Congresul Național de Medicină Fizică, de Recuperare și Balneoclimatologie
Covasna, 23 – 25 Aprilie 2026

STRATIF-AI Future Perspectives: Continuous Stratification Across the Stroke Pathway Using Digital Twins and Artificial Intelligence

Constantin Munteanu[1,2], Ana-Maria Vasile[2], Cristina Popescu[2], Gelu Onose [2,3]

1. Faculty of Medical Bioengineering, University of Medicine and Pharmacy "Grigore T. Popa" Iași, 700454, Romania
2. Teaching Emergency Hospital "Bagdasar-Arseni" (TEHBA), 041915 Bucharest, Romania
3. Faculty of Medicine, University of Medicine and Pharmacy "Carol Davila", Bucharest, RomaniaFaculty of Medicine, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania.

Relevant Financial Disclosure(s)

EUROPEAN HEALTH AND DIGITAL EXECUTIVE AGENCY (HADEA)

HADEA.A – Health and Food
A.3 – Health research

Gunnar CEDERSUND
LINKOPINGS UNIVERSITET
CAMPUS VALLA
581 83 LINKOPING
SWEDEN

Subject: Horizon Europe (HORIZON)
Call: HORIZON-HLTH-2022-TOOL-12-two-stage
Project: 101080875 — STRATIF-AI
GAP invitation letter

Dear Applicant,

I am writing in connection with your proposal for the above-mentioned call.

Having completed the evaluation, we are pleased to inform you that your proposal has passed this phase and that we would now like to start grant preparation.

Please find enclosed the evaluation summary report (ESR) for your proposal (for both stages of the evaluation).

Please be aware that there may be differences between the ESRs, since stage 1 evaluations are done on the outline of your proposal, while stage 2 evaluations cover the full proposal.

Invitation to grant preparation

Grant preparation will be based on the following:

1. **Project:**

   Project number and name: 101080875 — STRATIF-AI

   Topic: HORIZON-HLTH-2022-TOOL-12-01-two-stage — Computational models for new patient stratification strategies

   Type of action: HORIZON Research and Innovation Actions

   Requested grant amount (proposal): 5 969 100.00 EUR

   Maximum grant amount (after evaluation): 5 969 100.00 EUR

   Project duration: 48 months

Funding & tender opportunities
Single Electronic Data Interchange Area (SEDIA)

My Project: STRATIF-AI



STRATIF-AI proposes a paradigm shift from episodic stratification to continuous stratification, enabled by hybrid digital twins that dynamically integrate clinical, imaging, biological, behavioral, and wearable-derived data across the entire stroke condition. The platform is conceived as an interconnected, patient-centric architecture spanning prevention, acute treatment, and rehabilitation, with the overarching aim of improving personalization, prediction, monitoring, and long-term outcome optimization.



Data Collection and Analysis

AI can significantly enhance stroke therapeutic interventions by utilizing vast amounts of patient data to inform treatment plans. This data includes:

1. **Medical History: Comprehensive records of past medical conditions, treatments, and responses.**
2. **Genetic Information: Insights from genetic testing indicate predispositions to certain conditions.**
3. **Lifestyle Data: Information on diet, exercise, sleep patterns, and stress levels.**
4. **Environmental Factors: Details about the patient's living environment, such as pollution levels, that might affect health.**

BioMedInformatics

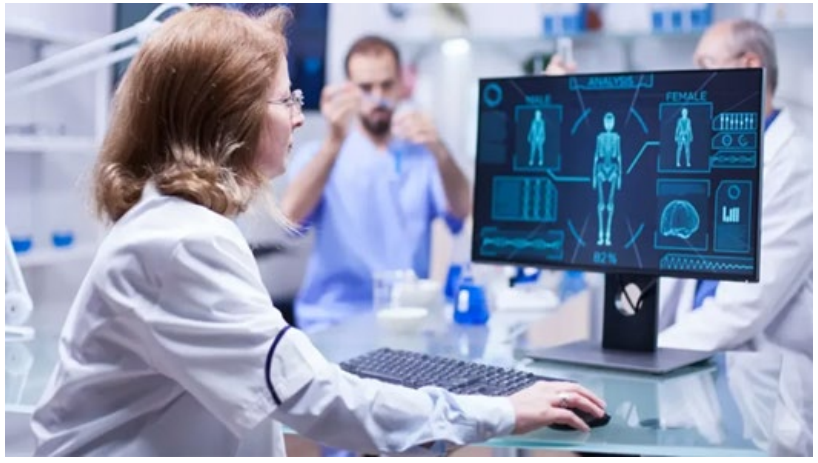
MDPI

Review

A Comprehensive Survey of Digital Twins in Healthcare in the Era of Metaverse

Muhammad Turab [1] and Sonain Jamil [1,2,*]





The central idea is simple, but clinically transformative: stroke care should not rely only on episodic risk assessment performed at isolated moments. Instead, we should move toward a continuously updated, patient-specific representation of risk, rehabilitation, and therapeutic opportunity. In other words, we should ask not only: What category does this patient belong to today? but rather: How is this individual patient's trajectory changing now, and what intervention is most likely to improve that trajectory?

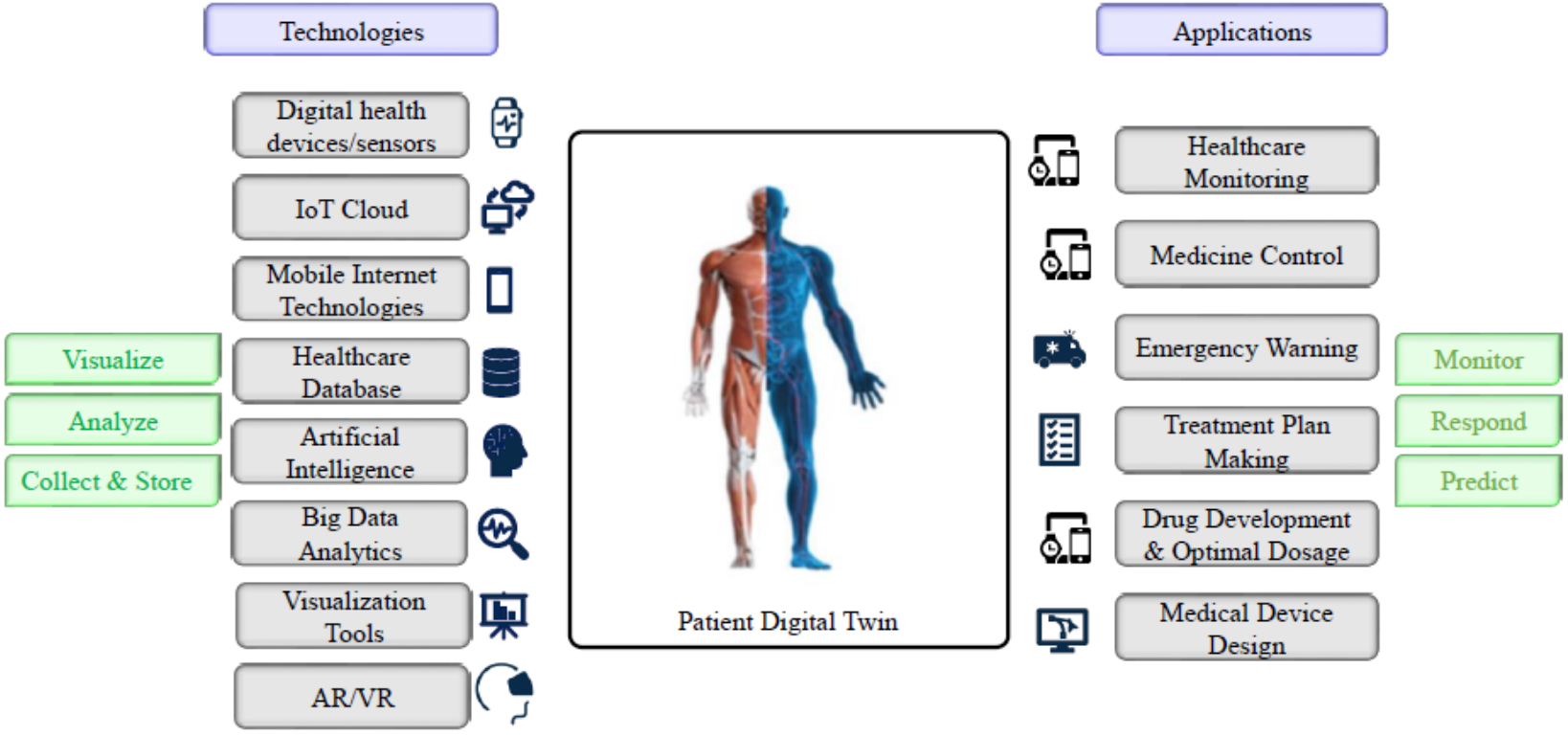
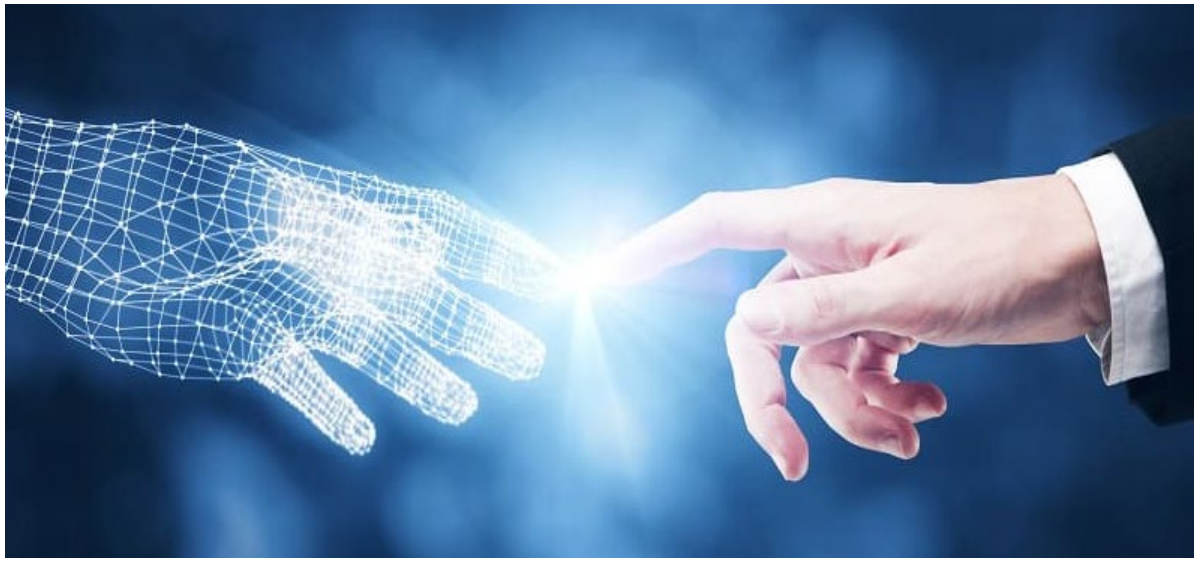


