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Artificial intelligence and digital technologies in preclinical research: from drug discovery to ethical animal studies

Ivona **Costachescu** [1]*, Maria-Raluca **Gogu** [1, 2], Gabriela-Dumitrița **Stanciu** [1], Bogdan-Ionel **Tamba** [1, 3]

[1] Prof. Ostin C. Mungiu Advanced Research and Development Center for Experimental Medicine – CEMEX, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania
[2] Faculty of Biology, Alexandru Ioan Cuza University, Iasi, Romania
[3] Department of Pharmacology, Clinical Pharmacology and Algesiology, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania

* **Correspondence to:** Ivona Costachescu, Prof. Ostin C. Mungiu Advanced Research and Development Center for Experimental Medicine – CEMEX, Grigore T. Popa University of Medicine and Pharmacy, 16 Universitatii Str., 700115, Iasi, Romania. E-mail: ivona.costachescu@umfiasi.ro

Abstract

Digitalization is profoundly transforming preclinical research by reshaping experimental design, data acquisition and result interpretation. This article reviews the role of artificial intelligence, automation and digital monitoring in novel drug discovery, the implementation of the 3R principles (Replacement, Reduction, Refinement) and the study of complex diseases. Digital platforms support virtual screening, automated behavioral analysis and continuous physiological monitoring, thereby improving data precision, reducing unnecessary animal use and enhancing animal welfare. These technologies are particularly valuable in preclinical models of neurodegenerative and metabolic disorders, where they enable early detection of functional alterations and improved longitudinal disease characterization. Overall, digitalization does not replace traditional preclinical research but strengthens it, making preclinical studies more precise, more ethical and more reproducible.

Keywords: artificial intelligence, preclinical research, digital technologies, animal models

Introduction

The past decade has witnessed a major digital transformation across the biomedical sciences. Artificial intelligence (AI), high-throughput automation platforms, advanced data analytics pipelines and integrated digital workflows now influence every stage of drug discovery. Machine-learning models support target prioritization, protein–ligand prediction and virtual compound generation, while robotic liquid-handling and microfluidic systems enable large-scale screening with high reproducibility [1, 2]. Complementary advances in cloud-based data infrastructures and standardized metadata frameworks facilitate seamless sharing, re-analysis and cross-study integration [3]. Together, these innovations reshape experimental planning: hypotheses become increasingly data-driven, protocols can be encoded as reproducible code and sensor-rich digital records create a “digital twin” of each biological experiment [4, 5]. In preclinical research, such capabilities are not intended to replace animal models but to augment their precision and scientific value.

Despite these developments, preclinical research still faces persistent limitations that constrain its predictive power. Biological variability within animal cohorts, along with procedural differences in handling, dosing and phenotyping, contributes to reduced reproducibility across laboratories [6]. Ethical and financial constraints often limit statistical power, hindering the detection of subtle therapeutic effects in complex diseases [6]. Moreover, multimodal datasets—from behavioral video and telemetry to histology and omics—can exceed the capacity of manual curation, resulting in incomplete documentation or selective reporting [3]. While these challenges are sometimes invoked to justify reduced animal use, they in fact highlight the need for digital tools that strengthen the rigor and responsible application of animal models. Digitalization offers practical solutions by improving experimental design, standardizing data capture and enhancing analytical robustness, while preserving the biological relevance uniquely provided by *in vivo* studies.

Digital tools also reinforce animal-based research in alignment with the Reduction and Refinement principles of the 3Rs. AI-driven power analyses and Bayesian adaptive designs help determine the minimum number of animals required to achieve adequate statistical confidence [6]. Automated monitoring technologies—computer-vision pose estimation, infrared sensors and implantable telemetry—generate continuous and unbiased assessments of health and behavior, reducing observer effects and enabling early detection of distress [6]. Such systems support Refinement by allowing timely adjustments to husbandry and experimental conditions. In addition, data-standardization frameworks aligned with the FAIR principles — Findable, Accessible, Interoperable and Reusable — together with ontology-based metadata, enhance transparency and ensure that datasets can be efficiently reused, thereby supporting robust validation across independent studies [3]. Digital "twins" of animal cohorts further enable in-silico exploration of dosing regimens and protocol permutations before execution, refining *in vivo* study plans and reducing unnecessary variation [4, 5]. Collectively, these approaches embed quantitative rigor into animal research while upholding ethical commitments.

