213. [CrossRef]
121. Kapoor, A.; Gulli, A.; Pal, S.; Chollet, F. Build and Deploy Supervised, Unsupervised, Deep, and Reinforcement Learning Models. In *Deep Learning with TensorFlow and Keras*, 3rd ed.; Packt Publishing Ltd.: Birmingham, UK, 2022.
122. Nussinov, R.; Zhang, M.; Liu, Y.; Jang, H. AlphaFold, Artificial Intelligence (AI), and Allostery. *J. Phys. Chem. B* **2022**, *126*, 6372–6383. [CrossRef] [PubMed]
123. Terwilliger, T.C.; Poon, B.K.; Afonine, P.V.; Schlicksup, C.J.; Croll, T.I.; Millán, C.; Richardson, J.S.; Read, R.J.; Adams, P.D. Improved AlphaFold modeling with implicit experimental information. *Nat. Methods* **2022**, *19*, 1376–1382. [CrossRef]
124. Pak, M.A.; Markhieva, K.A.; Novikova, M.S.; Petrov, D.S.; Vorobyev, I.S.; Maksimova, E.S.; Kondrashov, F.A.; Ivankov, D.N. Using AlphaFold to predict the impact of single mutations on protein stability and function. *PLoS ONE* **2023**, *18*, e0282689. [CrossRef]

125. Korshunova, M.; Huang, N.; Capuzzi, S.; Radchenko, D.S.; Savych, O.; Moroz, Y.S.; Wells, C.I.; Willson, T.M.; Tropsha, A.; Isayev, O. Generative and reinforcement learning approaches for the automated de novo design of bioactive compounds. *Commun. Chem.* **2022**, *5*, 129. [CrossRef]
126. Gangwal, A.; Lavecchia, A. Unleashing the power of generative AI in drug discovery. *Drug Discov. Today* **2024**, *29*, 103992. [CrossRef]
127. Bayley, O.; Savino, E.; Slattery, A.; Noël, T. Autonomous chemistry: Navigating self-driving labs in chemical and material sciences. *Matter* **2024**, *7*, 2382–2398. [CrossRef]
128. Tom, G.; Schmid, S.P.; Baird, S.G.; Cao, Y.; Darvish, K.; Hao, H.; Lo, S.; Pablo-García, S.; Rajaonson, E.M.; Skreta, M. Self-Driving Laboratories for Chemistry and Materials Science. *Chem. Rev.* **2024**, *124*, 9633–9732. [CrossRef]
129. Burger, B.; Maffettone, P.M.; Gusev, V.V.; Aitchison, C.M.; Bai, Y.; Wang, X.; Li, X.; Alston, B.M.; Li, B.; Clowes, R.; et al. A mobile robotic chemist. *Nature* **2020**, *583*, 237–241. [CrossRef]
130. Dai, T.; Vijayakrishnan, S.; Szczypiński, F.T.; Ayme, J.-F.; Simaei, E.; Fellowes, T.; Clowes, R.; Kotopanov, L.; Shields, C.E.; Zhou, Z. Autonomous mobile robots for exploratory synthetic chemistry. *Nature* **2024**, *635*, 890–897. [CrossRef]
131. Yang, Y.; Juntao, L.; Lingling, P. Multi-robot path planning based on a deep reinforcement learning DQN algorithm. *CAAI Trans. Intell. Technol.* **2020**, *5*, 177–183. [CrossRef]
132. Huang, D.; Ye, X.; Zhang, Y.; Sakurai, T. Collaborative analysis for drug discovery by federated learning on non-IID data. *Methods* **2023**, *219*, 1–7. [CrossRef] [PubMed]
133. Schouten, D.; Nicoletti, G.; Dille, B.; Chia, C.; Vendittelli, P.; Schuurmans, M.; Litjens, G.; Khalili, N. Navigating the landscape of multimodal AI in medicine: A scoping review on technical challenges and clinical applications. *Med. Image Anal.* **2025**, *105*, 103621. [CrossRef]
134. DeGroat, W.; Abdelhalim, H.; Peker, E.; Sheth, N.; Narayanan, R.; Zeeshan, S.; Liang, B.T.; Ahmed, Z. Multimodal AI/ML for discovering novel biomarkers and predicting disease using multi-omics profiles of patients with cardiovascular diseases. *Sci. Rep.* **2024**, *14*, 26503. [CrossRef]
135. Russell, S. Artificial intelligence: The future is superintelligent. *Nature* **2017**, *548*, 520–521. [CrossRef]
136. Tang, X.; Dai, H.; Knight, E.; Wu, F.; Li, Y.; Li, T.; Gerstein, M. A survey of generative AI for *de novo* drug design: New frontiers in molecule and protein generation. *Brief. Bioinform.* **2024**, *25*, bbae338. [CrossRef]
137. Withers, C.A.; Rufai, A.M.; Venkatesan, A.; Tirunagari, S.; Lobentanzer, S.; Harrison, M.; Zdrazil, B. Natural language processing in drug discovery: Bridging the gap between text and therapeutics with artificial intelligence. *Expert Opin. Drug Discov.* **2025**, *20*, 765–783. [CrossRef]
138. Guellil, I.; Wu, J.; Pradipta Gema, A.; Francis, F.; Berrachedi, Y.; Chenni, N.; Tobin, R.; Llewellyn, C.; Arakelyan, S.; Wu, H.; et al. Natural language processing for detecting adverse drug events: A systematic review protocol. *NIHR Open Res.* **2024**, *3*, 67. [CrossRef]
139. Roche, R.; Moussad, B.; Shuvo, M.H.; Bhattacharya, D. E(3) equivariant graph neural networks for robust and accurate protein-protein interaction site prediction. *PLoS Comput. Biol.* **2023**, *19*, e1011435. [CrossRef]
140. Xu, M.; Qian, P.; Zhao, Z.; Zeng, Z.; Chen, J.; Liu, W.; Yang, X. Graph Neural Networks for Protein-Protein Interactions—A Short Survey. *arXiv* **2024**, arXiv:2404.10450.
141. Nerella, S.; Bandyopadhyay, S.; Zhang, J.; Contreras, M.; Siegel, S.; Bumin, A.; Silva, B.; Sena, J.; Shickel, B.; Bihorac, A.; et al. Transformers and large language models in healthcare: A review. *Artif. Intell. Med.* **2024**, *154*, 102900. [CrossRef]
142. Chen, J.-Y.; Wang, J.-F.; Hu, Y.; Li, X.-H.; Qian, Y.-R.; Song, C.-L. Evaluating the advancements in protein language models for encoding strategies in protein function prediction: A comprehensive review. *Front. Bioeng. Biotechnol.* **2025**, *13*, 1506508. [CrossRef] [PubMed]
143. Yuan, Z.-H.; Yin, T.; Zhang, D.-B. Hybrid quantum-classical algorithms for solving quantum chemistry in Hamiltonian–wave-function space. *Phys. Rev. A* **2021**, *103*, 012413. [CrossRef]
144. Braga, D.M.; Rawal, B.S. Harnessing AI and Quantum Computing for Accelerated Drug Discovery: Regulatory Frameworks for In Silico to In Vivo Validation. *J. Pharm. BioTech Ind.* **2025**, *2*, 11. [CrossRef]
145. Cui, M.; Chang, L.; Chau, A.; Mekuria, H.; Adwankar, L.; Pendyala, S. Efficient and Optimized Small Organic Molecular Graph Generation Pathway Using a Quantum Generative Adversarial Network. In Proceedings of the 2024 IEEE International Conference on Quantum Computing and Engineering (QCE), Montreal, QC, Canada, 15–20 September 2024; IEEE: Piscataway, NJ, USA, 2024; pp. 1565–1570.
146. Bauer, N.; Siopsis, G. Post-Variational Ground State Estimation via QPE-Based Quantum Imaginary Time Evolution. *arXiv* **2025**, arXiv:2504.11549.
147. Ullah, S.; Shah, M.H.; Anjum, A. Quantum Enhanced Federated Learning with Differential Privacy. In Proceedings of the 2024 International Conference on Frontiers of Information Technology (FIT), Islamabad, Pakistan, 9–10 December 2024; IEEE: Piscataway, NJ, USA, 2024; pp. 1–6.

148. Bender, A.; Cortés-Ciriano, I. Artificial intelligence in drug discovery: What is realistic, what are illusions? Part 1: Ways to make an impact, and why we are not there yet. *Drug Discov. Today* **2021**, *26*, 511–524. [CrossRef]
149. Bender, A.; Cortes-Ciriano, I. Artificial intelligence in drug discovery: What is realistic, what are illusions? Part 2: A discussion of chemical and biological data. *Drug Discov. Today* **2021**, *26*, 1040–1052. [CrossRef]
150. Price, S.S.L. Computed Crystal Energy Landscapes for Understanding and Predicting Organic Crystal Structures and Polymorphism. *Acc. Chem. Res.* **2009**, *42*, 117–126. [CrossRef]
151. Davis, B.; Mcloughlin, K.; Allen, J.; Ellingson, S.R. Quantifying Overfitting Potential in Drug Binding Datasets. In Proceedings of the Computational Science—ICCS 2020, Amsterdam, The Netherlands, 15 June 2020; pp. 585–598.