Figure 2. Technologies and applications of DT as illustrated in [71].

Introduction to Digital Twins (DTs)

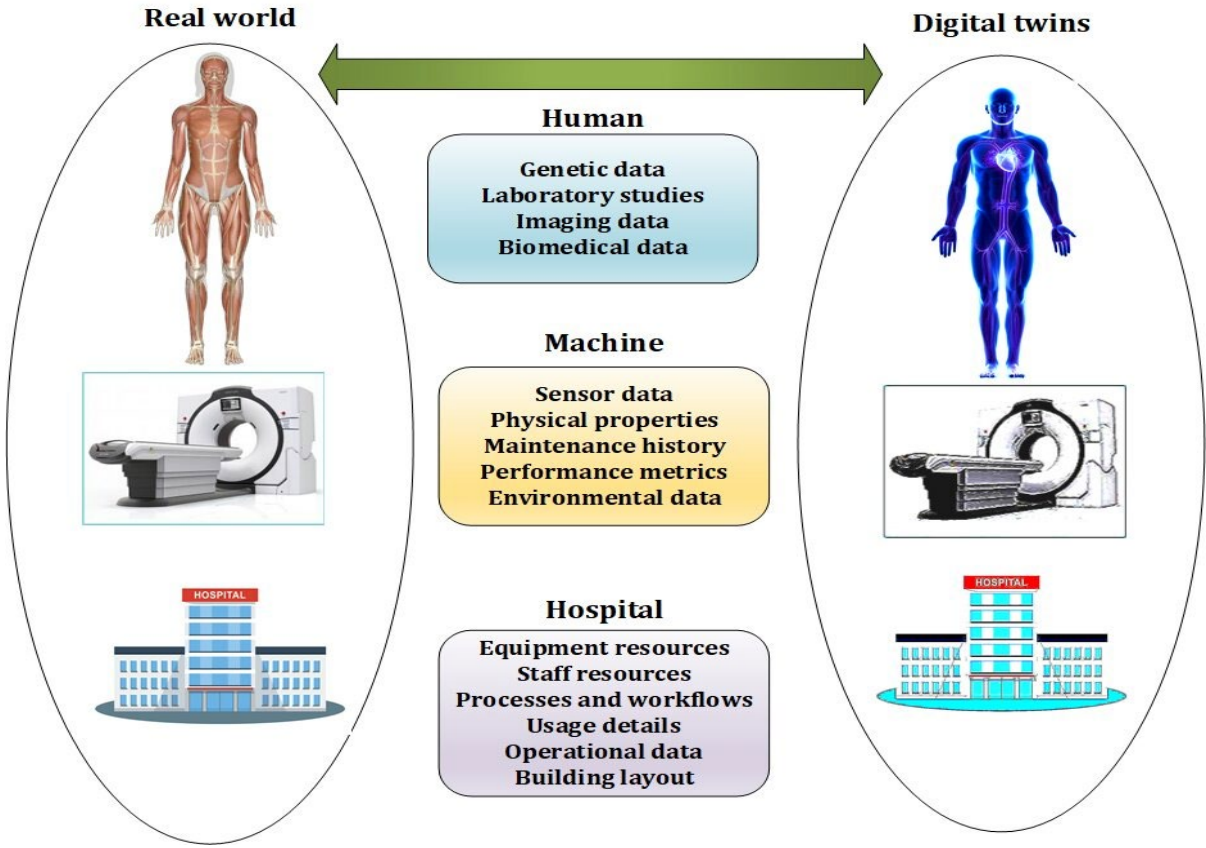
- Digital Twins (DTs) represent a groundbreaking technological advancement, creating virtual replicas of physical entities to monitor, simulate, and predict real-time behaviors.
- Initially developed for fields like aerospace and automotive engineering, Digital Twins are now extensively applied in healthcare. In this context, they allow clinicians to model individual patients, thereby predicting responses to treatments and optimizing outcomes.
- Digital Twins function by continuously updating virtual models based on real-world data from the physical counterpart. This allows simulations and analyses that were previously impossible. Through real-time modeling, Digital Twins provide a robust framework for precision medicine, where interventions are highly personalized.
- Digital Twins rely on biosensors, data analytics, and advanced imaging techniques to create accurate representations of biological systems, capturing physiological states that inform individualized care. As DT technology advances, it shows potential for complex, dynamic fields such as personalized therapies in stroke, an area that could greatly benefit from DT-based predictive modeling and patient-specific intervention strategies.