These benefits are particularly evident in the study of complex diseases such as neurodegeneration, metabolic disorders and autoimmune conditions. Such pathologies evolve gradually and require multimodal readouts that are difficult to capture. High-resolution video tracking coupled with deep-learning classifiers enables fine-grained quantification of gait, tremor and exploratory behavior, while sensor-integrated cages provide longitudinal physiological biomarkers—such as circadian rhythms, heart-rate variability and respiration—that can be correlated with molecular endpoints through advanced statistical models [3, 6]. Integrating these data streams into machine-learned disease signatures enhances the translational value of animal models by revealing pathways that more closely mirror human pathology [7]. In this way, digital tools add valuable information to animal studies and make disease models more reliable.

This review surveys the expanding digital toolbox that is reshaping preclinical research and discusses how these technologies can reinforce ethical standards, improve reproducibility and deepen the modeling of complex diseases. By focusing on how digital tools work together with traditional methods, we aim to show that digitalization strongly supports responsible and effective animal-based research and helps speed up therapeutic progress.

Digitalization and novel drug discovery

Artificial intelligence (AI) has become a central driver of innovation in early drug discovery, enabling the rapid identification of therapeutic targets and the efficient prioritization of candidate molecules. ML (machine learning) and DL (deep learning) models can extract patterns from genomic, proteomic and chemical datasets that exceed the analytical capacity of traditional approaches. For example, Gómez-Bombarelli *et al.* demonstrated that variational autoencoders can generate novel chemical structures optimized for drug-like properties, accelerating both hit and lead identification [8].

Similarly, Karimi *et al.* developed *DeepAffinity*, a deep learning framework capable of predicting compound–protein affinities directly from sequence information, outperforming classical docking-based workflows [9]. The use of large-scale virtual screening pipelines, supported by ML-enhanced scoring functions, has enabled pharmaceutical teams to screen millions of compounds computationally before selecting a smaller set for laboratory validation [10].

AI has also contributed to the design of clinically relevant molecules. Insilico Medicine reported an AI-generated small molecule (ISM001-055), now called *Rentosertib*, that advanced into Phase I clinical trials for idiopathic pulmonary fibrosis, illustrating how predictive models can shorten timelines. These computational successes do not eliminate the need for downstream *in vivo* studies, but they significantly reduce the number of low-probability candidates entering animal testing, increasing overall efficiency and scientific rigor [11].

Automation and high-throughput screening

Automation technologies amplify the efficiency and reproducibility of early drug discovery. High-throughput screening (HTS) platforms equipped with robotic liquid handling systems, automated microplate readers and barcode-tracked workflows enable controlled parallel testing of thousands of compounds. Macarron *et al.* highlight how modern HTS technologies have become indispensable for identifying lead molecules in large chemical libraries, significantly increasing assay reproducibility and throughput [12].

High-content screening (HCS), which couples automated microscopy with AI-based image analysis, has further expanded the discovery toolbox. Moen *et al.* describe how deep learning can interpret complex cellular phenotypes with high precision, enabling the detection of subtle morphological changes associated with drug activity [13].

Digital infrastructures also play a major role. FAIR-compliant data management systems facilitate transparent, traceable and reusable datasets across laboratories. Wilkinson *et al.* established the FAIR principles to support robust scientific data stewardship and these frameworks now underpin modern HTS and HCS workflows [14].

Together, automation and digital data integration accelerate target identification, improve assay quality, and support more rational selection of compounds that ultimately progress to *in vivo* studies.

Digitalization and the 3R principles

Digital transformation in preclinical research does not aim to remove animal experimentation but to make it more ethical, efficient and scientifically rigorous. The 3R framework — Replacement, Reduction, and Refinement — offers a structured approach for improving animal research and digital technologies now play a pivotal role in advancing each pillar.

Replacement

Digital technologies support the *Replacement* principle by enabling alternative methods that can partially substitute for exploratory *in vivo* studies.

Organs-on-chip platforms — microengineered systems that recapitulate functional units of human organs — allow researchers to test drug responses under physiologically relevant conditions. These systems improve the prediction of human toxicity and pharmacodynamics, reducing reliance on early-stage animal experiments [15, 16].

Digital twins, which are computational replicas of biological systems or entire organisms, integrate physiological, omics and pharmacological data to simulate drug responses under different conditions. Such models can predict dose–response relationships, toxicity windows, or metabolic outcomes before any *in vivo* exposure occurs [17].