152. Fan, Z.; Yu, J.; Zhang, X.; Chen, Y.; Sun, S.; Zhang, Y.; Chen, M.; Xiao, F.; Wu, W.; Li, X.; et al. Reducing overconfident errors in molecular property classification using Posterior Network. *Patterns* **2024**, *5*, 100991. [CrossRef]
153. Nyman, J.; Day, G.M. Static and lattice vibrational energy differences between polymorphs. *CrystEngComm* **2015**, *17*, 5154–5165. [CrossRef]
154. Ding, Q.-M.; Huang, Y.-M.; Yuan, X. Molecular docking via quantum approximate optimization algorithm. *Phys. Rev. Appl.* **2024**, *21*, 034036. [CrossRef]
155. Al-Dahlaki, M.H.; Mohammed, A.H. Quantum mechanics/molecular mechanics (QM/MM) methods in drug design: A comprehensive review of development and applications. *Int. J. Adv. Chem.* **2024**, *12*, 86–92. [CrossRef]
156. Hayashi, H.; Maeda, S.; Mita, T. Quantum chemical calculations for reaction prediction in the development of synthetic methodologies. *Chem. Sci.* **2023**, *14*, 11601–11616. [CrossRef]
157. Han, C.; Zhang, D.; Xia, S.; Zhang, Y. Accurate Prediction of NMR Chemical Shifts: Integrating DFT Calculations with Three-Dimensional Graph Neural Networks. *J. Chem. Theory Comput.* **2024**, *20*, 5250–5258. [CrossRef] [PubMed]
158. Wang, X.; Wu, X.; Brooks, B.R.; Wang, J. Accurate Free Energy Calculation via Multiscale Simulations Driven by Hybrid Machine Learning and Molecular Mechanics Potentials. *J. Chem. Theory Comput.* **2024**, *21*, 6979–6987. [CrossRef] [PubMed]
159. Yang, S.; Day, G.M. Global analysis of the energy landscapes of molecular crystal structures by applying the threshold algorithm. *Commun. Chem.* **2022**, *5*, 86. [CrossRef] [PubMed]
160. Asano, D.; Takakusa, H.; Nakai, D. Oral Absorption of Middle-to-Large Molecules and Its Improvement, with a Focus on New Modality Drugs. *Pharmaceutics* **2023**, *16*, 47. [CrossRef]
161. Kokudeva, M.; Vichev, M.; Naseva, E.; Miteva, D.G.; Velikova, T. Artificial intelligence as a tool in drug discovery and development. *World J. Exp. Med.* **2024**, *14*, 96042. [CrossRef]
162. Mustafa, H.; Morapakula, S.N.; Jain, P.; Ganguly, S. Variational Quantum Algorithms for Chemical Simulation and Drug Discovery. In Proceedings of the 2022 International Conference on Trends in Quantum Computing and Emerging Business Technologies, TQCEBT 2022, Pune, India, 13–15 October 2022.
163. Li, W.; Yin, Z.; Li, X.; Ma, D.; Yi, S.; Zhang, Z.; Zou, C.; Bu, K.; Dai, M.; Yue, J.; et al. A hybrid quantum computing pipeline for real world drug discovery. *Sci. Rep.* **2024**, *14*, 16942. [CrossRef]
164. Zubatyuk, R.; Biczysko, M.; Ranasinghe, K.; Moriarty, N.W.; Gokcan, H.; Kruse, H.; Poon, B.K.; Adams, P.D.; Waller, M.P.; Roitberg, A.E.; et al. AQuaRef: Machine learning accelerated quantum refinement of protein structures. *Nat. Commun.* **2024**, *16*, 9224.
165. Pasupuleti, M.K. Hybrid Quantum-Classical Algorithms for Drug Discovery and Molecular Simulation. *Int. J. Acad. Ind. Res. Innov.* **2025**, *5*, 303–314. [CrossRef]
166. Upama, P.B.; Kolli, A.; Kolli, H.; Alam, S.; Syam, M.; Shahriar, H.; Ahamed, S.I. Quantum Machine Learning in Disease Detection and Prediction: A survey of Applications and Future Possibilities. In Proceedings of the International Computer Software and Applications Conference, Torino, Italy, 26–30 June 2023.
167. Ghazi Vakili, M.; Gorgulla, C.; Snider, J.; Nigam, A.; Bezrukov, D.; Varoli, D.; Aliper, A.; Polykovsky, D.; Das, K.M.P.; Cox, H.; et al. Quantum-computing-enhanced algorithm unveils potential KRAS inhibitors. *Nat. Biotechnol.* **2025**, *43*, 1954–1959. [CrossRef]
168. Pyrkov, A.; Aliper, A.; Bezrukov, D.; Lin, Y.-C.; Polykovskiy, D.; Kamya, P.; Ren, F.; Zhavoronkov, A. Quantum computing for near-term applications in generative chemistry and drug discovery. *Drug Discov. Today* **2023**, *28*, 103675. [CrossRef]
169. Liu, J.-G.; Wang, L. Differentiable learning of quantum circuit Born machines. *Phys. Rev. A* **2018**, *98*, 062324. [CrossRef]
170. Pfau, D.; Axelrod, S.; Sutterud, H.; von Glehn, I.; Spencer, J.S. Accurate computation of quantum excited states with neural networks. *Science* **2024**, *385*, eadn0137. [CrossRef] [PubMed]
171. Sudarsanan Ragini, N.; Sazim, S. Higher-order incompatibility improves distinguishability of causal quantum networks. *New J. Phys.* **2024**, *26*, 123003. [CrossRef]
172. Zheng, K.; Fu, T.; Liang, Z. QCS-ADME: Quantum Circuit Search for Drug Property Prediction with Imbalanced Data and Regression Adaptation. *arXiv* **2025**, arXiv:2503.01927. [CrossRef]
173. Rath, M.; Date, H. Quantum Inspired Encoding Strategies for Machine Learning Models: Proposing and Evaluating Instance Level, Global Discrete, and Class Conditional Representations. *arXiv* **2025**, arXiv:2507.00019.

174. Alizadehsani, R.; Oyelere, S.S.; Hussain, S.; Jagatheesaperumal, S.K.; Calixto, R.R.; Rahouti, M. Explainable Artificial Intelligence for Drug Discovery and Development: A Comprehensive Survey. *IEEE Access* **2024**, *12*, 35796–35812. [CrossRef]
175. Salih, A.M.; Raisi-Estabragh, Z.; Galazzo, I.B.; Radeva, P.; Petersen, S.E.; Lekadir, K.; Menegaz, G. A Perspective on Explainable Artificial Intelligence Methods: SHAP and LIME. *Adv. Intell. Syst.* **2025**, *7*, 2400304. [CrossRef]
176. Wang, Q.; He, M.; Guo, L.; Chai, H. AFEI: Adaptive optimized vertical federated learning for heterogeneous multi-omics data integration. *Brief. Bioinform.* **2023**, *24*, bbad269. [CrossRef] [PubMed]
177. Fehlis, Y.; Mandel, P.; Crain, C.; Liu, B.; Fuller, D. Accelerating drug discovery with Artificial: A whole-lab orchestration and scheduling system for self-driving labs. *arXiv* **2025**, arXiv:2504.00986.
178. Häse, F.; Roch, L.M.; Aspuru-Guzik, A. Next-Generation Experimentation with Self-Driving Laboratories. *Trends Chem.* **2019**, *1*, 282–291. [CrossRef]
179. El Arab, R.A.; Abu-Mahfouz, M.S.; Abuadas, F.H.; Alzghoul, H.; Almari, M.; Ghannam, A.; Seweid, M.M. Bridging the Gap: From AI Success in Clinical Trials to Real-World Healthcare Implementation-A Narrative Review. *Healthcare* **2025**, *13*, 701. [CrossRef]
180. Babbush, R.; Huggins, W.J.; Berry, D.W.; Ung, S.F.; Zhao, A.; Reichman, D.R.; Neven, H.; Baczewski, A.D.; Lee, J. Quantum simulation of exact electron dynamics can be more efficient than classical mean-field methods. *Nat. Commun.* **2023**, *14*, 4058. [CrossRef]
181. Lappala, A. The next revolution in computational simulations: Harnessing AI and quantum computing in molecular dynamics. *Curr. Opin. Struct. Biol.* **2024**, *89*, 102919. [CrossRef]
182. Ahmed, M.; Maldonado, A.M.; Durrant, J.D. From byte to bench to bedside: Molecular dynamics simulations and drug discovery. *BMC Biol.* **2023**, *21*, 299. [CrossRef]
183. Mahdi, G.; Alamdary, A.; Kaghazian, H.; Ahmadi, N.; Mardani, R.; Gholami, A. Biopharmaceutical Analysis by HPLC: Practices and Challenges. *Chonnam Med. J.* **2025**, *61*, 19. [CrossRef] [PubMed]
184. Pienaar, E.; Theron, M.; Nelson, M.; Viljoen, H.J. A quantitative model of error accumulation during PCR amplification. *Comput. Biol. Chem.* **2006**, *30*, 102–111. [CrossRef]
185. Moinard, S.; Piau, D.; Laporte, F.; Rioux, D.; Taberlet, P.; Gonindard-Melodelima, C.; Coissac, E. Towards quantitative DNA Metabarcoding: A method to overcome PCR amplification bias. *bioRxiv* **2023**. [CrossRef]
186. Kiepas, A.; Voorand, E.; Mubaid, F.; Siegel, P.M.; Brown, C.M. Optimizing live-cell fluorescence imaging conditions to minimize phototoxicity. *J. Cell Sci.* **2020**, *133*, jcs242834. [CrossRef]
187. Godin, A.G.; Lounis, B.; Cognet, L. Super-resolution microscopy approaches for live cell imaging. *Biophys. J.* **2014**, *107*, 1777–1784. [CrossRef] [PubMed]
188. Mohs, R.C.; Greig, N.H. Drug discovery and development: Role of basic biological research. *Alzheimer's Dement.* **2017**, *3*, 651–657. [CrossRef] [PubMed]
189. Farid, S.S.; Baron, M.; Stamatis, C.; Nie, W.; Coffman, J. Benchmarking biopharmaceutical process development and manufacturing cost contributions to R&D. *MAbs* **2020**, *12*, 1754999. [CrossRef] [PubMed]
190. Pérez, I.; Krueger, A.; Wrachtrup, J.; Jelezko, F.; Börsch, M. Single NV Center in Nanodiamond for Quantum Sensing of Protein Dynamics in AN ABEL Trap. In Proceedings of the Single Molecule Spectroscopy and Superresolution Imaging XVII, San Francisco, CA, USA, 27 January–1 February 2024.