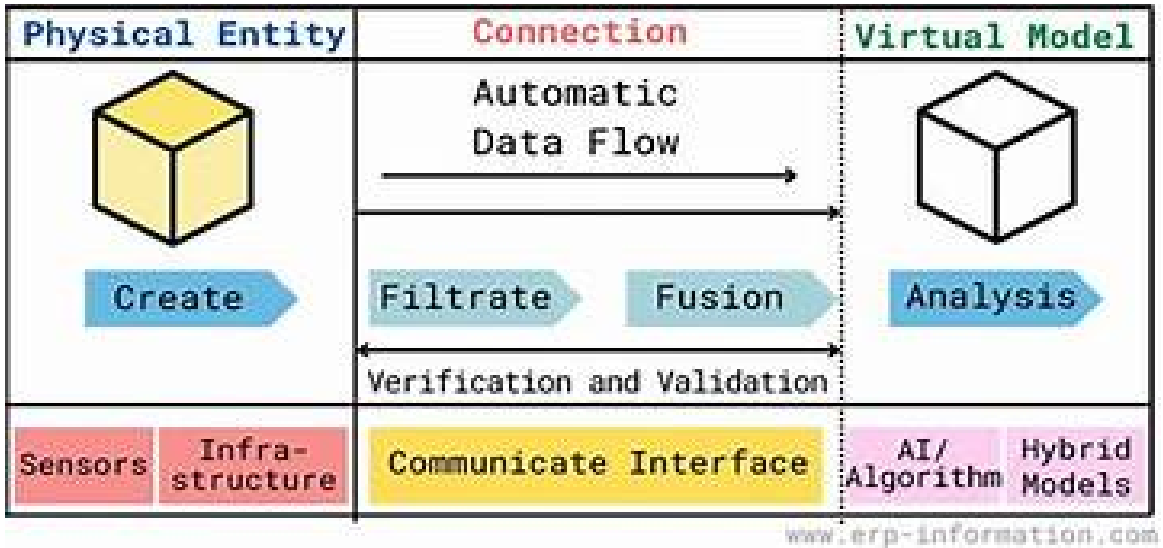




Intersection of Digital Twins and STROKE

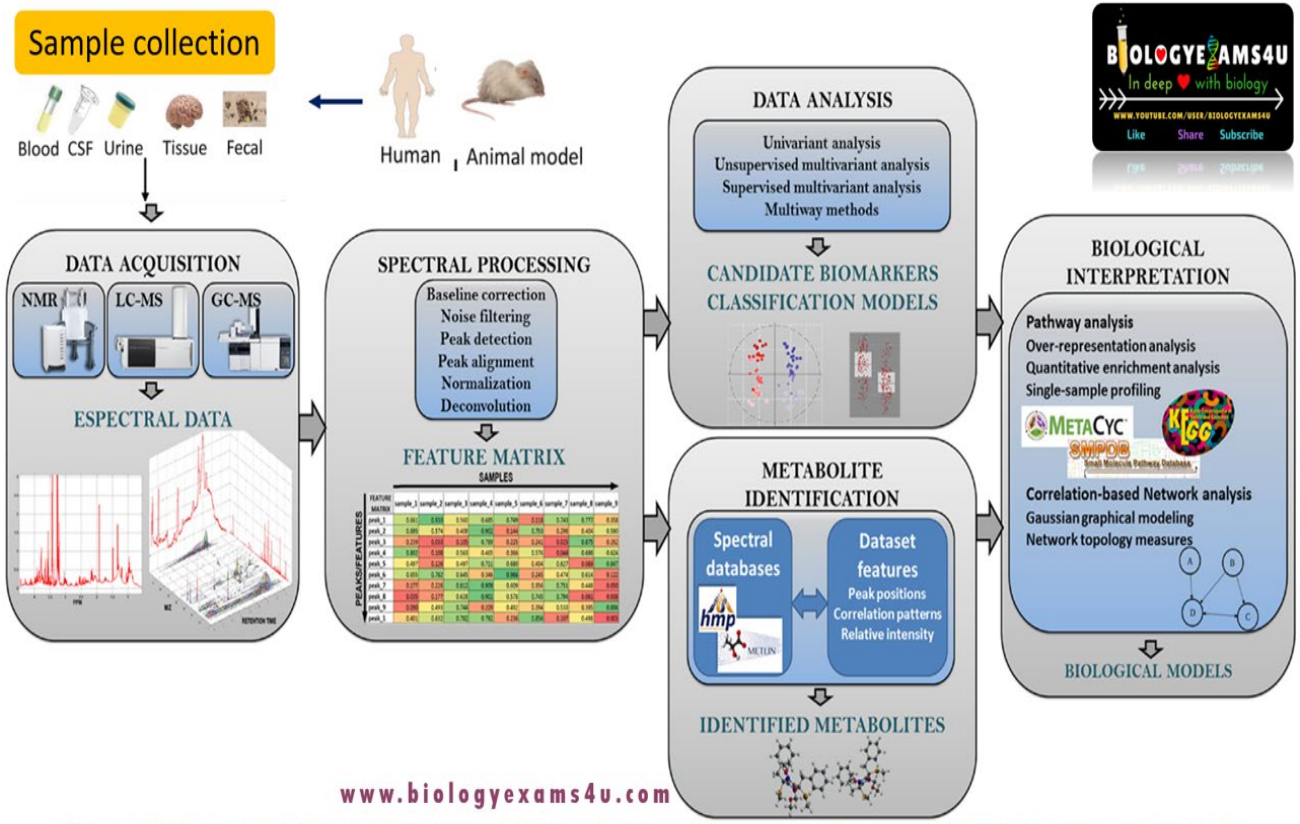
- The integration of Digital Twins in Stroke is intended to revolutionize therapeutic interventions by combining traditional rehabilitation treatments with cutting-edge digital modeling.
- A Digital Twin of a patient undergoing rehabilitation can simulate individual responses to various treatment parameters — physical therapy, rehabilitation, and pharmatherapy—allowing practitioners to tailor therapies based on unique health profiles. By leveraging the real-time data that DTs provide, clinicians can customize interventions to optimize efficacy and safety.
- This approach moves rehabilitation from a generalized therapy toward a model of precision care, where each treatment session uniquely suits the patient's evolving condition. Additionally, DTs in rehabilitation offer predictive insights, enabling clinicians to anticipate how a patient might respond to specific treatment changes. This personalized model can refine treatments, minimize side effects, and improve outcomes, paving the way for a modern, data-enhanced therapy.



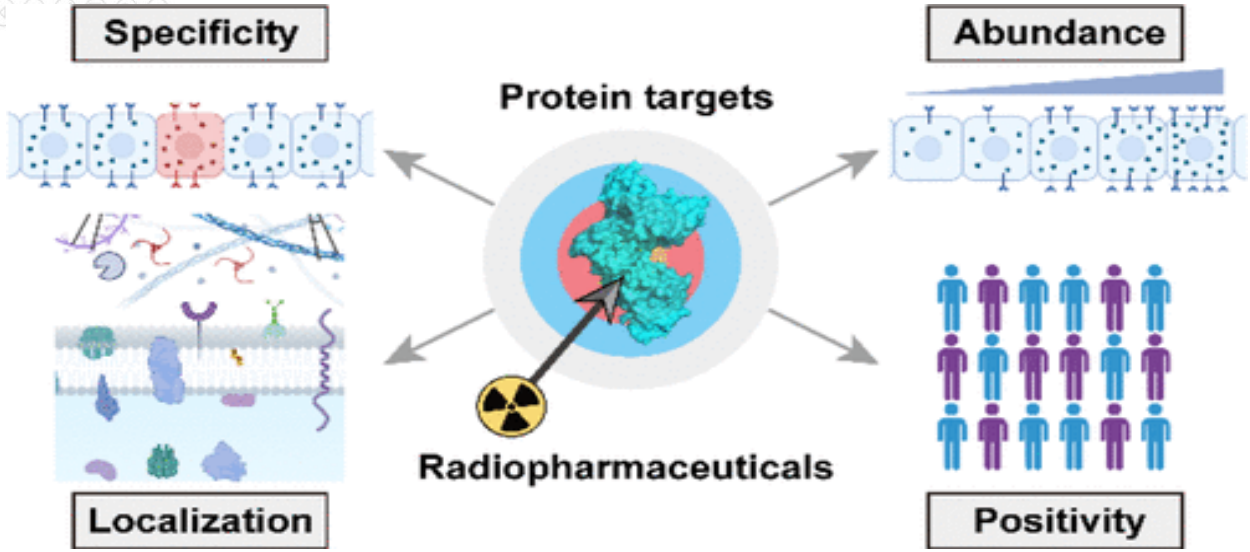


Mechanics of a Digital Twin

- A Digital Twin for rehabilitation functions by creating a comprehensive, virtual model of a patient, capturing physiological and pathological nuances that impact treatment outcomes.
- Data inputs from biosensors, patient health records, and imaging feed into the DT, allowing the virtual model to accurately simulate responses to different rehabilitation variables.
- The model continuously updates, reflecting the patient's real-time condition and adjusting simulated treatment protocols accordingly. Through advanced algorithms, the DT processes data on various parameters to simulate optimal therapeutic outcomes. The DT's core capability lies in its precision; by mirroring physiological changes, it provides clinicians with a powerful tool to test and refine rehabilitation regimens without trial and error on the patient. This model allows for customized therapies and supports clinical decision-making, advancing rehabilitation toward a future where personalized, precise treatments are routine.

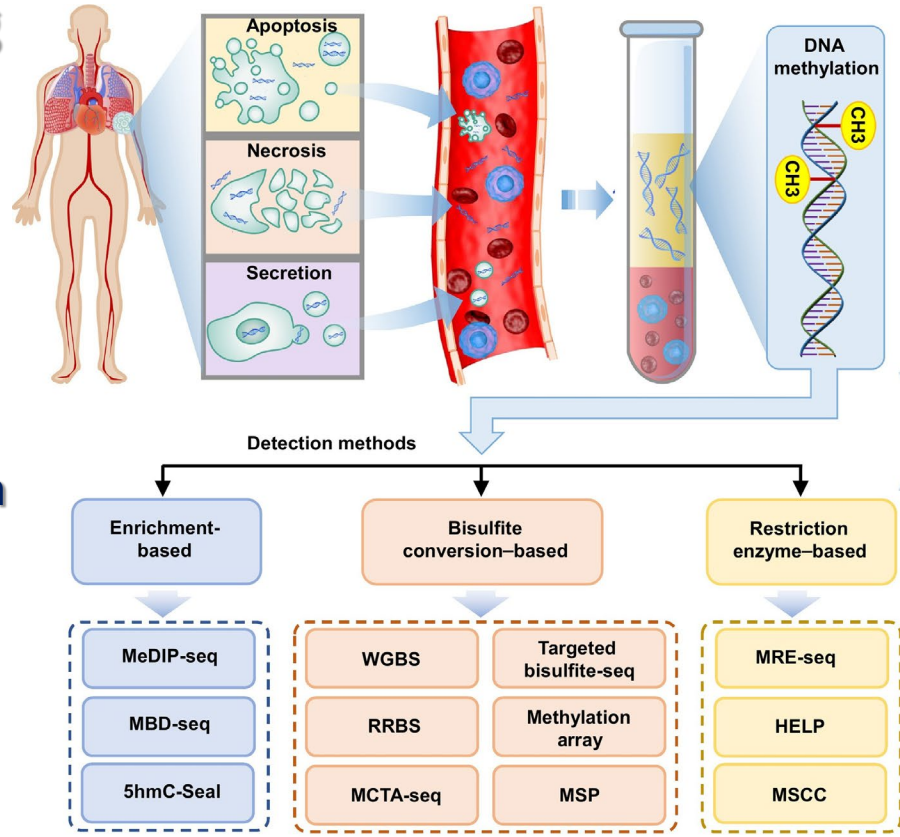


Alonso, A., Marsal, S., & Julià, A. (2015). Analytical methods in untargeted metabolomics: state of the art in 2015. *Frontiers in bioengineering and biotechnology*, *3*, 23.