Computational toxicology has become an important replacement strategy in early safety assessment. Machine learning models trained on historical toxicity datasets can predict hepatotoxicity, cardiotoxicity and genotoxicity without requiring new animal exposure [10, 18, 19].

Although these technologies cannot fully replace the complex biological processes observed only in whole organisms, they are useful tools in the early stages of research, helping to reduce the number of candidate compounds and to better select those that should move forward to animal studies.

Reduction

Digital technologies make a direct contribution to the Reduction principle by increasing measurement precision and statistical power, thereby allowing robust conclusions to be drawn from smaller animal cohorts. One of the most influential advances in this field is the development of markerless automated tracking systems based on deep learning. The DeepLabCut framework introduced by Mathis *et al.* enables high-precision pose estimation of freely moving animals without physical markers, significantly reducing observer bias and experimental variability [20].

In addition, home-cage monitoring systems allow continuous, long-term behavioral and physiological assessment without repeated handling. A comprehensive review by Voikar and Gaburro demonstrates that automated home-cage phenotyping improves sensitivity for detecting subtle behavioral changes while reducing stress and sample size requirements [21]. By combining continuous monitoring with automated data extraction, these platforms increase the informational yield per animal and markedly reduce the number of animals required for adequately powered studies.

Refinement through smart monitoring systems

The Refinement principle aims to minimize pain, stress and distress while improving the quality of experimental data. Digital monitoring technologies now play a central role in achieving this objective. RFID-based identification systems enable non-invasive tracking of individual animals housed in social groups, eliminating the need for repeated manual identification and handling [22].

Telemetry technologies allow real-time, continuous monitoring of physiological parameters such as heart rate, body temperature, EEG activity, and locomotion in freely moving animals. A detailed methodological review by Kramer and Kinter highlights how modern implantable telemetry systems improve both animal welfare and data reproducibility by avoiding repeated restraint-based measurements [23].

Computer vision–based behavioral analysis enables fully automated scoring of grooming, rearing, social interaction and seizure activity. Weissbrod *et al.* demonstrated that long-term automated tracking systems can quantify social behavior in group-housed mice with high temporal resolution and strong reproducibility [24]. Together, these smart monitoring systems enable early detection of distress, reduce experimenter-induced stress and substantially improve both animal welfare and scientific data quality, fully aligning with the Refinement component of the 3Rs framework.

Digital tools in preclinical models of complex pathologies

Complex diseases such as neurodegenerative disorders, psychiatric illnesses, chronic inflammatory conditions and metabolic diseases are characterized by profound biological heterogeneity, slow progression and strong inter-individual variability. Traditional preclinical models often rely on limited endpoint measurements, which may fail to capture subtle or early-stage phenotypic changes. In disorders such as Alzheimer's disease, Parkinson's disease, depression, or metabolic syndrome, early behavioral and physiological alterations frequently precede overt pathological hallmarks by weeks or months.

Longitudinal analysis is therefore critical for understanding disease dynamics. Continuous behavioral monitoring enables the detection of gradual functional decline, compensatory mechanisms and treatment responses over time. Moreover, complex diseases generate multimodal datasets, including behavior, electrophysiology, imaging and molecular profiling. Digital tools enable the integration of these heterogeneous data streams into unified analytical frameworks, enhancing the translational relevance of preclinical models [20, 21].

Behavioral monitoring through digital technologies

Recent advances in AI-based behavioral recognition now permit high-resolution quantification of movement, posture and social interaction. Deep-learning frameworks such as DeepLabCut enable markerless pose estimation with near-human accuracy, facilitating precise gait analysis, tremor detection and fine motor assessment [20]. Likewise, SLEAP – Social Leap estimates animal poses and related multi-animal tracking platforms allow automated extraction of social interaction patterns in group-housed animals [25].

Computer-vision–based systems increasingly replace manual behavioral scoring, which is time-consuming and prone to inter-observer variability. Automated scoring improves reproducibility and enables the detection of subtle phenotypes that are often missed during short observation sessions [26]. These technologies are now widely applied in rodent models of anxiety, depression, autism spectrum disorders and neurodegeneration.

Wearable and implantable telemetry sensors enable continuous monitoring of physiological parameters such as EEG (electroencephalography), ECG (electrocardiography), locomotion, body temperature, blood pressure and activity rhythms in freely moving animals. Unlike traditional wired recordings, modern implantable telemetry systems minimize restraint and stress while providing high-fidelity longitudinal data [23].