191. Noh, T.; Kindseth, A.; Chandrasekhar, V. Nonlocal superconducting quantum interference device. *Phys. Rev. B* **2021**, *104*, 064503. [CrossRef]
192. Bao, B.; Hua, Y.; Wang, R.; Li, D. Quantum-Based Magnetic Field Sensors for Biosensing. *Adv. Quantum Technol.* **2023**, *6*, 2200146. [CrossRef]
193. Modicano, P.; Trutschel, M.; Phan-Xuan, T.; Matarèse, B.F.E.; Urbano, L.; Green, M.; Mäder, K.; Dailey, L.A. Does Encapsulation of π-Conjugated Polymer Nanoparticles within Biodegradable PEG–PLGA Matrices Mitigate Photoinduced Free Radical Production and Phototoxicity? *Adv. Ther.* **2025**, *8*, 2400190. [CrossRef]
194. Feyen, P.L.C.; Matarèse, B.F.E.; Urbano, L.; Abelha, T.F.; Rahmoune, H.; Green, M.; Dailey, L.A.; de Mello, J.C.; Benfenati, F. Photosensitized and Photothermal Stimulation of Cellular Membranes by Organic Thin Films and Nanoparticles. *Front. Bioeng. Biotechnol.* **2022**, *10*, 932877. [CrossRef]
195. Rondin, L.; Tetienne, J.P.; Hingant, T.; Roch, J.-F.; Maletinsky, P.; Jacques, V. Magnetometry with nitrogen-vacancy defects in diamond. *Rep. Prog. Phys.* **2014**, *77*, 056503. [CrossRef] [PubMed]
196. Rodríguez, D. A quantum sensor for high-performance mass spectrometry. *Appl. Phys. B* **2012**, *107*, 1031–1042. [CrossRef]
197. Cautereels, J.; Blockhuys, F. Quantum Chemical Mass Spectrometry: Verification and Extension of the Mobile Proton Model for Histidine. *J. Am. Soc. Mass Spectrom.* **2017**, *28*, 1227–1235. [CrossRef]
198. Sarkar, A.; Jones, Z.R.; Parashar, M.; Druga, E.; Akkiraju, A.; Conti, S.; Krishnamoorthi, P.; Nachuri, S.; Aman, P.; Hashemi, M.; et al. High-precision chemical quantum sensing in flowing monodisperse microdroplets. *Sci. Adv.* **2024**, *10*, eadp4033. [CrossRef]
199. Fujiwara, M. Diamond quantum sensors in microfluidics technology. *Biomicrofluidics* **2023**, *17*, 054107. [CrossRef]

200. Lucivero, V.G.; Jiménez-Martínez, R.; Kong, J.; Mitchell, M.W. Squeezed-light spin noise spectroscopy. *Phys. Rev. A* **2016**, *93*, 053802. [CrossRef]
201. Tsao, C.; Ling, H.; Hinkle, A.; Chen, Y.; Jha, K.K.; Yan, Z.-L.; Utzat, H. Enhancing spectroscopy and microscopy with emerging methods in photon correlation and quantum illumination. *Nat. Nanotechnol.* **2025**, *20*, 1001–1016. [CrossRef] [PubMed]
202. Prajapati, N.; Niu, Z.; Novikova, I. Quantum-enhanced two-photon spectroscopy using two-mode squeezed light. *Opt. Lett.* **2021**, *46*, 1800. [CrossRef]
203. Zafar, A.; Takeda, C.; Manzoor, A.; Tanaka, D.; Kobayashi, M.; Wadayama, Y.; Nakane, D.; Majeed, A.; Iqbal, M.A.; Akitsu, T. Towards Industrially Important Applications of Enhanced Organic Reactions by Microfluidic Systems. *Molecules* **2024**, *29*, 398. [CrossRef] [PubMed]
204. Goutham, R.; Gopinath, K.P.; Ramprasath, A.; Srikanth, B.; Narayan, R.B. *High-Performance Photocatalysts for Organic Reactions*; Springer: Cham, Switzerland, 2019; pp. 219–270.
205. Levin, L.; Skomorowski, W.; Rybak, L.; Kosloff, R.; Koch, C.P.; Amitay, Z. Coherent Control of Bond Making. *Phys. Rev. Lett.* **2015**, *114*, 233003. [CrossRef]
206. Leibscher, M.; Pozzoli, E.; Pérez, C.; Schnell, M.; Sigalotti, M.; Boscain, U.; Koch, C.P. Full quantum control of enantiomer-selective state transfer in chiral molecules despite degeneracy. *Commun. Phys.* **2022**, *5*, 110. [CrossRef]
207. Furusho, Y.; Yagi, R.; Suda, M.; Maruhashi, T.; Takagi, I.; Kayanuma, Y.; Minami, F.; Nakamura, K.G. Ultrafast quantum-path interferometry of photo-absorption involving excitons in a GaAs multiple-quantum-well structure. *Solid State Commun.* **2023**, *360*, 115056. [CrossRef]
208. Camlik, G.; Bilakaya, B.; Güven, G.K.; Akkol, E.K.; Degim, Z.; Sobarzo-Sánchez, E.; Degim, I.T. Quantum Drugs (Q-Drugs): A New Discovery and Taboo Breaking Approach; Producing Carbon Quantum Dots from Drug Molecules. *Pharmaceuticals* **2025**, *18*, 767. [CrossRef]
209. Hartwig, S.; Albrecht, H.H.; Scheer, H.J.; Burghoff, M.; Trahms, L. A Superconducting Quantum Interference Device Measurement System for Ultra Low-Field Nuclear Magnetic Resonance. *Appl. Magn. Reson.* **2013**, *44*, 9–22. [CrossRef]
210. Vasyukov, D.; Anahory, Y.; Embon, L.; Halbertal, D.; Cuppens, J.; Neeman, L.; Finkler, A.; Segev, Y.; Myasoedov, Y.; Rappaport, M.L.; et al. A scanning superconducting quantum interference device with single electron spin sensitivity. *Nat. Nanotechnol.* **2013**, *8*, 639–644. [CrossRef] [PubMed]
211. Yong, K.T.; Wang, Y.; Roy, I.; Rui, H.; Swihart, M.T.; Law, W.-C.; Kwak, S.K.; Ye, L.; Liu, J.; Mahajan, S.D.; et al. Preparation of quantum dot/drug nanoparticle formulations for traceable targeted delivery and therapy. *Theranostics* **2012**, *2*, 681–694. [CrossRef] [PubMed]
212. Magann, A.B.; Grace, M.D.; Rabitz, H.A.; Sarovar, M. Digital quantum simulation of molecular dynamics and control. *Phys. Rev. Res.* **2021**, *3*, 023165. [CrossRef]
213. Gircha, A.I.; Boev, A.S.; Avchaciov, K.; Fedichev, P.O.; Fedorov, A.K. Hybrid quantum-classical machine learning for generative chemistry and drug design. *Sci. Rep.* **2023**, *13*, 8250. [CrossRef]
214. Wang, L.; Zhou, Z.; Yang, X.; Shi, S.; Zeng, X.; Cao, D. The present state and challenges of active learning in drug discovery. *Drug Discov. Today* **2024**, *29*, 103985. [CrossRef]
215. Kadam, E.A.J.J.; Kharmate, G.M.; Jadhav, M.R.; Howal, S.A.; Pandit, V.U. Quantum Machine Learning Technique for Automatic Retrosynthetic Reaction Pathway Search Method. *Int. J. Recent Innov. Trends Comput. Commun.* **2023**, *11*, 2111–2122. [CrossRef]
216. Zhou, Y.; Chen, J.; Cheng, J.; Cao, X.; Zhang, Y.; Karemore, G.; Zitnik, M.; Chong, F.T.; Liu, J.; Fu, T.; et al. Quantum-Machine-Assisted Drug Discovery: Survey and Perspective. *arXiv* **2025**, arXiv:2408.13479.
217. Banchi, L.; Fingerhuth, M.; Babej, T.; Ing, C.; Arrazola, J.M. Molecular docking with Gaussian Boson Sampling. *Sci. Adv.* **2020**, *6*, eaax1950. [CrossRef]
218. Niu, Z.; Xiao, X.; Wu, W.; Cai, Q.; Jiang, Y.; Jin, W.; Wang, M.; Yang, G.; Kong, L.; Jin, X.; et al. PharmaBench: Enhancing ADMET benchmarks with large language models. *Sci. Data* **2024**, *11*, 985. [CrossRef]
219. Tran, T.T.; Van Tayara, H.; Chong, K.T. Recent Studies of Artificial Intelligence on In Silico Drug Absorption. *J. Chem. Inf. Model.* **2023**, *63*, 6198–6211. [CrossRef]
220. Speybroeck, V.; Van Gani, R.; Meier, R.J. The calculation of thermodynamic properties of molecules. *Chem. Soc. Rev.* **2010**, *39*, 1764–1779. [CrossRef] [PubMed]
221. Ali, R.S.A.E.; Meng, J.; Khan, M.E.I.; Jiang, X. Machine learning advancements in organic synthesis: A focused exploration of artificial intelligence applications in chemistry. *Artif. Intell. Chem.* **2024**, *2*, 100049. [CrossRef]
222. Bogojeski, M.; Vogt-Maranto, L.; Tuckerman, M.E.; Müller, K.-R.; Burke, K. Quantum chemical accuracy from density functional approximations via machine learning. *Nat. Commun.* **2020**, *11*, 5223. [CrossRef]
223. Zhuang, M.; Chen, S.; Huang, J.; Lee, C. Quantum lock-in measurement of weak alternating signals. *Quantum Front.* **2024**, *3*, 4. [CrossRef]
224. Qi, J.; Ko, T.W.; Wood, B.C.; Pham, T.A.; Ong, S.P. Robust training of machine learning interatomic potentials with dimensionality reduction and stratified sampling. *npj Comput. Mater.* **2024**, *10*, 43. [CrossRef]

225. Bannigan, P.; Aldeghi, M.; Bao, Z.; Häse, F.; Aspuru-Guzik, A.; Allen, C. Machine learning directed drug formulation development. *Adv. Drug Deliv. Rev.* **2021**, *175*, 113806. [CrossRef]
226. Wang, Y.; Hu, Z.; Chang, J.; Yu, B. Thinking on the Use of Artificial Intelligence in Drug Discovery. *J. Med. Chem.* **2025**, *68*, 4996–4999. [CrossRef]
227. Zhang, X.; Deng, H.; Wu, R.; Ren, J.; Ren, Y. PQSF: Post-quantum secure privacy-preserving federated learning. *Sci. Rep.* **2024**, *14*, 23553. [CrossRef]
228. Morin, L.; Weber, V.; Meijer, G.I.; Yu, F.; Staar, P.W.J. PatCID: An open-access dataset of chemical structures in patent documents. *Nat. Commun.* **2024**, *15*, 6532. [CrossRef]
229. Saratkar, S.Y.; Langote, M.; Kumar, P.; Gote, P.; Weerarathna, I.; Mishra, G. Digital twin for personalized medicine development. *Front. Digit. Health* **2025**, *7*, 1583466. [CrossRef]
230. Khater, T.; Alkhatib, S.A.; AlShehhi, A.; Pitsalidis, C.; Pappa, A.; Ngo, S.; Chan, V.; Truong, V. Generative artificial intelligence based models optimization towards molecule design enhancement. *J. Cheminform.* **2025**, *17*, 116. [CrossRef] [PubMed]
231. Udrescu, S.M.; Tegmark, M. AI Feynman: A physics-inspired method for symbolic regression. *Sci. Adv.* **2020**, *6*, eaay2631. [CrossRef] [PubMed]
232. Xu, T.; Zhao, J.; Xiong, M. Graphical Learning and Causal Inference for Drug Repurposing. *medRxiv* **2023**. [CrossRef] [PubMed]
233. Wang, G.; Wang, C.; Zhang, X.; Li, Z.; Zhou, J.; Sun, Z. Machine learning interatomic potential: Bridge the gap between small-scale models and realistic device-scale simulations. *iScience* **2024**, *27*, 109673. [CrossRef]
234. Della Pia, F.; Shi, B.X.; Kapil, V.; Zen, A.; Alfè, D.; Michaelides, A. Accurate and efficient machine learning interatomic potentials for finite temperature modelling of molecular crystals. *Chem. Sci.* **2025**, *16*, 11419–11433. [CrossRef]
235. Lin, J.C.; Glover, Z.K.; Sreedhara, A. Assessing the Utility of Circular Dichroism and FTIR Spectroscopy in Monoclonal-Antibody Comparability Studies. *J. Pharm. Sci.* **2015**, *104*, 4459–4466. [CrossRef]
236. Schlawin, F.; Gessner, M. Theory of Quantum-Enhanced Stimulated Raman Scattering. *arXiv* **2025**, arXiv:2502.19344. [CrossRef]
237. Kalashnikov, D.A.; Pan, Z.; Kuznetsov, A.I.; Krivitsky, L.A. Quantum Spectroscopy of Plasmonic Nanostructures. *Phys. Rev. X* **2014**, *4*, 011049. [CrossRef]
238. Michoel, T.; Zhang, J.D. Causal inference in drug discovery and development. *Drug Discov. Today* **2023**, *28*, 103737. [CrossRef]
239. Deepasree, K.; Venugopal, S. Molecular docking and molecular dynamic simulation studies to identify potential terpenes against Internalin A protein of Listeria monocytogenes. *Front. Bioinform.* **2024**, *4*, 1463750. [CrossRef] [PubMed]
240. Liu, S.; An, J.; Zhao, J.; Zhao, S.; Lv, H.; Wang, S. Drug-Target Interaction Prediction Based on Multisource Information Weighted Fusion. *Contrast Media Mol. Imaging* **2021**, *2021*, 6044256. [CrossRef]
241. Heifetz, A. *Accelerating COVID-19 Drug Discovery with High-Performance Computing*; Humana: New York, NY, USA, 2024; pp. 405–411.