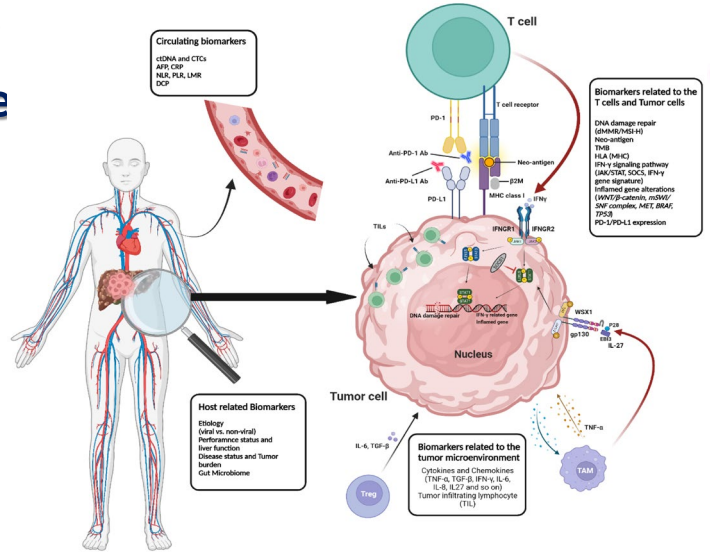


Role of Biosensors in Dynamic Monitoring

- Biosensors play an essential role in feeding real-time physiological data into Digital Twins, allowing dynamic and responsive modeling.
- These sensors, which can monitor heart rate, skin temperature, blood pressure, and other metrics, offer insights into how a patient's body responds during and after a rehabilitation session. For instance, if a patient's heart rate or skin temperature indicates discomfort or overexertion, the DT can signal the need for immediate adjustments, such as lowering intensity or shortening the session.
- Continuous data from biosensors ensures that the DT remains a highly accurate reflection of the patient's physical state, enabling real-time adjustments that maximize therapeutic benefits while minimizing potential adverse effects. In rehabilitation, this data-driven adaptability represents a shift from generalized treatment to a refined, continuously optimized intervention.

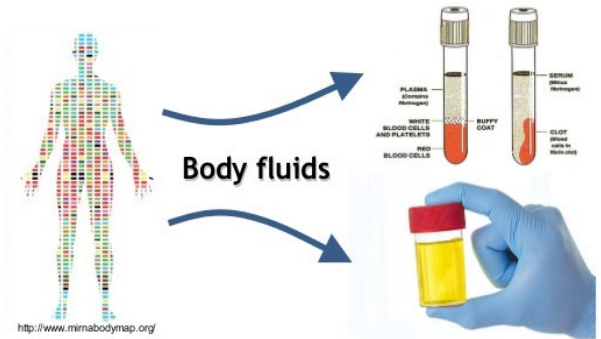


- Cancer detection: screening or earlier diagnosis
- Molecular profiling or prognostication
- Minimal residual disease monitoring
- Assessing treatment response
- Tracing the tissue origin of ctDNA



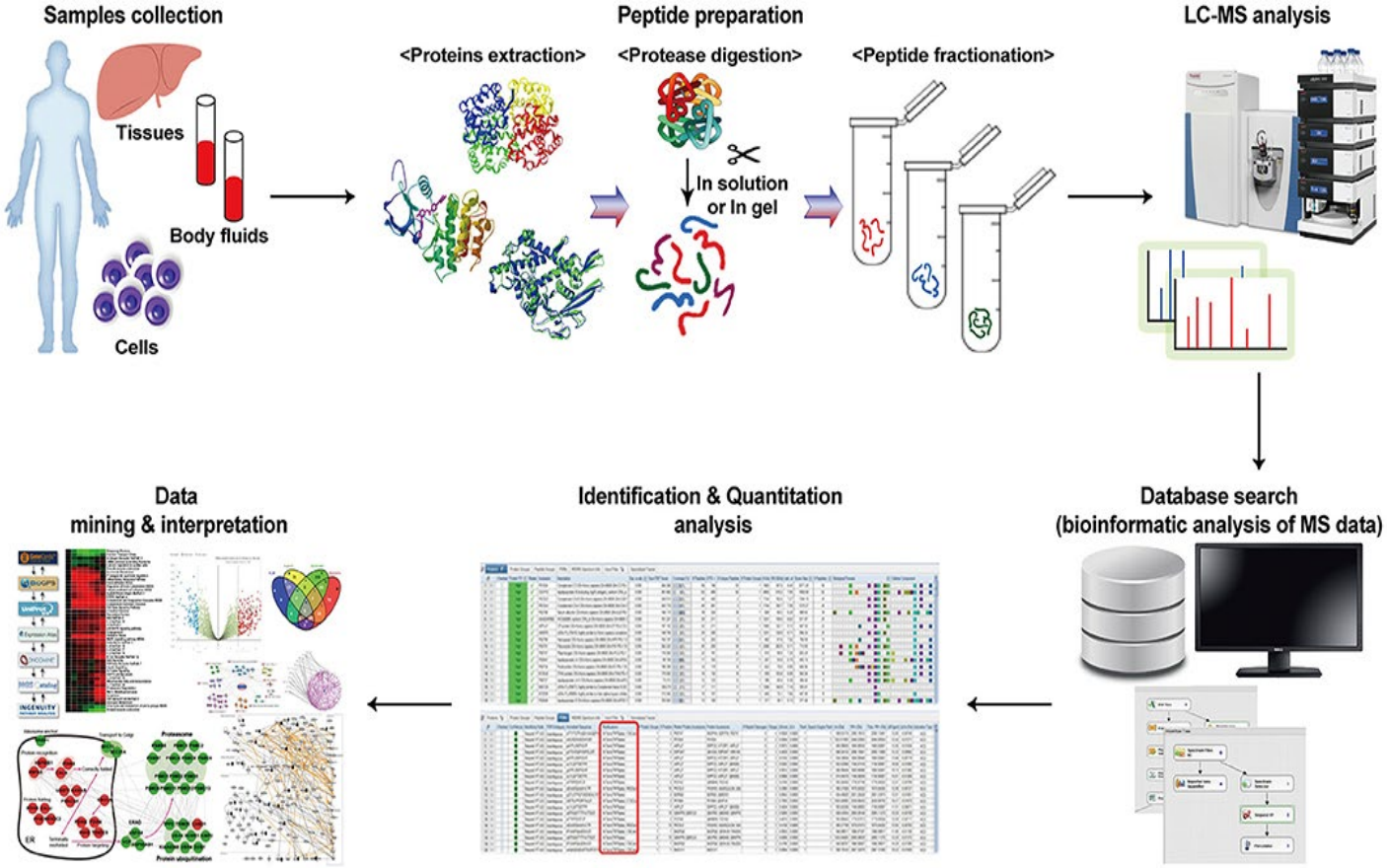
Biomarker

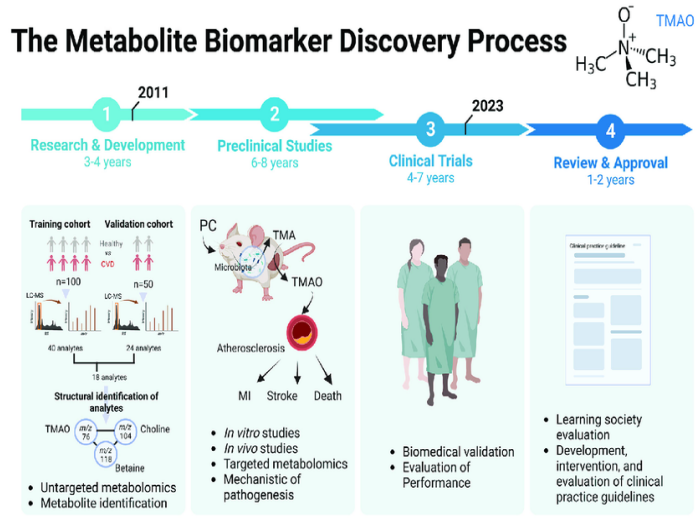
- miRNAs can be detected in serum, plasma, urine, and other biological fluids

