

Breakthroughs in Bioinformatics and Biomedical Engineering

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Modern healthcare, biomedicine, and translational medicine are becoming increasingly dependent on innovations and achievements in bioinformatics and biomedical engineering. Artificial intelligence and machine learning, medical imaging and predictive analytics, deep learning, wearable technologies and computational genomics are all major technologies that help to improve our understanding of biological processes, support informed decision-making and diagnostics and personalized treatment options, and facilitate improved distribution of healthcare technologies. Nevertheless, these innovations are accompanied by multiple methodological, ethical, regulatory, and translational issues that require careful consideration of various factors that influence the success of biomedical inventions.

This Special Issue “Breakthroughs in Bioinformatics and Biomedical Engineering,” aims to showcase high-quality scientific achievements in the field of biomedical computing and engineering. Bioinformatics and biomedical engineering is currently characterized by strong disciplinary intersections, calling for a joint contribution of computational techniques, domain knowledge, data management and processing, validation of results, clinical relevance, usability, etc. The convergence of these components has led to the development of a new generation of biomedical technologies that represent a significant breakthrough in research and healthcare practice.

Artificial intelligence (AI) and machine learning are widely used in biomedical research [1,2]. Nowadays, AI models are successfully employed in numerous tasks, from interpreting images and identifying biomarkers to stratifying patients and making decisions. Deep learning algorithms in particular have contributed significantly to progress in pattern recognition within biomedical data, including genomic sequences, images, electronic health records, and other sources [2]. However, the increased efficiency and accuracy of these models should be accompanied by clinical generalizability, reproducibility, and transparency. Though experiments have produced satisfactory results, some AI models face serious challenges when employed in a real-life setting [1].

One of the most sophisticated and productive areas of biomedical AI development is based on image analysis techniques [3,4]. Medical imaging data represents a huge source of information which can be effectively used for diagnostic and monitoring purposes, among other potential uses. Furthermore, thanks to AI-powered analysis, it is now possible to perform segmentation, registration, classification, reconstruction, denoising, visualization, biomarker extraction, and other operations on imaging data [4]. Nevertheless, despite all the advances in this field, there are still many issues related to dataset imbalances, interpretability problems, differences in imaging protocols, and challenges associated with applying imaging analysis in clinical practice [3,4]. Hence, the implementation of image analysis algorithms in healthcare requires extensive cooperation between researchers from various fields of expertise.



Received: 18 June 2026

Accepted: 1 July 2026

Published: 4 July 2026

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It is also worth acknowledging the incredible progress that has recently been achieved in bioinformatics and computational genomics [5,6]. With the advent of high-throughput sequencing technologies and other related innovations, large amounts of genomic, transcriptomic, and other omics data have started accumulating, and novel analytical tools are required to make sense of the information collected. RNA sequencing, analysis of genomic variants, pathway modeling, and other techniques may contribute substantially to the study of disease mechanisms, biomarker discovery, precision medicine, etc. In the future, researchers should focus on integrating biological data across different levels from molecular and cellular processes to individuals, groups, and populations in order to develop a more comprehensive understanding of the underlying disease mechanisms.

Finally, wearable health devices and biomedical sensors represent another important area of research [7,8]. These technologies can be employed to continuously monitor the patient's physiological parameters and can support preventive healthcare, telemedicine, activity recognition, and other vital functions. Thanks to machine learning algorithms, wearable biomedical systems can provide clinicians with a substantial amount of clinically meaningful information from time-series data. However, wearable biomedical devices require calibration, energy efficiency, user involvement, signal quality control, and data transmission security in order to operate successfully. Consequently, further research in this field should involve hardware development, embedded systems, signal processing, data analytics, cloud and edge computing, and human-centered design aspects [8].

The use of AI technologies in healthcare poses many concerns from an ethical and governance perspective. The World Health Organization recommends paying particularly close attention to ethics, human rights, transparency, accountability, inclusiveness, and trust in the development and implementation of AI for health [9,10]. These factors are especially important in the biomedical sector, since AI algorithms typically work with highly sensitive data and can influence diagnostics and other clinical decisions made by the physician. Hence, when creating biomedical systems, one needs to consider data privacy, informed consent, data responsibility, fairness, explainability, cybersecurity, and other relevant issues. Ethical and trustworthy AI innovation cannot be considered an additional requirement after technical innovation, but a key aspect of the research.