242. Švajger, U.; Horvat, Ž.; Knez, D.; Rožman, P.; Turk, S.; Gobec, S. New antagonists of toll-like receptor 7 discovered through 3D ligand-based virtual screening. *Med. Chem. Res.* **2015**, *24*, 362–371. [CrossRef]
243. Belsley, A. Quantum-Enhanced Absorption Spectroscopy with Bright Squeezed Frequency Combs. *Phys. Rev. Lett.* **2023**, *130*, 133602. [CrossRef] [PubMed]
244. Brad, S. Enhancing Creativity in Deep Learning Models with SAVE-Inspired Activation Functions. In *IFIP Advances in Information and Communication Technology*; Springer: Cham, Switzerland, 2023.
245. Pal, S.; Bhattacharya, M.; Lee, S.S.; Chakraborty, C. Quantum Computing in the Next-Generation Computational Biology Landscape: From Protein Folding to Molecular Dynamics. *Mol. Biotechnol.* **2024**, *66*, 163–178. [CrossRef]
246. Miessen, A.; Ollitrault, P.J.; Tacchino, F.; Tavernelli, I. Quantum algorithms for quantum dynamics. *Nat. Comput. Sci.* **2022**, *3*, 25–37. [CrossRef]
247. Day, E.C.; Chittari, S.S.; Bogen, M.P.; Knight, A.S. Navigating the Expansive Landscapes of Soft Materials: A User Guide for High-Throughput Workflows. *ACS Polym. Au* **2023**, *3*, 406–427. [CrossRef]
248. Shapira, L.; Lerner, S.; Assayag, G.; Vardi, A.; Haham, D.; Bar, G.; Kozokaro, V.; Robicsek, M.; Lerner, I.; Michaeli, A. Discovery of novel spike/ACE2 inhibitory macrocycles using in silico reinforcement learning. *Front. Drug Discov.* **2022**, *2*, 1085701. [CrossRef]
249. Lee, T.-S.; Hu, Y.; Sherborne, B.; Guo, Z.; York, D.M. Toward Fast and Accurate Binding Affinity Prediction with pmemdGTI: An Efficient Implementation of GPU-Accelerated Thermodynamic Integration. *J. Chem. Theory Comput.* **2017**, *13*, 3077–3084. [CrossRef]
250. Ye, C.; Sun, Y.; Zhang, X. Entanglement-Assisted Quantum Chiral Spectroscopy. *J. Phys. Chem. Lett.* **2021**, *12*, 8591–8597. [CrossRef] [PubMed]
251. Cheng, X.; Miao, T.; Qian, Y.; Zhang, Z.; Zhang, W.; Zhu, X. Supramolecular Chirality in Azobenzene-Containing Polymer System: Traditional Postpolymerization Self-Assembly Versus In Situ Supramolecular Self-Assembly Strategy. *Int. J. Mol. Sci.* **2020**, *21*, 6186. [CrossRef]
252. Gupta, A.; Dey, S.; Hicks, A.; Zhou, H.-X. Artificial intelligence guided conformational mining of intrinsically disordered proteins. *Commun. Biol.* **2022**, *5*, 610. [CrossRef]

253. Richardson, J.O. Nonadiabatic Tunneling in Chemical Reactions. *J. Phys. Chem. Lett.* **2024**, *15*, 7387–7397. [CrossRef] [PubMed]
254. Das, S.; Mazumdar, H.; Khondakar, K.R.; Mishra, Y.; Kaushik, A. Review—Quantum Biosensors: Principles and Applications in Medical Diagnostics. *ECS Sens. Plus* **2024**, *3*, 025001. [CrossRef]
255. Jinich, A.; Rappoport, D.; Dunn, I.; Sanchez-Lengeling, B.; Olivares-Amaya, R.; Noor, E.; Bar Even, A.; Aspuru-Guzik, A. Quantum Chemical Approach to Estimating the Thermodynamics of Metabolic Reactions. *Sci. Rep.* **2014**, *4*, 7022. [CrossRef] [PubMed]
256. Vidossich, P.; De Vivo, M. The role of first principles simulations in studying (bio)catalytic processes. *Chem. Catal.* **2021**, *1*, 69–87. [CrossRef]
257. Sagar Shrikrishna, N.; Sharma, R.; Sahoo, J.; Kaushik, A.; Gandhi, S. Navigating the landscape of optical biosensors. *Chem. Eng. J.* **2024**, *490*, 151661. [CrossRef]
258. Aly, S.M.; Fathi, M. Advancing aquaculture biosecurity: A scientometric analysis and future outlook for disease prevention and environmental sustainability. *Aquac. Int.* **2024**, *32*, 8763–8789. [CrossRef]
259. Yu, T.; Guo, H. Understanding Enzyme Catalysis Mechanism Using QM/MM Simulation Methods. *Mech. Enzymol. Bridg. Struct. Funct.* **2020**, *1357*, 121–137.
260. Hernandez, A.B.; Cortés-Arriagada, D.; García, H.C.; Anota, E.; Villanueva, M. Quantum molecular study on doping effect in titanium and vanadium clusters: Their application to remove some chemical species. *Appl. Nanosci.* **2020**, *10*, 37–49. [CrossRef]
261. Wang, T.; He, X.; Li, M.; Li, Y.; Bi, R.; Wang, Y.; Cheng, C.; Shen, X.; Meng, J.; Zhang, H.; et al. Ab initio characterization of protein molecular dynamics with AI2BMD. *Nature* **2024**, *635*, 1019–1027. [CrossRef]
262. Li, X.; Huo, P. Investigating Tunneling-Controlled Chemical Reactions through Ab Initio Ring Polymer Molecular Dynamics. *J. Phys. Chem. Lett.* **2021**, *12*, 6714–6721. [CrossRef]
263. Wen, J.; Mai, S.; González, L. Excited-State Dynamics Simulations of a Light-Driven Molecular Motor in Solution. *J. Phys. Chem. A* **2023**, *127*, 9520–9529. [CrossRef]
264. Thürlemann, M.; Riniker, S. Hybrid classical/machine-learning force fields for the accurate description of molecular condensed-phase systems. *Chem. Sci.* **2023**, *14*, 12661–12675. [CrossRef] [PubMed]
265. Lin, F.-Y.; MacKerell, A.D. Force Fields for Small Molecules. *Methods Mol. Biol.* **2019**, *2022*, 21–54. [CrossRef]
266. Skogh, M.; Dobrautz, W.; Lolur, P.; Warren, C.; Biznárová, J.; Osman, A.; Tancredi, G.; Bylander, J.; Rahm, M. The electron density: A fidelity witness for quantum computation. *Chem. Sci.* **2024**, *15*, 2257–2265. [CrossRef] [PubMed]
267. Niazi, S.K. The Quantum Paradox in Pharmaceutical Science: Understanding Without Comprehending—A Centennial Reflection. *Int. J. Mol. Sci.* **2025**, *26*, 4658. [CrossRef] [PubMed]
268. Zhang, Y.-L.; Li, B. Reliability of Computing van der Waals Bond Lengths of Some Rare Gas Diatomics. *Int. J. Mol. Sci.* **2022**, *23*, 13944. [CrossRef] [PubMed]
269. Świderek, K.; Bertran, J.; Zinovjev, K.; Tuñón, I.; Moliner, V. Advances in the Simulations of Enzyme Reactivity in the Dawn of the Artificial Intelligence Age. *WIREs Comput. Mol. Sci.* **2025**, *15*, e70003. [CrossRef]
270. Tiwari, A.; Honingh, C.; Ensing, B. Accurate calculation of zero point energy from molecular dynamics simulations of liquids and their mixtures. *J. Chem. Phys.* **2019**, *151*, 244124. [CrossRef] [PubMed]
271. Bakowies, D.; Von Lilienfeld, O.A. Density Functional Geometries and Zero-Point Energies in Ab Initio Thermochemical Treatments of Compounds with First-Row Atoms (H, C, N, O, F). *J. Chem. Theory Comput.* **2021**, *17*, 4872–4890. [CrossRef] [PubMed]
272. Karandashev, K.; Xu, Z.-H.; Meuwly, M.; Vaníček, J.; Richardson, J. Kinetic isotope effects and how to describe them. *Struct. Dyn.* **2017**, *4*, 061501. [CrossRef]
273. Dale, H.J.A.; Leach, A.G.; Lloyd-Jones, G.C. Heavy-Atom Kinetic Isotope Effects: Primary Interest or Zero Point? *J. Am. Chem. Soc.* **2021**, *143*, 21079–21099. [CrossRef]
274. Choi, D.-J.; Phark, S.; Heinrich, A.J.; Lorente, N. Electron spin resonance with scanning tunneling microscopy: A tool for an on-surface quantum platform of identical qubits. *Nanoscale Adv.* **2025**, *7*, 4551–4558. [CrossRef]
275. Hishikawa, A.; Matsuda, A.; Fushitani, M. Ultrafast reaction imaging and control by ultrashort intense laser pulses. *Bull. Chem. Soc. Jpn.* **2020**, *93*, 1293–1304. [CrossRef]
276. Lorenz, R. Quantum causal models: The merits of the spirit of Reichenbach's principle for understanding quantum causal structure. *Synthese* **2022**, *200*, 424. [CrossRef]
277. Alvarez-Mendoza, R.; Uboldi, L.; Lyons, A.; Cogdell, R.; Cerullo, G.; Faccio, D. Entangled-photon time- and frequency-resolved optical spectroscopy. *arXiv* **2025**, arXiv:2505.02940.