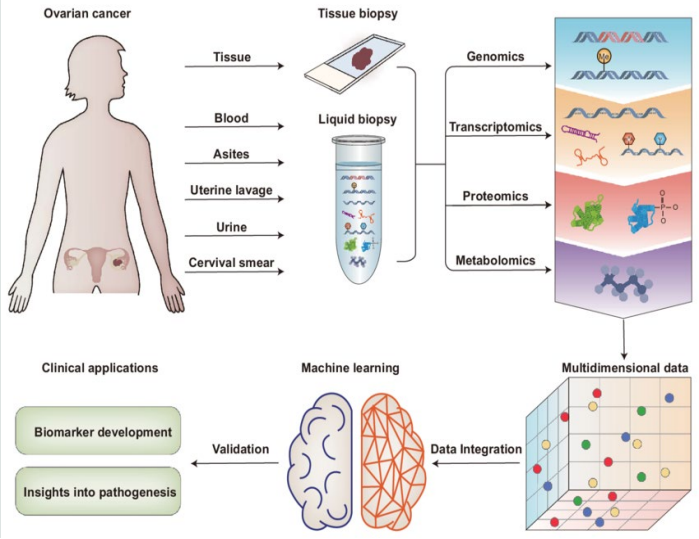


Personalized Treatment Modeling

- Digital Twins empower rehabilitation to offer genuinely personalized treatment by simulating individual physiological responses to various treatment parameters.
- Rather than applying a one-size-fits-all approach, DTs consider each patient's unique characteristics—such as cardiovascular health, skin sensitivity, and existing medical conditions—to model how they would react to specific therapies. For example, a DT might simulate a patient's response to higher intensity exercises, adjusting the treatment if it predicts a possible adverse reaction.
- By offering a tailored approach, DTs enhance both safety and efficacy, creating a therapeutic experience tailored to the individual's needs and maximizing the potential for positive outcomes.
- This shift from standardization to personalization marks a significant leap forward in rehabilitation, aligning the field with broader trends in precision medicine.

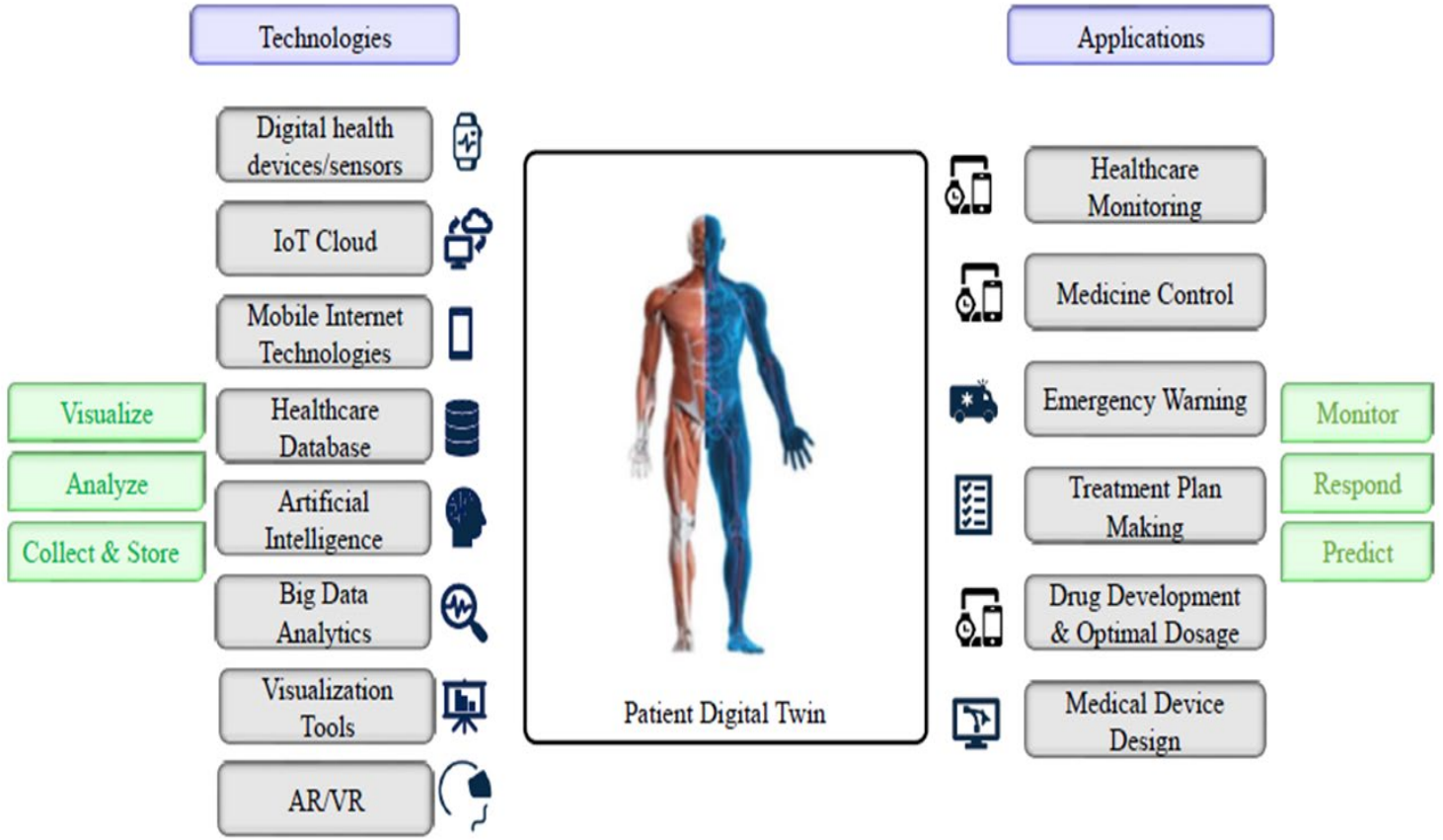






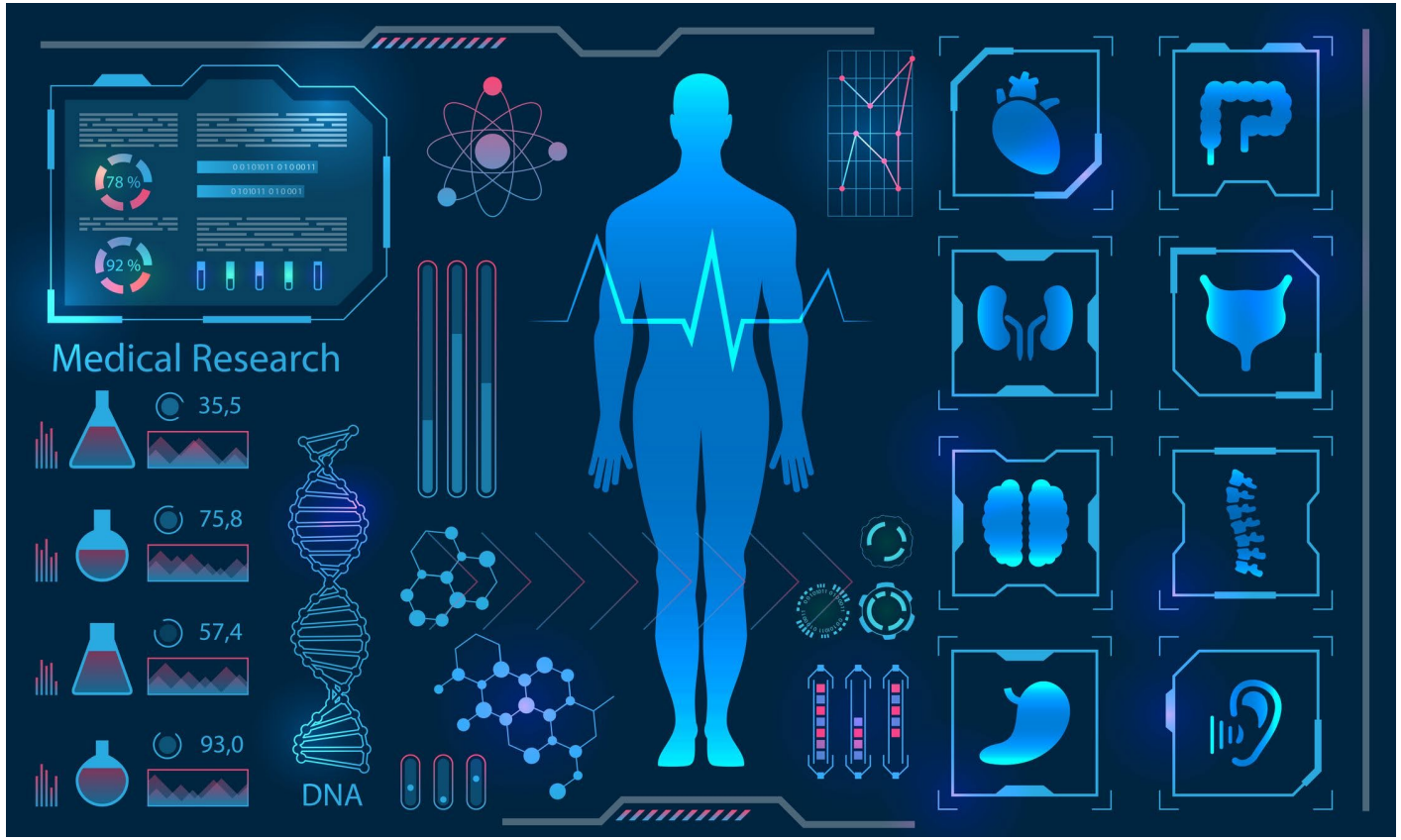
Integrating AI in DT-driven rehabilitation