Additionally, it is necessary to introduce methodological and reporting standards when developing predicting models, intervention design, decision-making systems, or other similar components. Recently, some reporting guidelines have been proposed—TRIPOD+AI, CONSORT-AI, and SPIRIT-AI. These recommendations provide guidelines on the requirements concerning the dataset, model development, model validation, interventions, human-machine interaction, error analysis, and clinical implementation [11–13]. Adherence to these recommendations will support the peer review process, allow the results to be reproduced, and promote clinical implementation of AI technologies.

Further innovations reinforce the notion that the future of biomedical engineering and bioinformatics will be substantially impacted by reliable, generative, and multi-modal AI. The WHO highlights that multi-modal systems open up new possibilities in the fields of healthcare, medical research, public health, and drug development, but that they need to be properly governed, made transparent, accountable, supervised, and safeguarded to prevent them from undermining patients' rights. In parallel, the recently published international guideline on FUTURE-AI offers recommendations for building and using trustworthy AI in healthcare throughout the whole healthcare AI lifecycle, considering its design, validation, and regulation; its implementation in clinical practice, and post-deployment monitoring [14]. These recommendations are especially applicable for AI systems that are designed to be used within clinical settings, where technical effectiveness alone is not sufficient.

Finally, another growing trend that is anticipated to play an increasingly important role in the field of biomedical engineering and bioinformatics is generative AI and the application of large language models in medicine [15]. Recently, several promising studies have investigated the use of conversational diagnostic AI and differential diagnosis by means of large language models [16,17]. These advancements should be viewed with a critical eye, since recent evaluations of large language models in medicine may overestimate the clinical utility of such AI if they utilize narrow benchmarks, simple tasks, or unrepresentative data [18]. Therefore, future biomedical AI systems should undergo a comprehensive evaluation process based on clinically valid, transparent, and context-dependent criteria prior to their practical application.

Several important future directions in biomedical sciences deserve special consideration. Firstly, it is possible to combine various types of information—including imaging, genomic, clinical, and laboratory data, signals from wearable biomedical devices, and patients' reports—to provide a more comprehensive description of disease mechanisms, progression, and responses to treatments. Secondly, federated learning and privacy-preserving AI may help researchers and organizations collaborate on the development of prediction models without needing to share patient data [19]. Thirdly, techniques for the explanation of AI system behavior and creation of trustworthy models may promote wider applications of biomedical innovations; however, one should evaluate the concept of explainability critically and carefully [20]. Fourthly, edge computing may help extend the use of biomedical technologies by performing analysis near patients in dynamic environments.

In conclusion, it is clear that the future of bioinformatics and biomedical engineering depends on the activities of the interdisciplinary scientific community. Scientists from spheres such as engineering, computer science, biology, medicine, statistics, law, ethics, and public health must collaborate to develop effective, convenient, sustainable, inclusive, and safe technologies. At the moment, the healthcare industry is experiencing several issues related to an aging population, the presence of chronic diseases, a shortage of medical specialists, increased costs, and the need for personalized healthcare services. Under these circumstances, there is an acute need for advanced technologies in the healthcare industry.

Author Contributions: Conceptualization, P.T. and E.M.; writing—original draft preparation, P.T. and E.M.; writing—review and editing, P.T. and E.M. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Topol, E.J. High-performance medicine: The convergence of human and artificial intelligence. *Nat. Med.* **2019**, *25*, 44–56.
2. Esteva, A.; Robicquet, A.; Ramsundar, B.; Kuleshov, V.; DePristo, M.; Chou, K.; Cui, C.; Corrado, G.; Thrun, S.; Dean, J. A guide to deep learning in healthcare. *Nat. Med.* **2019**, *25*, 24–29.
3. Liu, X.; Faes, L.; Kale, A.U.; Wagner, S.K.; Fu, D.J.; Bruynseels, A.; Mahendiran, T.; Moraes, G.; Shamdas, M.; Kern, C.; et al. A comparison of deep learning performance against health-care professionals in detecting diseases from medical imaging: A systematic review and meta-analysis. *Lancet Digit. Health* **2019**, *1*, e271–e297.
4. Zhou, S.K.; Greenspan, H.; Davatzikos, C.; Duncan, J.S.; Van Ginneken, B.; Madabhushi, A.; Prince, J.L.; Rueckert, D.; Summers, R.M. A review of deep learning in medical imaging: Imaging traits, technology trends, case studies with progress highlights, and future promises. *Proc. IEEE* **2021**, *109*, 820–838.
5. Makris, E.; Kolaitis, A.; Andrikos, C.; Moulos, V.; Tsanakas, P.; Pavlatos, C. Knotify+: Toward the Prediction of RNA H-Type Pseudoknots, Including Bulges and Internal Loops. *Biomolecules* **2023**, *13*, 308. <https://doi.org/10.3390/biom13020308>.
6. Koroulis, C.; Makris, E.; Kolaitis, A.; Tsanakas, P.; Pavlatos, C. Syntactic Pattern Recognition for the Prediction of L-Type Pseudoknots in RNA. *Appl. Sci.* **2023**, *13*, 5168. <https://doi.org/10.3390/app13085168>.
7. Kim, J.; Campbell, A.S.; de Avila, B.E.-F.; Wang, J. Wearable biosensors for healthcare monitoring. *Nat. Biotechnol.* **2019**, *37*, 389–406.