278. Walling, M.A.; Novak, J.A.; Shepard, J.R.E. Quantum Dots for Live Cell and In Vivo Imaging. *Int. J. Mol. Sci.* **2009**, *10*, 441–491. [CrossRef] [PubMed]
279. Yukawa, H.; Kono, H.; Ishiwata, H.; Igarashi, R.; Takakusagi, Y.; Arai, S.; Hirano, Y.; Suhara, T.; Baba, Y. Quantum life science: Biological nano quantum sensors, quantum technology-based hyperpolarized MRI/NMR, quantum biology, and quantum biotechnology. *Chem. Soc. Rev.* **2025**, *54*, 3293–3322. [CrossRef] [PubMed]

280. Nagarajan, K.; Thomas, A.; Ebbesen, T.W. Chemistry under Vibrational Strong Coupling. *J. Am. Chem. Soc.* **2021**, *143*, 16877–16889. [CrossRef]
281. Lindoy, L.P.; Mandal, A.; Reichman, D.R. Quantum dynamical effects of vibrational strong coupling in chemical reactivity. *Nat. Commun.* **2023**, *14*, 2733. [CrossRef] [PubMed]
282. Shen, Y.-Y.; Wang, B.; Ke, D.-Q.; Zheng, D.-D.; Li, Z.-H.; Wen, H.-F.; Guo, H.; Li, X.; Tang, J.; Ma, Z.-M.; et al. High-frequency resolution diamond nitrogen-vacancy center wide-spectrum imaging technology. *Acta Phys. Sin.* **2024**, *73*, 067601. [CrossRef]
283. Hiura, H.; Shalabney, A.; George, J. Cavity Catalysis—Accelerating Reactions under Vibrational Strong Coupling. *ChemRxiv* **2018**. Available online: https://chemrxiv.org/engage/chemrxiv/article-details/60c759bd0f50db605439873c (accessed on 6 January 2026).
284. Burd, S.C.; Bagheri, N.; Ingaramo, M.; Condon, A.F.; Mondal, S.; Dowlatshahi, D.P.; Summers, J.A.; Mukherjee, S.; York, A.G.; Wakatsuki, S.; et al. Magnetic resonance control of reaction yields through genetically-encoded protein:flavin spin-correlated radicals in a live animal. *bioRxiv* **2025**. [CrossRef]
285. von Burg, V.; Low, G.H.; Häner, T.; Steiger, D.S.; Reiher, M.; Roetteler, M.; Troyer, M. Quantum computing enhanced computational catalysis. *Phys. Rev. Res.* **2021**, *3*, 033055. [CrossRef]
286. Cheng, Y.; Ling, S.; Geng, Y.; Wang, Y.; Xu, J. Microfluidic synthesis of quantum dots and their applications in bio-sensing and bio-imaging. *Nanoscale Adv.* **2021**, *3*, 2180–2195. [CrossRef]
287. Freddolino, L.; Harrison, C.B.; Liu, Y.; Schulten, K. Challenges in protein folding simulations: Timescale, representation, and analysis. *Nat. Phys.* **2010**, *6*, 751–758. [CrossRef]
288. Samantray, S.; Schumann, W.; Illig, A.M.; Carballo-Pacheco, M.; Paul, A.; Barz, B.; Strodel, B. Molecular Dynamics Simulations of Protein Aggregation: Protocols for Simulation Setup and Analysis with Markov State Models and Transition Networks. In *Methods in Molecular Biology*; Humana: New York, NY, USA, 2022.
289. Wang, W.; Singh, S.K.; Li, N.; Toler, M.R.; King, K.R.; Nema, S. Immunogenicity of protein aggregates—Concerns and realities. *Int. J. Pharm.* **2012**, *431*, 1–11. [CrossRef]
290. Gillet, J.N. From molecular dynamics to quantum mechanics of misfolded proteins and amyloid-like macroaggregates applied to neurodegenerative diseases. *J. Mol. Graph. Model.* **2022**, *110*, 108046. [CrossRef] [PubMed]
291. Wong, R.; Chang, W.L. Fast quantum algorithm for protein structure prediction in hydrophobic-hydrophilic model. *J. Parallel Distrib. Comput.* **2022**, *164*, 178–190. [CrossRef]
292. Noshay, J.M.; Walker, T.; Alexander, W.G.; Klingeman, D.M.; Romero, J.; Walker, A.M.; Prates, E.; Eckert, C.; Irle, S.; Kainer, D.; et al. Quantum biological insights into CRISPR-Cas9 sgRNA efficiency from explainable-AI driven feature engineering. *Nucleic Acids Res.* **2023**, *51*, 10147–10161. [CrossRef] [PubMed]
293. Wang, Y.; Zhou, X. Efficient quantum algorithm for lattice protein folding. *Quantum Sci. Technol.* **2025**, *10*, 015056. [CrossRef]
294. Sarkar, M.; Roy, L.; Gutal, A.; Kumar, A.; Paranjothy, M. Quantum Simulations of Chemical Reactions: Achieving Accuracy with NISQ Devices. *arXiv* **2025**, arXiv:2503.12084. [CrossRef]
295. Guan, H.; Sun, H.; Zhao, X. Application of Density Functional Theory to Molecular Engineering of Pharmaceutical Formulations. *Int. J. Mol. Sci.* **2025**, *26*, 3262. [CrossRef]
296. Bartlett, R.J.; Musiał, M. Coupled-cluster theory in quantum chemistry. *Rev. Mod. Phys.* **2007**, *79*, 291–352. [CrossRef]
297. Vimal, D. PIMA Diabetes Prediction Using Machine Learning and Quantum Machine Learning Techniques. In Proceedings of the 2024 ITU Kaleidoscope: Innovation and Digital Transformation for a Sustainable World (ITU K), New Delhi, India, 21–23 October 2024; IEEE: Piscataway, NJ, USA, 2024; pp. 1–7.
298. Senthil, G.A.; Monica, K.M.; Prabha, R.; Prinslin, L.; Elavarasi, R. Quantum AI: A Cognitive Machine Learning Technique based on Nurturing Food Security Sustainability Predictive Analysis for Life Science—Bioengineering in Healthcare. *BIO Web Conf.* **2025**, *172*, 02002. [CrossRef]
299. Neuling, N.R.; Allert, R.D.; Bucher, D.B. Prospects of single-cell nuclear magnetic resonance spectroscopy with quantum sensors. *Curr. Opin. Biotechnol.* **2023**, *83*, 102975. [CrossRef]
300. Zaporski, L.; Liu, Q.; Velez, G.; Radzihovsky, M.; Li, Z.; Colombo, S.; Pedrozo-Peñafiel, E.; Vuletić, V. Quantum-amplified global-phase spectroscopy on an optical clock transition. *Nature* **2025**, *646*, 309–314. [CrossRef]
301. Wu, W.; Davis, E.J.; Hughes, L.B.; Ye, B.; Wang, Z.; Kufel, D.; Ono, T.; Meynell, S.A.; Block, M.; Liu, C.; et al. Spin squeezing in an ensemble of nitrogen–vacancy centres in diamond. *Nature* **2025**, *646*, 74–80. [CrossRef]
302. Dietze, K.; Pelzer, L.; Krinner, L.; Dawel, F.; Kramer, J.; Spethmann, N.C.H.; Kielinski, T.; Hammerer, K.; Stahl, K.; Klose, J.; et al. Entanglement-Enhanced Optical Ion Clock. *arXiv* **2025**, arXiv:2506.11810. [CrossRef]
303. Marques, J.M.C.; Prudente, F.V.; Pirani, F. Intermolecular Forces: From Atoms and Molecules to Nanostructures. *Molecules* **2022**, *27*, 3072. [CrossRef] [PubMed]
304. Ritter, S.K. The art of the chemical bond. *ACS Cent. Sci.* **2016**, *2*, 769–772. [CrossRef]
305. Korchef, A. Chemical Bonding and Molecular Geometry. In *Understanding General Chemistry*; CRC Press: Boca Raton, FL, USA, 2022.

306. Akman, F.; Demirpolat, A.; Kazachenko, A.S.; Kazachenko, A.S.; Issaoui, N.; Al-Dossary, O. Molecular Structure, Electronic Properties, Reactivity (ELF, LOL, and Fukui), and NCI-RDG Studies of the Binary Mixture of Water and Essential Oil of Phlomis bruguieri. *Molecules* **2023**, *28*, 2684. [CrossRef]
307. Ng, S.; Masarone, S.; Watson, D.; Barnes, M.R. The benefits and pitfalls of machine learning for biomarker discovery. *Cell Tissue Res.* **2023**, *394*, 17–31. [CrossRef] [PubMed]
308. Liu, C.; Denzler, L.; Chen, Y.; Martin, A.; Paige, B. AsEP: Benchmarking Deep Learning Methods for Antibody-specific Epitope Prediction. *arXiv* **2024**, arXiv:2407.18184.