- Artificial Intelligence (AI) augments Digital Twin capabilities by analyzing vast datasets to optimize rehabilitation treatments. Through machine learning, AI systems can identify patterns within the DT's data, learning how different patient types respond to specific therapies.
- AI enhances the DT's predictive accuracy, fine-tuning the rehabilitation protocol to better suit evolving patient needs. For instance, by analyzing data from previous sessions, AI can detect subtle trends and suggest preventive adjustments, such as gradually increasing exposure time.
- Furthermore, AI integration supports continuous learning within the DT, refining its recommendations based on new data. This symbiotic relationship between AI and DTs ensures that rehabilitation interventions are not only reactive but proactively optimized, delivering consistently superior outcomes.



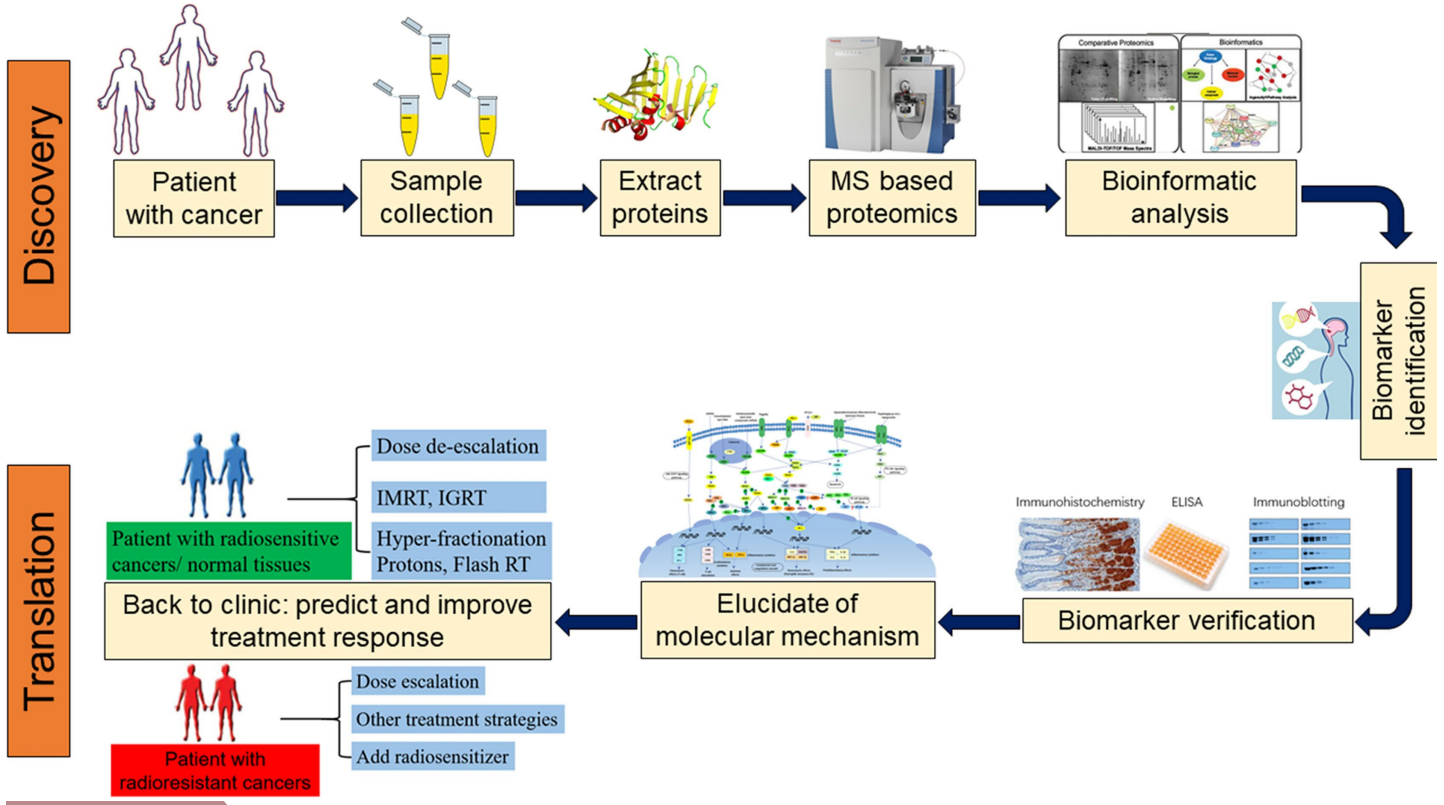
Precision-Driven Therapy

- Digital Twins enable precision-driven therapy by simulating individual responses to specific exercises and varying therapeutic parameters.
- Rather than applying generic treatment protocols, DTs can fine-tune factors like intensity levels to align with patient-specific therapeutic needs.
- This customized approach enhances the efficacy of rehabilitation therapy, potentially accelerating recovery for musculoskeletal conditions, skin disorders, and more.
- Digital Twins can, for instance, simulate how increased exercises intensity levels might affect a patient with joint inflammation, allowing the treatment to be customized without risking adverse reactions.
- By optimizing treatment precision, Digital Twins set a new standard for targeted, patient-centric therapy in rehabilitation.

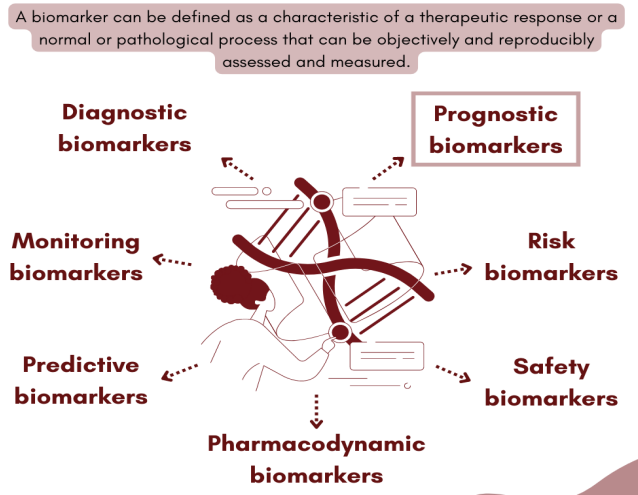


Longitudinal Patient Data for Chronic Conditions

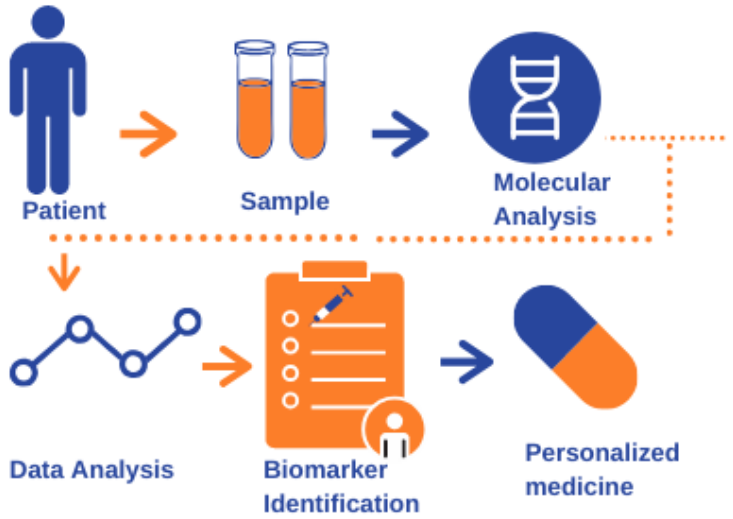
- For patients with chronic conditions, a DT can track treatment responses over time, building a comprehensive dataset that allows for increasingly refined therapeutic approaches. This long-term monitoring capability is invaluable for managing diseases that require periodic interventions, such as arthritis or stroke.
- Over time, the DT accumulates detailed data on how the patient's body reacts to specific treatments, creating a foundation for progressively more effective therapies. With this longitudinal perspective, clinicians can make data-driven decisions about treatment frequency, intensity, and adjustments based on accumulated insights, optimizing patient care across multiple sessions.