In rodent models of epilepsy, telemetric EEG is widely used for continuous seizure detection and treatment-response monitoring, enabling accurate quantification of spontaneous seizure burden [27]. In Parkinson's disease models, telemetry-based locomotor and circadian rhythm analysis reveals early motor asymmetries and non-motor symptoms that precede overt dopaminergic neuronal loss [28]. Similarly, in Alzheimer's disease models, implantable temperature and activity sensors reveal disruptions in sleep–wake cycles and circadian rhythms well before cognitive impairment becomes evident [29].

These wearable technologies thus provide a crucial link between physiological dynamics and behavioral expression, supporting both mechanistic insight and therapeutic evaluation.

Digital biomarkers in preclinical neurodegeneration

Digital biomarkers are quantitative, objective measurements derived from continuous digital monitoring and they have become increasingly valuable in preclinical neurodegeneration research. Unlike traditional behavioral tests that capture isolated time points, digital biomarkers reflect continuous functional trajectories, improving sensitivity to early disease onset. In Alzheimer's disease models, subtle alterations in locomotor complexity, exploratory behavior, sleep fragmentation and circadian rhythm stability can be detected months before amyloid plaque deposition using automated home-cage and telemetry systems [29, 30]. In Parkinsonian models, fine-grained gait abnormalities and reduced movement initiation serve as early digital biomarkers of dopaminergic dysfunction [28].

Crucially, digital behavioral and physiological biomarkers can be integrated with histological, molecular and imaging endpoints, enabling multiscale disease characterization. For example, longitudinal behavioral decline can be directly linked to synaptic loss, neuroinflammation and neurodegeneration through post-mortem histology and *in vivo* imaging. This multimodal alignment strengthens mechanistic interpretation and improves the translational validity of animal models [21].

Challenges and limitations

While digitalization has profoundly advanced preclinical research, the integration of digital tools also introduces a series of technical, ethical, organizational and methodological challenges that must be carefully addressed to ensure responsible and effective implementation. One of the most significant technical challenges associated with digital preclinical research is the sheer volume and complexity of data generated by high-throughput screening, continuous behavioral monitoring, telemetry, imaging and multi-omics platforms. These large datasets require substantial computational infrastructure for storage, processing and long-term preservation. Without adequate infrastructure, data loss, inconsistent preprocessing and analytical bottlenecks become major risks [31].

Another major limitation is interoperability. Many digital platforms operate using proprietary data formats and heterogeneous metadata standards, which complicates data sharing and cross-study integration. Although the FAIR principles were introduced to address these issues, full implementation remains uneven across institutions [14]. Lack of interoperability limits large-scale meta-analyses and reduces the reproducibility and translational value of preclinical findings.

Ethical considerations

Despite their potential to improve animal welfare, continuous digital monitoring systems also raise ethical questions. Constant surveillance through video tracking, telemetry and biosensors generates massive amounts of sensitive biological data and may introduce new forms of experimental burden if not properly managed. Although many of these systems are non-invasive, implantable devices still require surgical procedures and carry risks of infection, discomfort, or altered behavior [23].

Additionally, ethical oversight frameworks were developed primarily for traditional experimental designs and are still adapting to AI-driven decision-making and automated phenotyping. The use of algorithms to classify pain, stress, or disease severity introduces concerns about transparency, accountability and validation of automated welfare assessments [32].

Expertise and high costs

Digital preclinical research requires highly specialized expertise that extends beyond classical biomedical training. Effective implementation of AI, automated monitoring and advanced data analytics depends on close collaboration between biologists, veterinarians, computer scientists, data engineers and statisticians. A major limitation is the shortage of researchers with interdisciplinary training, capable of both designing biological experiments and developing or validating complex computational models. Without such expertise, there is a risk of improper algorithm selection, incorrect data interpretation, and overreliance on black-box predictions [33].

Although digital technologies promise long-term gains in efficiency and data quality, the initial investment costs remain substantial. Telemetry systems, automated home-cage monitoring platforms, high-content imaging systems and dedicated computational infrastructure require considerable capital expenditure, which can be prohibitive for small academic laboratories and institutions in resource-limited settings. Analyses of high-throughput and digital research infrastructures show that advanced screening, imaging and data-processing platforms involve not only high acquisition costs but also expensive long-term operational demands [31, 33].