309. Zeng, X.; Bai, G.; Sun, C.; Ma, B. Recent Progress in Antibody Epitope Prediction. *Antibodies* **2023**, *12*, 52. [CrossRef]
310. Hearty, S.; Leonard, P.; O'Kennedy, R. Measuring Antibody-Antigen Binding Kinetics Using Surface Plasmon Resonance. In *Antibody Engineering*; Humana Press: Totowa, NJ, USA, 2018; pp. 421–455. [CrossRef]
311. Wu, K.; Vedelaar, T.A.; Damle, V.G.; Morita, A.; Mougnaud, J.; Martin, C.R.S.; Zhang, Y.; van der Pol, D.P.I.; Ende-Metselaar, H.; Rodenhuis-Zybert, I.; et al. Applying NV center-based quantum sensing to study intracellular free radical response upon viral infections. *Redox Biol.* **2022**, *52*, 102279. [CrossRef]
312. Zheng, Y.; Song, K.; Cai, K.; Liu, L.; Tang, D.; Long, W.; Zhai, B.; Chen, J.; Tao, Y.; Zhao, Y.; et al. B-Cell-Epitope-Based Fluorescent Quantum Dot Biosensors for SARS-CoV-2 Enable Highly Sensitive COVID-19 Antibody Detection. *Viruses* **2022**, *14*, 1031. [CrossRef]
313. Robert, A.; Barkoutsos, P.K.; Woerner, S.; Tavernelli, I. Resource-efficient quantum algorithm for protein folding. *npj Quantum Inf.* **2021**, *7*, 38. [CrossRef]
314. Náray-Szabó, G.; Oláh, J.; Krámos, B. Quantum Mechanical Modeling: A Tool for the Understanding of Enzyme Reactions. *Biomolecules* **2013**, *3*, 662–702. [CrossRef]
315. Tong, X.; Shi, S.; Tong, C.; Iftikhar, A.; Long, R.; Zhu, Y. Quantum/carbon dots-based fluorescent assays for enzyme activity. *TrAC Trends Anal. Chem.* **2020**, *131*, 116008. [CrossRef]
316. Mzyk, A.; Sigaeva, A.; Schirhagl, R. Relaxometry with Nitrogen Vacancy (NV) Centers in Diamond. *Acc. Chem. Res.* **2022**, *55*, 3572–3580. [CrossRef] [PubMed]
317. Roman-Vicharra, C.; Cai, J.J. Quantum gene regulatory networks. *npj Quantum Inf.* **2023**, *9*, 67. [CrossRef]
318. Green, C.M.; Spangler, J.; Susumu, K.; Stenger, D.A.; Medintz, I.L.; Díaz, S.A. Quantum Dot-Based Molecular Beacons for Quantitative Detection of Nucleic Acids with CRISPR/Cas(N) Nucleases. *ACS Nano* **2022**, *16*, 20693–20704. [CrossRef]
319. Giovannetti, V.; Lloyd, S.; Maccone, L. Quantum-enhanced measurements: Beating the standard quantum limit. *Science* **2004**, *306*, 1330–1336. [CrossRef] [PubMed]
320. Yu, Y.-H.; Zhang, R.-Z.; Xu, Y.; Chen, X.-Q.; Zheng, H.; Li, Q.; Liu, R.-B.; Pan, X.-Y.; Budker, D.; Liu, G.-Q. Optically detected magnetic resonance of nitrogen-vacancy centers in diamond under weak laser excitation. *Phys. Rev. Appl.* **2024**, *21*, 044051. [CrossRef]
321. Hansen, N.W.; Webb, J.L.; Troise, L.; Olsson, C.; Tomasevic, L.; Brinza, O.; Achard, J.; Staacke, R.; Kieschnick, M.; Meijer, J.; et al. Microscopic-scale magnetic recording of brain neuronal electrical activity using a diamond quantum sensor. *Sci. Rep.* **2023**, *13*, 12407. [CrossRef]
322. Tan, Y.; Hu, X.; Hou, Y.; Chu, Z. Emerging Diamond Quantum Sensing in Bio-Membranes. *Membranes* **2022**, *12*, 957. [CrossRef]
323. Crane, J.M.; Haggie, P.M.; Verkman, A.S. Quantum Dot Single Molecule Tracking Reveals a Wide Range of Diffusive Motions of Membrane Transport Proteins. In Proceedings of the Colloidal Quantum Dots for Biomedical Applications IV, San Jose, CA, USA, 24–26 January 2009.
324. Hall, L.T.; Hill, C.D.; Cole, J.H.; Städler, B.; Caruso, F.; Mulvaney, P.; Wrachtrup, J.; Hollenberg, L.C.L. Monitoring ion-channel function in real time through quantum decoherence. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 18777–18782. [CrossRef] [PubMed]
325. Yu, C.J.; Von Kugelgen, S.; Laorenza, D.W.; Freedman, D.E. A Molecular Approach to Quantum Sensing. *ACS Cent. Sci.* **2021**, *7*, 712–723. [CrossRef]
326. Li, X.; Zhao, W.; Liu, J.; Li, R.; Jia, S.; Li, C.; Bao, D.; Zhu, S.; Wang, P.; Huang, L.; et al. Harnessing non-equilibrium hot electrons in a quantum-engineered ternary heterostructure for sub-ppb C9 biomarker detection. *Chem. Sci.* **2025**, *16*, 17200–17206. [CrossRef]
327. Pogorzelski, J.; Horsthemke, L.; Homrighausen, J.; Stiegekötter, D.; Gregor, M.; Glösekötter, P. Compact and Fully Integrated LED Quantum Sensor Based on NV Centers in Diamond. *Sensors* **2024**, *24*, 743. [CrossRef]
328. Ajoy, A. High-Throughput in-Flow Quantum Sensing Based on Droplet Microfluidics. In Proceedings of the Quantum Effects and Measurement Techniques in Biology and Biophotonics, San Francisco, CA, USA, 27–30 January 2024.
329. Al Shammri, F.K.; Al-Shareeda, M.A.; Abbood, A.A.J.; Almaiah, M.A.; AlAli, R. Quantum-Enhanced AI and Machine Learning: Transforming Predictive Analytics. In *Recent Advances in Electrical & Electronic Engineering (Formerly Recent Patents on Electrical & Electronic Engineering)*; Bentham Science: Sharjah, United Arab Emirates, 2025; p. 18. [CrossRef]
330. Kim, J.; McFee, M.; Fang, Q.; Abdin, O.; Kim, P.M. Computational and artificial intelligence-based methods for antibody development. *Trends Pharmacol. Sci.* **2023**, *44*, 175–189. [CrossRef]

331. Basu, S.; Born, J.; Bose, A.; Capponi, S.; Chalkia, D.; Chan, T.A.; Doga, H.; Flother, F.F.; Getz, G.; Goldsmith, M.; et al. Towards Quantum-Enabled Cell-Centric Therapeutics. *arXiv* **2023**, arXiv:2307.05734.
332. Utro, F.; Tolunay, M.; Rhrissorrakrai, K.; Gujarati, T.P.; Shi, J.; Capponi, S.; Amico, M.; Earnest-Noble, N.; Parida, L. Enhanced Prediction of CAR T-Cell Cytotoxicity with Quantum-Kernel Methods. *arXiv* **2025**, arXiv:2507.22710.
333. Reymond, J.-L.; van Deursen, R.; Blum, L.C.; Ruddigkeit, L. Chemical space as a source for new drugs. *Medchemcomm* **2010**, *1*, 30. [CrossRef]
334. Han, P.; Zhao, P.; Lu, C.; Huang, J.; Wu, J.; Shang, S.; Yao, B.; Zhang, X. GNN-Retro: Retrosynthetic Planning with Graph Neural Networks. In Proceedings of the 36th AAAI Conference on Artificial Intelligence, AAAI 2022, Vancouver, BC, Canada, 22 February–8 March 2022.
335. Zhao, P.-C.; Wei, X.-X.; Wang, Q.; Wang, Q.-H.; Li, J.-N.; Shang, J.; Lu, C.; Shi, J.-Y. Single-step retrosynthesis prediction via multitask graph representation learning. *Nat. Commun.* **2025**, *16*, 814. [CrossRef] [PubMed]
336. Koch, M.; Duigou, T.; Faulon, J.L. Reinforcement learning for bioretrosynthesis. *ACS Synth. Biol.* **2020**, *9*, 157–168. [CrossRef]
337. Lu, J.-M.; Pan, J.-Z.; Mo, Y.-M.; Fang, Q. Automated Intelligent Platforms for High-Throughput Chemical Synthesis. *Artif. Intell. Chem.* **2024**, *2*, 100057. [CrossRef]
338. Cavasotto, C.N.; Di Filippo, J.I. Artificial intelligence in the early stages of drug discovery. *Arch. Biochem. Biophys.* **2021**, *698*, 108730. [CrossRef]
339. Wang, Y.; Pang, C.; Wang, Y.; Jin, J.; Zhang, J.; Zeng, X.; Su, R.; Zou, Q.; Wei, L. Retrosynthesis prediction with an interpretable deep-learning framework based on molecular assembly tasks. *Nat. Commun.* **2023**, *14*, 6155. [CrossRef]
340. Reiher, M.; Wiebe, N.; Svore, K.M.; Wecker, D.; Troyer, M. Elucidating reaction mechanisms on quantum computers. *Proc. Natl. Acad. Sci. USA* **2017**, *114*, 7555–7560. [CrossRef]
341. Fox, D.M.; MacDermaid, C.M.; Schreij, A.M.A.; Zwierzyna, M.; Walker, R.C. RNA folding using quantum computers. *PLoS Comput. Biol.* **2022**, *18*, e1010032. [CrossRef]
342. Conde-Torres, D.; Mussa-Juane, M.; Faílde, D.; Gómez, A.; García-Fandiño, R.; Piñeiro, Á. Interface-Driven Peptide Folding: Quantum Computations on Simulated Membrane Surfaces. *arXiv* **2024**, arXiv:2401.05075. [CrossRef]
343. de la Fuente, J.; Contreras, M. Quantum vaccinomics platforms to advance in vaccinology. *Front. Immunol.* **2023**, *14*, 1172734. [CrossRef]
344. Liu, J.; Guan, S.; Zou, Q.; Wu, H.; Tiwari, P.; Ding, Y. AMDGT: Attention aware multi-modal fusion using a dual graph transformer for drug–disease associations prediction. *Knowl. Based Syst.* **2024**, *284*, 111329. [CrossRef]
345. Shen, S.; Qi, W.; Liu, X.; Zeng, J.; Li, S.; Zhu, X.; Dong, C.; Wang, B.; Shi, Y.; Yao, J.; et al. From virtual to reality: Innovative practices of digital twins in tumor therapy. *J. Transl. Med.* **2025**, *23*, 348. [CrossRef] [PubMed]
346. Mohkam, M.; Sadraeian, M.; Lauto, A.; Gholami, A.; Nabavizadeh, S.H.; Esmaeilzadeh, H.; Alyasin, S. Exploring the potential and safety of quantum dots in allergy diagnostics. *Microsyst. Nanoeng.* **2023**, *9*, 145. [CrossRef]
347. Papalitsas, C.; Guan, Y.; Waghe, S.; Liakos, A.; Balatsos, I.; Pantazopoulos, V. Quantum Approximate Optimization Algorithms for Molecular Docking. *arXiv* **2025**, arXiv:2503.04239. [CrossRef]
348. Jameel, F.; Stein, M. Chemical accuracy for ligand-receptor binding Gibbs energies through multi-level SQM/QM calculations. *Phys. Chem. Chem. Phys.* **2024**, *26*, 21197–21203. [CrossRef] [PubMed]
349. Hoja, J.; Tkatchenko, A. First-principles stability ranking of molecular crystal polymorphs with the DFT+MBD approach. *Faraday Discuss.* **2018**, *211*, 253–274. [CrossRef]
350. Hoja, J.; Ko, H.Y.; Neumann, M.A.; Car, R.; DiStasio, R.A.; Tkatchenko, A. Reliable and practical computational description of molecular crystal polymorphs. *Acta Hortic. Sin.* **2019**, *45*, eaau3338. [CrossRef]
351. Feller, D. Climbing mount PSI: The level of theory needed to obtain 1 KCAL:/MOL accuracy in thermochemical properties. In *Abstracts of Papers of the American Chemical Society*; American Chemical Society: Washington, DC, USA, 1999; Volume 44.