Types of biomarkers



Role of Biomarker



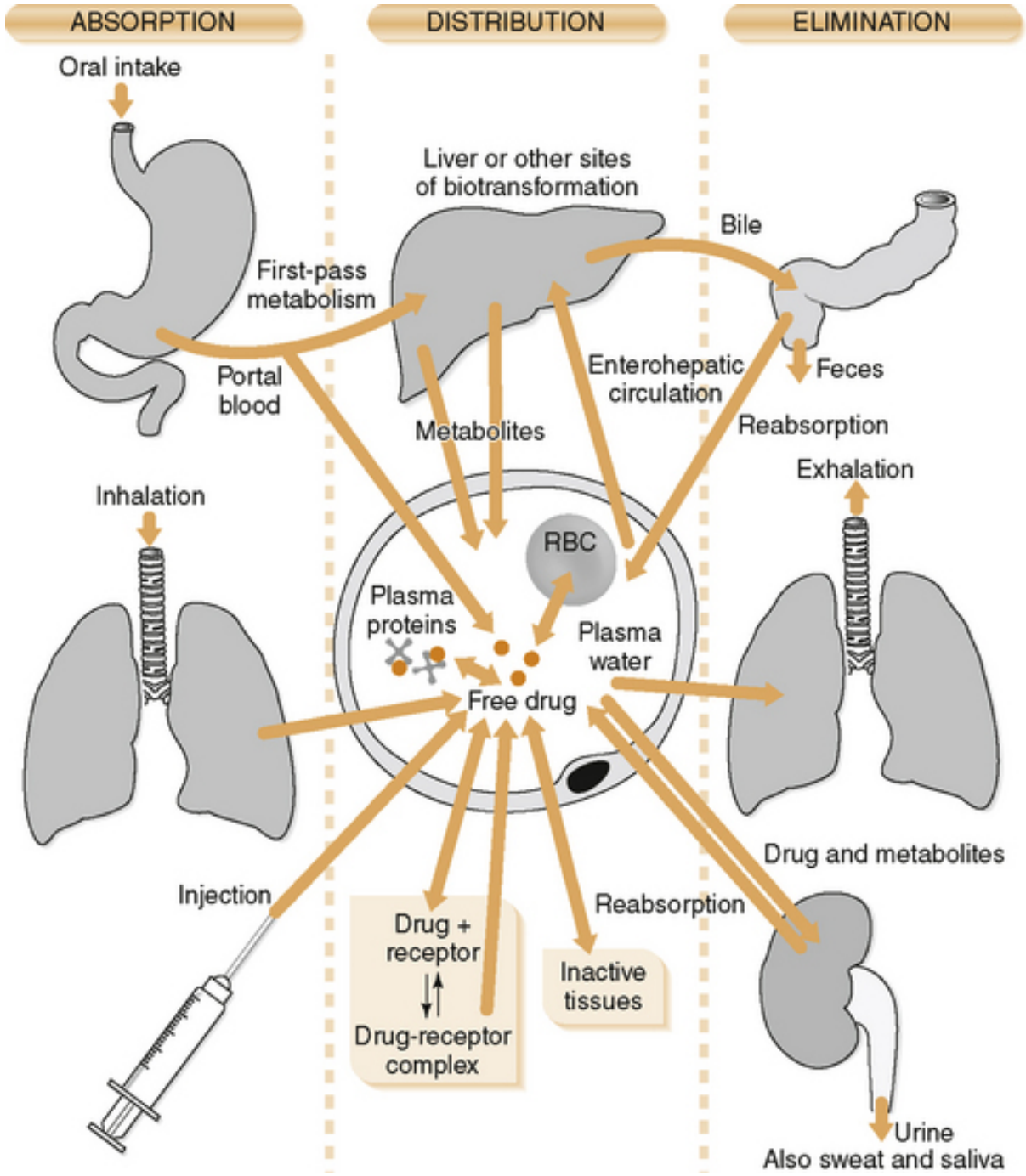
Ethical Considerations and Patient Privacy

- The adoption of Digital Twins in healthcare, including stroke, requires careful ethical consideration, particularly regarding patient privacy and data security.
- Digital Twins rely on highly sensitive patient data, necessitating robust protocols to protect information from unauthorized access.
- Compliance with data protection laws, such as GDPR, is essential, and health institutions need transparent protocols for data collection, storage, and sharing.
- Additionally, clinicians should obtain explicit patient consent, ensuring that individuals are fully informed about how their data will be used.
- Ethical governance in Digital Twins-based medicine also includes managing AI biases to ensure equitable treatment recommendations across diverse patient populations.



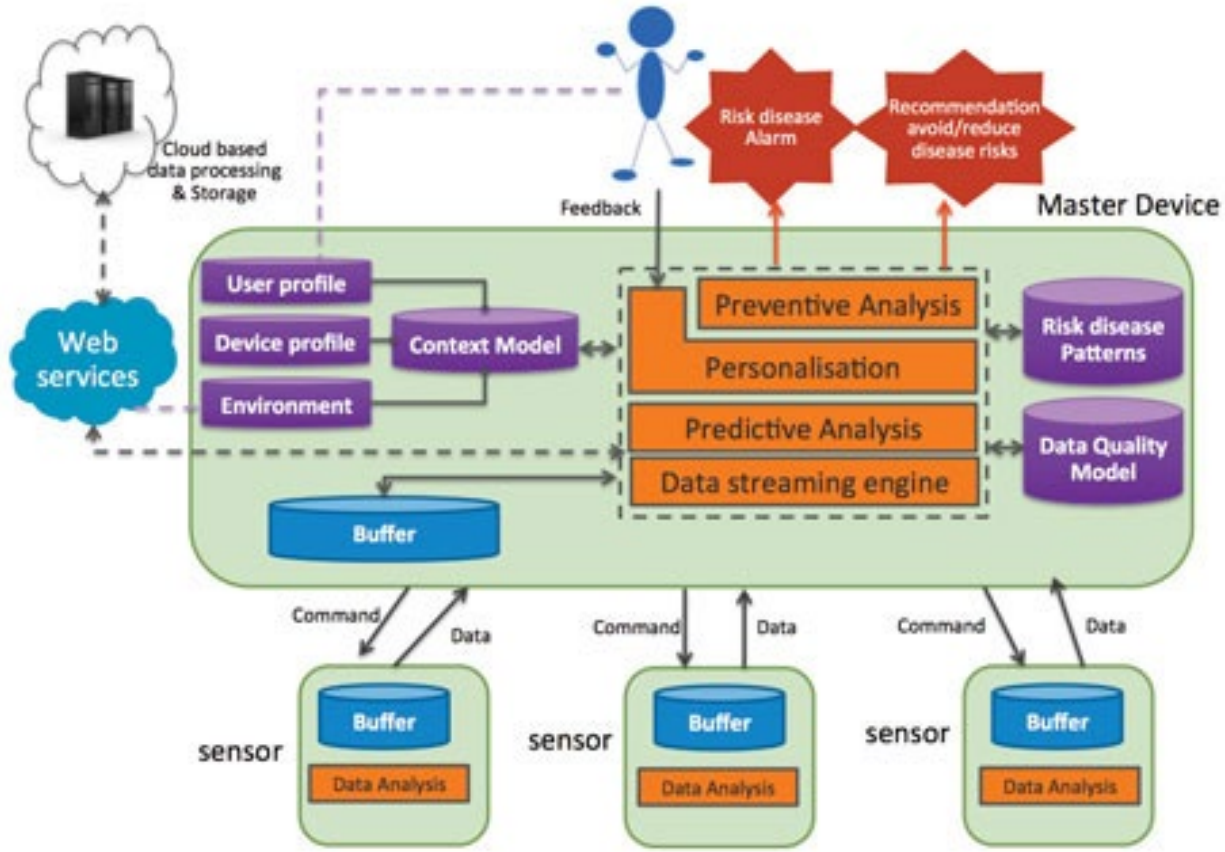
Technical Challenges and Limitations

- Implementing DTs in rehabilitation poses technical challenges, particularly in accurately modeling complex physiological responses.
- The intricacies of the human body—such as individual variations in skin permeability or exercises intensity—make it difficult to create universally reliable models.
- Additionally, current biosensors may not capture all necessary data, potentially limiting the DT's precision.
- Developing more sophisticated sensors, advanced data integration techniques, and improved machine learning models are crucial to overcome these challenges.
- Addressing these technical limitations is essential for ensuring that DTs in rehabilitation provide accurate, reliable, and clinically meaningful insights.