Beyond hardware, ongoing expenses related to maintenance, software licensing, cybersecurity, large-scale data storage and personnel training further restrict accessibility [33]. Studies examining the implementation of digital health and AI-based technologies consistently identify limited funding, insufficient infrastructure and lack of specialized workforce as major barriers, particularly in low- and middle-income environments [34]. As a result, digital innovation risks becoming concentrated in well-funded research centers, potentially widening global disparities in access to advanced preclinical technologies and in the capacity to generate data-rich, high-resolution animal models.

Conclusion

Digitalization is becoming an essential part of modern preclinical research by improving experimental design, supporting ethical standards based on the 3R principles and enhancing the study of complex diseases. Tools such as artificial intelligence, automation and digital monitoring help researchers obtain more accurate data, reduce unnecessary animal use and improve animal welfare. Digital technologies are particularly valuable in preclinical models of complex disorders, such as neurodegenerative and metabolic diseases, where long-term monitoring and data integration enable the earlier detection of functional changes and a deeper understanding of disease progression. At the same time, these digital approaches support the identification and testing of new therapeutic strategies, improving the quality and reliability of preclinical evidence.

Overall, digitalization does not replace traditional preclinical research, but rather strengthens it, making preclinical studies more precise, more ethical and more reproducible.

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Conflict of interest

The authors declare no conflict of interest.

Declaration of generative AI and AI-assisted technologies in the writing process:

The authors used ChatGPT (GPT-5.1, OpenAI, San Francisco, CA; accessed June 2025) to support language refinement and improve the clarity and coherence of the manuscript. All content was subsequently reviewed and revised by the authors, who take full responsibility for the accuracy and integrity of the final work.