352. Baker, T.E.; Burke, K.; White, S.R. Accurate correlation energies in one-dimensional systems from small system-adapted basis functions. *Phys. Rev. B* **2018**, *97*, 085139. [CrossRef]
353. Behera, S.; Hahn, D.F.; Wilson, C.J.; Marsili, S.; Tresadern, G.; Gapsys, V.; de Groot, B.L. Quantification of the Impact of Structure Quality on Predicted Binding Free Energy Accuracy. *J. Chem. Inf. Model.* **2025**, *65*, 6927–6938. [CrossRef] [PubMed]
354. Salo-Ahen, O.M.H.; Alanko, I.; Bhadane, R.; Bonvin, A.M.J.J.; Honorato, R.V.; Hossain, S.; Juffer, A.H.; Kabedev, A.; Lahtela-Kakkonen, M.; Larsen, A.S.; et al. Molecular dynamics simulations in drug discovery and pharmaceutical development. *Processes* **2021**, *9*, 71. [CrossRef]
355. Kállay, M.; Horváth, R.A.; Gyevi-Nagy, L.; Nagy, P.R. Basis Set Limit CCSD(T) Energies for Extended Molecules via a Reduced-Cost Explicitly Correlated Approach. *J. Chem. Theory Comput.* **2023**, *19*, 174–189. [CrossRef]
356. Lesiuk, M. Quintic-scaling rank-reduced coupled cluster theory with single and double excitations. *J. Chem. Phys.* **2022**, *156*, 064103. [CrossRef]

357. Nandi, A.; Pandey, P.; Houston, P.L.; Qu, C.; Yu, Q.; Conte, R.; Tkatchenko, A.; Bowman, J.M. Δ-Machine Learning to Elevate DFT-based Potentials and a Force Field to the CCSD(T) Level Illustrated for Ethanol. *J. Chem. Theory Comput.* **2024**, *20*, 8807–8819. [CrossRef]
358. Nandi, A.; Qu, C.; Houston, P.L.; Conte, R.; Bowman, J.M. Δ-machine learning for potential energy surfaces: A PIP approach to bring a DFT-based PES to CCSD(T) level of theory. *J. Chem. Phys.* **2021**, *154*, 051102. [CrossRef]
359. Abdolmaleki, S.; Aliabadi, A.; Khaksar, S. Riding the metal wave: A review of the latest developments in metal-based anticancer agents. *Coord. Chem. Rev.* **2024**, *501*, 215579. [CrossRef]
360. Sheng, X.; Kazemi, M.; Planas, F.; Himo, F. Modeling Enzymatic Enantioselectivity using Quantum Chemical Methodology. *ACS Catal.* **2020**, *10*, 6430–6449. [CrossRef]
361. Robo, M.T.; Hayes, R.L.; Ding, X.; Pulawski, B.; Vilseck, J.Z. Fast free energy estimates from λ-dynamics with bias-updated Gibbs sampling. *Nat. Commun.* **2023**, *14*, 8515. [CrossRef]
362. Champion, C.; Gall, R.; Ries, B.; Rieder, S.R.; Barros, E.P.; Riniker, S. Accelerating Alchemical Free Energy Prediction Using a Multistate Method: Application to Multiple Kinases. *J. Chem. Inf. Model.* **2023**, *63*, 7133–7147. [CrossRef]
363. Bueno, P.R. Quantum electroanalysis in drug discovery. *Chem. Commun.* **2025**, *61*, 8632–8642. [CrossRef] [PubMed]
364. Santos, J.; Pujols, J.; Pallarès, I.; Iglesias, V.; Ventura, S. Computational prediction of protein aggregation: Advances in proteomics, conformation-specific algorithms and biotechnological applications. *Comput. Struct. Biotechnol. J.* **2020**, *18*, 1403–1413. [CrossRef] [PubMed]
365. Hu, H. Quantum Computer Simulation of Protein Protonation. *J. Chem. Theory Comput.* **2023**, *19*, 5671–5676. [CrossRef]
366. Takaya, D.; Ohno, S.; Miyagishi, T.; Tanaka, S.; Okuwaki, K.; Watanabe, C.; Kato, K.; Tian, Y.-S.; Fukuzawa, K. Quantum chemical calculation dataset for representative protein folds by the fragment molecular orbital method. *Sci. Data* **2024**, *11*, 1164. [CrossRef]
367. Danhof, M.; Klein, K.; Stolk, P.; Aitken, M.; Leufkens, H. The future of drug development: The paradigm shift towards systems therapeutics. *Drug Discov. Today* **2018**, *23*, 1990–1995. [CrossRef]
368. Posey Norris, S.M.; Pankevich, D.E.; Davis, M.; Altevogt, B.M. *Improving and Accelerating Therapeutic Development for Nervous System Disorders: Workshop Summary*; National Academies Press: Washington, DC, USA, 2014.
369. Ocana, A.; Pandiella, A.; Privat, C.; Bravo, I.; Luengo-Oroz, M.; Amir, E.; Gyorffy, B. Integrating artificial intelligence in drug discovery and early drug development: A transformative approach. *Biomark. Res.* **2025**, *13*, 45. [CrossRef]
370. Malheiro, V.; Santos, B.; Figueiras, A.; Mascarenhas-Melo, F. The Potential of Artificial Intelligence in Pharmaceutical Innovation: From Drug Discovery to Clinical Trials. *Pharmaceuticals* **2025**, *18*, 788. [CrossRef] [PubMed]
371. Woo, H.-M.; Qian, X.; Tan, L.; Jha, S.; Alexander, F.J.; Dougherty, E.R.; Yoon, B.-J. Optimal decision-making in high-throughput virtual screening pipelines. *Patterns* **2023**, *4*, 100875. [CrossRef] [PubMed]
372. Hu, S.; Hu, J.; Zhang, X.; Jin, S.; Xu, X. Drug target affinity prediction based on multi-scale gated power graph and multi-head linear attention mechanism. *PLoS ONE* **2025**, *20*, e0315718. [CrossRef]
373. Fromer, J.C.; Graff, D.E.; Coley, C.W. Pareto optimization to accelerate multi-objective virtual screening. *Digit. Discov.* **2024**, *3*, 467–481. [CrossRef]
374. Wang, W.; Liu, Y.; Wang, Z.; Hao, G.; Song, B. The way to AI-controlled synthesis: How far do we need to go? *Chem. Sci.* **2022**, *13*, 12604–12615. [CrossRef] [PubMed]
375. Philippidis, A. Pipeline Pruning: Exscientia Cuts Programs to Sharpen Precision Oncology Focus. *GEN Edge* **2023**, *5*, 889–897. [CrossRef]
376. Philippidis, A. In the Pipeline: Recursion's Approach to AI and Machine Learning. *GEN Biotechnol.* **2024**, *3*, 269–273. [CrossRef]
377. Redl, I.; Fisicaro, C.; Dutton, O.; Hoffmann, F.; Henderson, L.; Owens, B.M.J.; Heberling, M.; Paci, E.; Tamiola, K. ADOPT: Intrinsic protein disorder prediction through deep bidirectional transformers. *NAR Genom. Bioinform.* **2023**, *5*, lqad041. [CrossRef]
378. Thomas, D.A.; Fleming, T.A.; Bittner, M.-I. Abstract 295: Implementing fully automated kinase inhibitor characterization using a robotic system. *Cancer Res.* **2021**, *81*, 295. [CrossRef]
379. Segal, M. An operating system for the biology lab. *Nature* **2019**, *573*, S112–S113. [CrossRef]
380. YWong, G.K.; Costa, K.D.; Fermini, B.; Li, R.A. Modeling the Heart with Novoheart's Myheart^{TM} Platform. *Future Drug Discov.* **2020**, *2*, FDD32. [CrossRef]
381. Hough, S.H.; Ajetunmobi, A.; Brody, L.; Humphryes-Kirilov, N.; Perello, E. Desktop genetics. *Pers. Med.* **2016**, *13*, 517–521. [CrossRef] [PubMed]
382. Kumar, K.; Chupakhin, V.; Vos, A.; Morrison, D.; Rassokhin, D.; Dellwo, M.J.; McCormick, K.; Paternoster, E.; Ceulemans, H.; DesJarlais, R.L. Development and implementation of an enterprise-wide predictive model for early absorption, distribution, metabolism and excretion properties. *Future Med. Chem.* **2021**, *13*, 1639–1654. [CrossRef]
383. Ghiandoni, G.M.; Evertsson, E.; Riley, D.J.; Tyrchan, C.; Rathi, P.C. Augmenting DMTA using predictive AI modelling at AstraZeneca. *Drug Discov. Today* **2024**, *29*, 103945. [CrossRef] [PubMed]
384. Benson, B.M.; Ingman, V.M.; Agarwal, A.; Keinan, S. A CQM-Based Approach to Solving a Combinatorial Problem with Applications in Drug Design. *arXiv* **2023**, arXiv:2303.15419. [CrossRef]

385. Chandran, A. Biopharma foresees a 'quantum advantage': They could be right. *Nat. Biotechnol.* **2024**, *42*, 690–692. [CrossRef]
386. Feniou, C.; Hassan, M.; Claudon, B.; Courtat, A.; Adjoua, O.; Maday, Y.; Piquemal, J.-P. Greedy gradient-free adaptive variational quantum algorithms on a noisy intermediate scale quantum computer. *Sci. Rep.* **2025**, *15*, 18689. [CrossRef]
387. Petch, J.; Di, S.; Nelson, W. Opening the Black Box: The Promise and Limitations of Explainable Machine Learning in Cardiology. *Can. J. Cardiol.* **2022**, *38*, 204–213. [CrossRef]
388. Liu, Y. Superconducting quantum computing optimization based on multi-objective deep reinforcement learning. *Sci. Rep.* **2025**, *15*, 3828. [CrossRef]
389. Zhong, H.; Ju, K.; Shen, J.; Zhang, X.; Qin, X.; Ohtsuki, T.; Pan, M.; Han, Z. Differential Privacy Preserving Distributed Quantum Computing. *arXiv* **2025**, arXiv:2412.12387.