8. Ates, H.C.; Nguyen, P.Q.; Gonzalez-Macia, L.; Morales-Narvaez, E.; Guder, F.; Collins, J.J.; Dincer, C. End-to-end design of wearable sensors. *Nat. Rev. Mater.* **2022**, *7*, 887–907.
9. World Health Organization. *Ethics and Governance of Artificial Intelligence for Health: WHO Guidance*; World Health Organization: Geneva, Switzerland, 2021.
10. World Health Organization. *Ethics and Governance of Artificial Intelligence for Health: Guidance on Large Multi-Modal Models*; World Health Organization: Geneva, Switzerland, 2025.
11. Collins, G.S.; Moons, K.G.M.; Dhiman, P.; Riley, R.D.; Beam, A.L.; Van Calster, B.; Ghassemi, M.; Liu, X.; Reitsma, J.B.; van Smeden, M.; et al. TRIPOD + AI statement: Updated guidance for reporting clinical prediction models that use regression or machine learning methods. *BMJ* **2024**, *385*, e078378.
12. Liu, X.; Rivera, S.C.; Moher, D.; Calvert, M.J.; Denniston, A.K.; SPIRIT-AI and CONSORT-AI Working Group. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: The CONSORT-AI extension. *Nat. Med.* **2020**, *26*, 1364–1374.
13. Rivera, S.C.; Liu, X.; Chan, A.-W.; Denniston, A.K.; Calvert, M.J.; SPIRIT-AI and CONSORT-AI Working Group. Guidelines for clinical trial protocols for interventions involving artificial intelligence: The SPIRIT-AI extension. *Nat. Med.* **2020**, *26*, 1351–1363.
14. Lekadir, K.; Frangi, A.F.; Porras, A.R.; Glocker, B.; Cintas, C.; Langlotz, C.P.; Weicken, E.; Asselbergs, F.W.; Prior, F.; Collins, G.S.; et al. FUTURE-AI: International consensus guideline for trustworthy and deployable artificial intelligence in healthcare. *BMJ* **2025**, *388*, e081554. <https://doi.org/10.1136/bmj-2024-081554>.
15. Teo, Z.L.; Thirunavukarasu, A.J.; Elangovan, K.; Cheng, H.; Moova, P.; Soetikno, B.; Nielsen, C.; Pollreisz, A.; Ting, D.S.J.; Morris, R.J.T.; et al. Generative artificial intelligence in medicine. *Nat. Med.* **2025**, *31*, 3270–3282. <https://doi.org/10.1038/s41591-025-03983-2>.
16. Tu, T.; Schaekermann, M.; Palepu, A.; Saab, K.; Freyberg, J.; Tanno, R.; Wang, A.; Li, B.; Amin, M.; Cheng, Y.; et al. Towards conversational diagnostic artificial intelligence. *Nature* **2025**, *642*, 442–450. <https://doi.org/10.1038/s41586-025-08866-7>.
17. McDuff, D.; Schaekermann, M.; Tu, T.; Palepu, A.; Wang, A.; Garrison, J.; Singhal, K.; Sharma, Y.; Azizi, S.; Kulkarni, K.; et al. Towards accurate differential diagnosis with large language models. *Nature* **2025**, *642*, 451–457. <https://doi.org/10.1038/s41586-025-08869-4>.
18. Agrawal, M.; Chen, I.Y.; Gulamali, F.; Joshi, S. The evaluation illusion of large language models in medicine. *npj Digit. Med.* **2025**, *8*, 600. <https://doi.org/10.1038/s41746-025-01963-x>.
19. Rieke, N.; Hancock, J.; Li, W.; Milletari, F.; Roth, H.R.; Albarqouni, S.; Bakas, S.; Galtier, M.N.; Landman, B.A.; Maier-Hein, K.; et al. The future of digital health with federated learning. *npj Digit. Med.* **2020**, *3*, 119.
20. Ghassemi, M.; Oakden-Rayner, L.; Beam, A.L. The false hope of current approaches to explainable artificial intelligence in health care. *Lancet Digit. Health* **2021**, *3*, e745–e750.

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