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References

1. Bell, L.; Simonneau, C.; Zanini, C.; Kassianidou, E.; Zundel, C.; Neff, R.; Steinhuber, B.; Tecilla, M.; Odermatt, A.; Villaseñor, R.; et al. Advanced Tissue Technologies of Blood-Brain Barrier Organoids as High Throughput Toxicity Readouts in Drug Development. 2024, doi:10.2139/SSRN.4965471.
2. The Smart Benefit of Digital Systems in Preclinical Studies | BioPharm International Available online: https://www.biopharminternational.com/view/the-smart-benefit-of-digital-systems-in-preclinical-studies (accessed on 6 December 2025).
3. Vijayan, R.S.K.; Kihlberg, J.; Cross, J.B.; Poongavanam, V. Enhancing Preclinical Drug Discovery with Artificial Intelligence. Drug Discov Today 2022, 27, 967–984, doi:10.1016/J.DRUDIS.2021.11.023.
4. Gangwal, A.; Lavecchia, A. Artificial Intelligence in Preclinical Research: Enhancing Digital Twins and Organ-on-Chip to Reduce Animal Testing. Drug Discov Today 2025, 30, 104360, doi:10.1016/J.DRUDIS.2025.104360.
5. Deng, S.; Li, C.; Cao, J.; Cui, Z.; Du, J.; Fu, Z.; Yang, H.; Chen, P. Organ-on-a-Chip Meets Artificial Intelligence in Drug Evaluation. Issue 13 Theranostics 2023, 13, 4526–4558, doi:10.7150/thno.87266.
6. Berridge, B.R.; Baran, S.W.; Kumar, V.; Bratcher-Petersen, N.; Ellis, M.; Liu, C.N.; Robertson, T.L. Digitalization of Toxicology: Improving Preclinical to Clinical Translation. Frontiers in Toxicology 2024, 6, 1377542, doi:10.3389/FTOX.2024.1377542/BIBTEX.
7. Loewa, A.; Feng, J.J.; Hedtrich, S. Human Disease Models in Drug Development. Nature Reviews Bioengineering | 2023, 1, 545–559, doi:10.1038/s44222-023-00063-3.
8. Gómez-Bombarelli, R.; Wei, J.N.; Duvenaud, D.; Hernández-Lobato, J.M.; Sánchez-Lengeling, B.; Sheberla, D.; Aguilera-Iparraguirre, J.; Hirzel, T.D.; Adams, R.P.; Aspuru-Guzik, A. Automatic Chemical Design Using a Data-Driven Continuous Representation of Molecules. ACS Cent Sci 2018, 4, 268, doi:10.1021/ACSCENTSCI.7B00572.
9. Karimi, M.; Wu, D.; Wang, Z.; Shen, Y. DeepAffinity: Interpretable Deep Learning of Compound-Protein Affinity through Unified Recurrent and Convolutional Neural Networks. Bioinformatics 2019, 35, 3329–3338, doi:10.1093/BIOINFORMATICS/BTZ111.
10. Ekins, S.; Puhl, A.C.; Zorn, K.M.; Lane, T.R.; Russo, D.P.; Klein, J.J.; Hickey, A.J.; Clark, A.M. Exploiting Machine Learning for End-to-End Drug Discovery and Development. Nat Mater 2019, 18, 435–441, doi:10.1038/S41563-019-0338-Z.
11. Xu, Z.; Ren, F.; Wang, P.; Cao, J.; Tan, C.; Ma, D.; Zhao, L.; Dai, J.; Ding, Y.; Fang, H.; et al. A Generative AI-Discovered TNIK Inhibitor for Idiopathic Pulmonary Fibrosis: A Randomized Phase 2a Trial. Nature Medicine 2025 31:8 2025, 31, 2602–2610, doi:10.1038/s41591-025-03743-2.
12. MacArron, R.; Banks, M.N.; Bojanic, D.; Burns, D.J.; Cirovic, D.A.; Garyantes, T.; Green, D.V.S.; Hertzberg, R.P.; Janzen, W.P.; Paslay, J.W.; et al. Impact of High-Throughput Screening in Biomedical Research. Nat Rev Drug Discov 2011, 10, 188–195, doi:10.1038/NRD3368.
13. Moen, E.; Bannon, D.; Kudo, T.; Graf, W.; Covert, M.; Van Valen, D. Deep Learning for Cellular Image Analysis. Nat Methods 2019, 16, 1233–1246, doi:10.1038/S41592-019-0403-1.
14. Wilkinson, M.D.; Dumontier, M.; Aalbersberg, Ij.J.; Appleton, G.; Axton, M.; Baak, A.; Blomberg, N.; Boiten, J.W.; da Silva Santos, L.B.; Bourne, P.E.; et al. The FAIR Guiding Principles for Scientific Data Management and Stewardship. Scientific Data 2016 3:1 2016, 3, 160018-, doi:10.1038/sdata.2016.18.
15. Huh, D. A Human Breathing Lung-on-a-Chip. Ann Am Thorac Soc 2015, 12, S42, doi:10.1513/ANNALSATS.201410-442MG.
16. Low, L.A.; Mummery, C.; Berridge, B.R.; Austin, C.P.; Tagle, D.A. Organs-on-Chips: Into the next Decade. Nature Reviews Drug Discovery 2020 20:5 2020, 20, 345–361, doi:10.1038/s41573-020-0079-3.
17. Corral-Acero, J.; Margara, F.; Marciniak, M.; Rodero, C.; Loncaric, F.; Feng, Y.; Gilbert, A.; Fernandes, J.F.; Bukhari, H.A.; Wajdan, A.; et al. The “Digital Twin” to Enable the Vision of Precision Cardiology. Eur Heart J 2020, 41, 4556-4564B, doi:10.1093/EURHEARTJ/EHAA159.
18. Rusyn, I.; Daston, G.P. Computational Toxicology: Realizing the Promise of the Toxicity Testing in the 21st Century. Environ Health Perspect 2010, 118, 1047–1050, doi:10.1289/EHP.1001925.
19. Raies, A.B.; Bajic, V.B. In Silico Toxicology: Computational Methods for the Prediction of Chemical Toxicity. Wiley Interdiscip Rev Comput Mol Sci 2016, 6, 147–172, doi:10.1002/WCMS.1240;SUBPAGE:STRING:FULL.
20. Mathis, A.; Mamidanna, P.; Cury, K.M.; Abe, T.; Murthy, V.N.; Mathis, M.W.; Bethge, M. DeepLabCut: Markerless Pose Estimation of User-Defined Body Parts with Deep Learning. Nature Neuroscience 2018 21:9 2018, 21, 1281–1289, doi:10.1038/s41593-018-0209-y.
21. Voikar, V.; Gaburro, S. Three Pillars of Automated Home-Cage Phenotyping of Mice: Novel Findings, Refinement,

and Reproducibility Based on Literature and Experience. Front Behav Neurosci 2020, 14, 575434, doi:10.3389/FNBEH.2020.575434/EPUB.