390. Kannan, E.; MJ, C.M.B.; Ravikumar, S.; Alex, D.S.; Sriram, K.; Vijay, K. Quantum-Safe Federated Learning: Enhancing Data Privacy and Security. In Proceedings of the 2024 International Conference on Emerging Research in Computational Science (ICERCS), Coimbatore, India, 12–14 December 2024; IEEE: Piscataway, NJ, USA, 2024; pp. 1–6.
391. Gao, X.; Zhang, Z.Y.; Duan, L.M. A quantum machine learning algorithm based on generative models. *Sci. Adv.* **2018**, *4*, eaat9004. [CrossRef] [PubMed]
392. Dang, T.L.P.; Sadreddin, A.; Ahuja, S. Readily available technologies in low-resource communities: A review and synthesis. *Inf. Technol. Dev.* **2024**, *30*, 132–172. [CrossRef]
393. Knapik, E.; Brandimarte, L.; Usher, M. Maintenance in sustainable stormwater management: Issues, barriers and challenges. *J. Environ. Plan. Manag.* **2025**, *68*, 2769–2795. [CrossRef]
394. Whalen, C.J.; Donnell, D.; Tartakovsky, M. Supporting research sites in resource-limited settings: Challenges in implementing information technology infrastructure. *J. Acquir. Immune Defic. Syndr.* **2014**, *65*, S44–S49. [CrossRef]
395. Jindal, M. How Can Hybrid Algorithms Combining Quantum Machine Learning and Classical Machine Learning be Optimised for Performance and Accuracy? *Int. J. Multidiscip. Res.* **2024**, *6*, 33629. [CrossRef]
396. Zhang, X.-M.; Li, T.; Yuan, X. Quantum State Preparation with Optimal Circuit Depth: Implementations and Applications. *Phys. Rev. Lett.* **2022**, *129*, 230504. [CrossRef]
397. Aiello, C.D.; Awschalom, D.D.; Bernien, H.; Brower, T.; Brown, K.R.; Brun, T.A.; Caram, J.R.; Chitambar, E.; Di Felice, R.; Edmonds, K.M. Achieving a quantum smart workforce. *Quantum Sci. Technol.* **2021**, *6*, 030501. [CrossRef]
398. De Michielis, M.; Ferraro, E. Energy and power scaling in quantum computers based on rotated surface codes with silicon flip-flop qubits. *EPJ Quantum Technol.* **2025**, *12*, 64. [CrossRef]
399. Ennab, M.; Mcheick, H. Enhancing interpretability and accuracy of AI models in healthcare: A comprehensive review on challenges and future directions. *Front. Robot. AI* **2024**, *11*, 1444763. [CrossRef]
400. Lellouch, S.; Holynski, M. Integration of a high-fidelity model of quantum sensors with a map-matching filter for quantum-enhanced navigation. *Quantum Sci. Technol.* **2025**, *10*, 045007. [CrossRef]
401. Christensen, M.; Yunker, L.P.E.; Shiri, P.; Zepel, T.; Prieto, P.L.; Grunert, S.; Borka, F.; Hein, J.E. Automation isn't automatic. *Chem. Sci.* **2021**, *12*, 15473–15490. [CrossRef]
402. Hosseinzadehtaher, M.; D'silva, S.; Baker, M.; Kumar, R.; Hein, N.T.; Shadmand, M.B.; Jagadish, S.V.K.; Ghanbarian, B. On Design Challenges of Portable Nuclear Magnetic Resonance System. *J. Nucl. Eng.* **2023**, *4*, 323–337. [CrossRef]
403. Kennedy, I.G.; Whitehead, D.; Ferdinand-James, D. Serendipity: A way of stimulating researchers' creativity. *J. Creat.* **2022**, *32*, 100014. [CrossRef]
404. Kothari, A.R.; Bickford, J.J.; Edwards, N.; Dobbins, M.J.; Meyer, M. Uncovering tacit knowledge: A pilot study to broaden the concept of knowledge in knowledge translation. *BMC Health Serv. Res.* **2011**, *11*, 198. [CrossRef]
405. Guedes, M.; de la Serna Bazan, A.; Rubio-Martín, E.; Pulido, L.B.; Palomo, V.; Piljić, A.; Leclerc, Q.J.; Aris, E.; Vella, V.; Dambrauskienė, A.; et al. How to: Share and reuse data—Challenges and solutions from predicting the impact of monoclonal antibodies & vaccines on antimicrobial resistance project. *Clin. Microbiol. Infect.* **2025**, *31*, 753–760. [CrossRef] [PubMed]
406. Ballantyne, A. How should we think about clinical data ownership? *J. Med. Ethics* **2020**, *46*, 289–294. [CrossRef]
407. Patino, R.M. Moving research to patient applications through commercialization: Understanding and evaluating the role of intellectual property. *J. Am. Assoc. Lab. Anim. Sci.* **2010**, *49*, 147–154.
408. Pratt, B.; Hyder, A.A. Governance of global health research consortia: Sharing sovereignty and resources within Future Health Systems. *Soc. Sci. Med.* **2017**, *174*, 113–121. [CrossRef]
409. Dutta, M.; Ramasubramanian, S.; Barrett, M.; Elers, C.; Sarwatay, D.; Raghunath, P.; Kaur, S.; Dutta, D.; Jayan, P.; Rahman, M.; et al. Decolonizing Open Science: Southern Interventions. *J. Commun.* **2021**, *71*, 803–826. [CrossRef]
410. Wilkinson, B.D. The Limits of Neuroscience in Counseling: A Humanistic Perspective and Proposed Model. *J. Humanist. Couns.* **2018**, *57*, 70–78. [CrossRef]
411. Frank, A.; Gleiser, M.; Thompson, E. *The Blind Spot: Why Science Cannot Ignore Human Experience*; The MIT Press: Cambridge, MA, USA, 2024.

412. Ricci, G. Pharmacological Human Enhancement: An Overview of the Looming Bioethical and Regulatory Challenges. *Front. Psychiatry* **2020**, *11*, 53. [CrossRef]
413. Barra, M.E.; Solt, K.; Yu, X.; Edlow, B.L. Restoring consciousness with pharmacologic therapy: Mechanisms, targets, and future directions. *Neurotherapeutics* **2024**, *21*, e00374. [CrossRef]
414. Wenzel, T. Open hardware: From DIY trend to global transformation in access to laboratory equipment. *PLoS Biol.* **2023**, *21*, e3001931. [CrossRef]
415. Sarkar, S.; Mateus, S. Doing more with less—How frugal innovations can contribute to improving healthcare systems. *Soc. Sci. Med.* **2022**, *306*, 115127. [CrossRef] [PubMed]
416. Mugambi, M.L.; Peter, T.; Martins, S.F.; Giachetti, C. How to implement new diagnostic products in low-resource settings: An end-to-end framework. *BMJ Glob. Health* **2018**, *3*, e000914. [CrossRef] [PubMed]
417. Pearce, J.M. Economic savings for scientific free and open source technology: A review. *HardwareX* **2020**, *8*, e00139. [CrossRef] [PubMed]
418. D'Alton, L.; Carrara, S.; Barbante, G.J.; Hoxley, D.; Hayne, D.J.; Francis, P.S.; Hogan, C.F. A simple, low-cost instrument for electrochemiluminescence immunoassays based on a Raspberry Pi and screen-printed electrodes. *Bioelectrochemistry* **2022**, *146*, 108107. [CrossRef]
419. Rujano, M.A.; Boiten, J.-W.; Ohmann, C.; Canham, S.; Contrino, S.; David, R.; Ewbank, J.; Filippone, C.; Connellan, C.; Custers, I.; et al. Sharing sensitive data in life sciences: An overview of centralized and federated approaches. *Brief. Bioinform.* **2024**, *25*, bbae262. [CrossRef]
420. Kotev, M.; Diaz Gonzalez, C. Molecular Dynamics and Other HPC Simulations for Drug Discovery. *Methods Mol. Biol.* **2024**, *2716*, 265–291. [CrossRef]
421. Kushwaha, P.; Srivastava, N.; Kushwaha, S.P. Enhancing clinical drug trial monitoring with blockchain technology. *Contemp. Clin. Trials* **2024**, *146*, 107684. [CrossRef] [PubMed]
422. Keršič, V.; Karakatič, S.; Turkanović, M. On-chain zero-knowledge machine learning: An overview and comparison. *J. King Saud Univ. Comput. Inf. Sci.* **2024**, *36*, 102207. [CrossRef]
423. Cha, Y.; Erez, T.; Reynolds, I.J.; Kumar, D.; Ross, J.; Koytiger, G.; Kusko, R.; Zeskind, B.; Risso, S.; Kagan, E.; et al. Drug repurposing from the perspective of pharmaceutical companies. *Br. J. Pharmacol.* **2018**, *175*, 168–180. [PubMed]
424. Stevens, W. Good clinical laboratory practice (GCLP): The need for a hybrid of good laboratory practice and good clinical practice guidelines/standards for medical testing laboratories conducting clinical trials in developing countries. *Qual. Assur.* **2003**, *10*, 83–89. [CrossRef]
425. Satterthwaite, E.V.; Bax, N.J.; Miloslavich, P.; Ratnarajah, L.; Canonico, G.; Dunn, D.; Simmons, S.E.; Carini, R.J.; Evans, K.; Allain, V.; et al. Establishing the Foundation for the Global Observing System for Marine Life. *Front. Mar. Sci.* **2021**, *8*, 737416. [CrossRef]
426. Matarése, B.F.E.; Desai, R.; Oughton, D.H.; Motherisill, C. EGO to ECO: Tracing the History of Radioecology from the 1950s to the Present Day. *Radiat. Res.* **2024**, *202*, 273–288. [CrossRef]

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