22. Pernold, K.; Iannello, F.; Low, B.E.; Rigamonti, M.; Rosati, G.; Scavizzi, F.; Wang, J.; Raspa, M.; Wiles, M. V; Ulfhake Id, B. Towards Large Scale Automated Cage Monitoring-Diurnal Rhythm and Impact of Interventions on in-Cage Activity of C57BL/6J Mice Recorded 24/7 with a Non-Disrupting Capacitive-Based Technique. 2019, doi:10.1371/journal.pone.0211063.
23. Kramer, K.; Kinter, L.B. Evaluation and Applications of Radiotelemetry in Small Laboratory Animals. Physiol Genomics 2003, 13, 197–205, doi:10.1152/PHYSIOLGENOMICS.00164.2002.
24. Weissbrod, A.; Shapiro, A.; Vasserman, G.; Edry, L.; Dayan, M.; Yitzhaky, A.; Hertzberg, L.; Feinerman, O.; Kimchi, T. Automated Long-Term Tracking and Social Behavioural Phenotyping of Animal Colonies within a Semi-Natural Environment. Nat Commun 2013, 4, doi:10.1038/NCOMMS3018.
25. Pereira, T.D.; Tabris, N.; Matsliah, A.; Turner, D.M.; Li, J.; Ravindranath, S.; Papadoyannis, E.S.; Normand, E.; Deutsch, D.S.; Wang, Z.Y.; et al. SLEAP: A Deep Learning System for Multi-Animal Pose Tracking. Nat Methods 2022, 19, 486–495, doi:10.1038/S41592-022-01426-1.
26. Wiltschko, A.B.; Johnson, M.J.; Iurilli, G.; Peterson, R.E.; Katon, J.M.; Pashkovski, S.L.; Abraira, V.E.; Adams, R.P.; Datta, S.R. Mapping Sub-Second Structure in Mouse Behavior. Neuron 2015, 88, 1121–1135, doi:10.1016/j.neuron.2015.11.031.
27. Pitkänen, A.; Löscher, W.; Vezzani, A.; Becker, A.J.; Simonato, M.; Lukasiuk, K.; Gröhn, O.; Bankstahl, J.P.; Friedman, A.; Aronica, E.; et al. Advances in the Development of Biomarkers for Epilepsy. Lancet Neurol 2016, 15, 843–856, doi:10.1016/S1474-4422(16)00112-5.
28. Duty, S.; Jenner, P. Animal Models of Parkinson's Disease: A Source of Novel Treatments and Clues to the Cause of the Disease. Br J Pharmacol 2011, 164, 1357–1391, doi:10.1111/J.1476-5381.2011.01426.X.
29. Musiek, E.S.; Bhimasani, M.; Zangrilli, M.A.; Morris, J.C.; Holtzman, D.M.; Ju, Y.E.S. Circadian Rest-Activity Pattern Changes in Aging and Preclinical Alzheimer Disease. JAMA Neurol 2018, 75, 582–590, doi:10.1001/JAMANEUROL.2017.4719.
30. Jhuang, H.; Garrote, E.; Yu, X.; Khilnani, V.; Poggio, T.; Steele, A.D.; Serre, T. Automated Home-Cage Behavioural Phenotyping of Mice. Nat Commun 2010, 1, doi:10.1038/NCOMMS1064.
31. Marx, V. The Big Challenges of Big Data. Nature 2013 498:7453 2013, 498, 255–260, doi:10.1038/498255a.
32. Prescott, M.J.; Lidster, K. Improving Quality of Science through Better Animal Welfare: The NC3Rs Strategy. Lab Animal 2017 46:4 2017, 46, 152–156, doi:10.1038/laban.1217.
33. Topol, E.J. High-Performance Medicine: The Convergence of Human and Artificial Intelligence. Nature Medicine 2019 25:1 2019, 25, 44–56, doi:10.1038/s41591-018-0300-7.
34. Kaboré, S.S.; Ngangue, P.; Soubeiga, D.; Barro, A.; Pilabré, A.H.; Bationo, N.; Pafadnam, Y.; Drabo, K.M.; Hien, H.; Savadogo, G.B.L. Barriers and Facilitators for the Sustainability of Digital Health Interventions in Low and Middle-Income Countries: A Systematic Review. Front Digit Health 2022, 4, 1014375, doi:10.3389/FDGTH.2022.1014375