Patient-centered P4 Medicine and Digital Twins

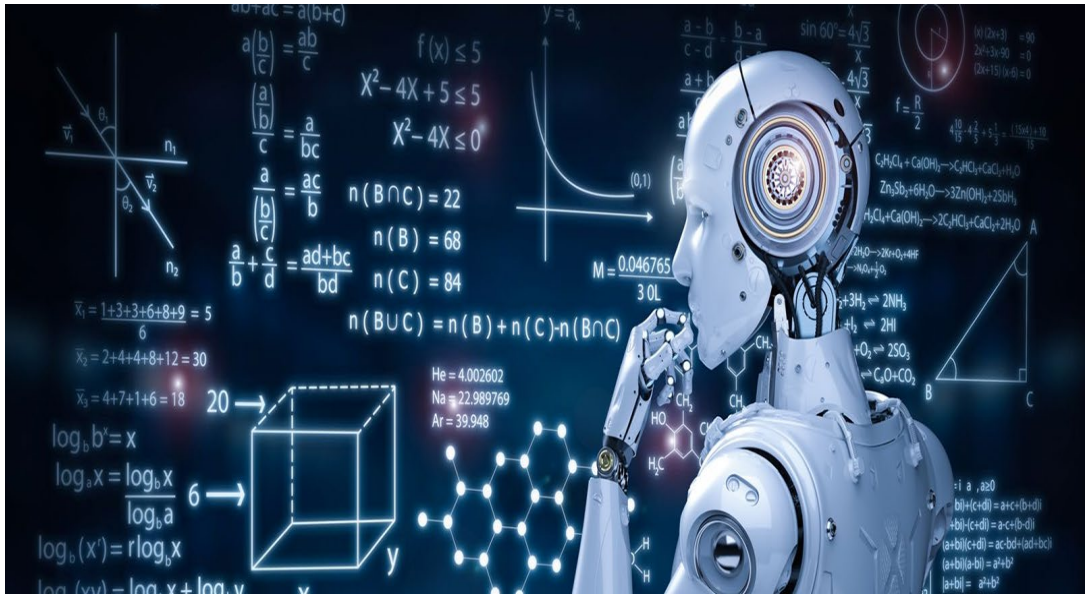
- Digital Twins naturally align with P4 medicine's four pillars: predictive, preventive, personalized, and participatory care.
- Digital Twins excel at predictive and preventive modeling, simulating patient responses to anticipate adverse reactions or ineffective treatments before they occur.
- Personalized care is embedded in the Digital Twins framework, as each model adapts to individual patient needs.
- Furthermore, Digital Twins support participatory medicine by involving patients in their care journey; for instance, patients could monitor their own progress through Digital Twins visualizations, gaining insights into how their bodies react to different therapies.
- This participatory approach fosters patient empowerment, encouraging adherence to treatment plans and active engagement with health outcomes.



The architecture: data, models, feedback, action

- The digital twin system can be described as a loop.
- First, there is the physical patient: the person living with vascular risk, stroke injury, functional limitations, and recovery potential.
- Second, there is data acquisition: electronic health records, imaging, laboratory values, physiological monitoring, medication data, wearable sensors, rehabilitation assessments, gait metrics, speech measures, cognitive testing, and patient-reported outcomes.
- Third, there is the middleware layer: data storage, semantic harmonization, preprocessing, quality control, interoperability, and secure exchange. Without this layer, the digital twin cannot be clinically reliable, because the model will inherit the fragmentation and noise of the source systems.
- Fourth, there is the modeling layer: mechanistic models, statistical models, machine learning, deep learning, and explainable AI. This is where prediction becomes possible.
- Fifth, there is the clinical interface: a decision-support environment that presents information in a way that is interpretable, actionable, and compatible with workflow.
- Finally, there is the feedback loop. The clinician acts, the patient responds, new data are generated, and the model updates. This is the difference between a static model and a learning clinical system.





STRATIF-AI across the whole stroke pathway

A major strength of the STRATIF-AI vision is that it is not limited to a single clinical episode. It covers the whole stroke pathway: prevention, acute treatment, rehabilitation, and long-term follow-up.

This is essential because stroke does not begin at hospital admission, and it does not end at discharge. The pre-stroke phase may include hypertension, atrial fibrillation, diabetes, carotid disease, sedentary behavior, inflammation, or previous transient ischemic events. The acute phase includes diagnostic uncertainty, time pressure, imaging interpretation, reperfusion decisions, peri-procedural risks, and early complications. The post-acute phase includes secondary prevention, neurorehabilitation, cognitive impairment, fatigue, spasticity, depression, social reintegration, and recurrence risk.

The official STRATIF-AI project description states that the project aims to refine and validate a scalable platform for continuous stratification to improve prevention, treatment, and rehabilitation of stroke patients using digital twins and AI. It also describes the ambition to connect apps across the entire patient journey, using six new clinical studies involving eight partner hospitals.

This is precisely the perspective needed in modern stroke medicine: not a single model for a single question, but a platform of connected models supporting the patient across transitions of care.

Prevention: identifying risk before the event

In prevention, continuous stratification can help move from generic population-level risk toward individualized, dynamic prevention.

For example, two patients may have similar conventional risk scores, but very different trajectories. One may show stable blood pressure, good adherence, improving physical activity, and no evidence of silent vascular progression. Another may show increasing blood pressure variability, poor sleep, atrial fibrillation burden, worsening metabolic control, or declining cognitive performance. Their nominal risk category may be similar, but their biological trajectories are different.

A digital twin can integrate these data streams and simulate alternative scenarios: What happens if blood pressure is controlled more aggressively? What is the likely benefit of improved adherence? How might exercise affect vascular risk and metabolic status? Which patient requires escalation, and which patient may be safely monitored?

The goal is not to replace clinical judgment. The goal is to make prevention more anticipatory. A useful prevention twin should support earlier recognition of instability, clearer patient communication, and personalized recommendations that are understandable enough to improve adherence.

This is where digital twins also have behavioral value. When patients see their own projected risk trajectory, prevention may become less abstract and more personally meaningful.

Acute stroke: time-critical stratification and decision support

The acute stroke phase is where minutes matter, but it is also where uncertainty is greatest.

In acute care, AI already has important roles in image segmentation, lesion detection, large-vessel occlusion triage, perfusion analysis, and workflow acceleration. However, the digital twin perspective goes beyond image classification. It asks: Can we integrate imaging, physiology, comorbidities, medication history, laboratory data, and evolving bedside observations into a coherent patient-specific model?

In practice, an acute digital twin could support several functions. It could help interpret whether a patient is deteriorating because of infarct progression, hemorrhagic transformation, edema, infection, seizures, or systemic instability. It could estimate complication risk after intervention. It could guide post-acute monitoring intensity. It could also link acute injury characteristics with probable rehabilitation needs.

The challenge is that acute decision support must be fast, explainable, and robust. A model that is accurate but opaque may be difficult to trust. A model that is interpretable but poorly calibrated may be unsafe. Therefore, acute digital twins must be validated not only by statistical performance but also by their effect on workflow, treatment timing, safety, and patient outcomes.

The clinical aim is not automation for its own sake. The aim is better decisions under time pressure.

Rehabilitation: from impairment measurement to adaptive recovery modeling

Rehabilitation is perhaps one of the most promising fields for digital twins, because recovery is longitudinal, heterogeneous, and highly dependent on feedback.

After stroke, patients differ in lesion location, corticospinal tract integrity, spasticity, balance, endurance, cognition, language, mood, fatigue, motivation, family support, and access to therapy. A static discharge score cannot capture this complexity.

A rehabilitation digital twin can model recovery trajectories across motor function, gait, upper limb activity, speech, swallowing, cognition, and participation. It can integrate hospital assessments, wearable movement data, home-exercise adherence, patient-reported fatigue, sleep, and therapy intensity.

The clinical question becomes: Is this patient improving as expected? Is recovery plateauing? Is the rehabilitation dose adequate? Should we change from compensatory training to impairment-focused therapy, introduce robotics, virtual reality, neuromodulation, or cognitive rehabilitation? Which patient needs more frequent reassessment?

STRATIF-AI describes work focused on rehabilitation and chronic follow-up, including prediction of cognitive function after rehabilitation and hybrid models for exercise and movement applicable to physical rehabilitation.

This is a future in which rehabilitation becomes adaptive, continuously evaluated, and biologically informed rather than delivered as a fixed protocol.

AI

MDPI

Opinion

What Is the Role of AI for Digital Twins?

Frank Emmert-Streib

Artificial intelligence contributes to digital twins at several levels.

The first level is perception: extracting structured information from complex data. This includes imaging segmentation, motion analysis, speech analysis, electrocardiographic pattern recognition, and signal processing from wearables.

The second level is prediction: estimating risk, deterioration, response to therapy, recurrence, functional recovery, or cognitive outcome.

The third level is prescription: identifying which action is likely to improve the trajectory. This may include optimization of monitoring, therapy intensity, medication adherence strategies, lifestyle intervention, or rehabilitation planning.

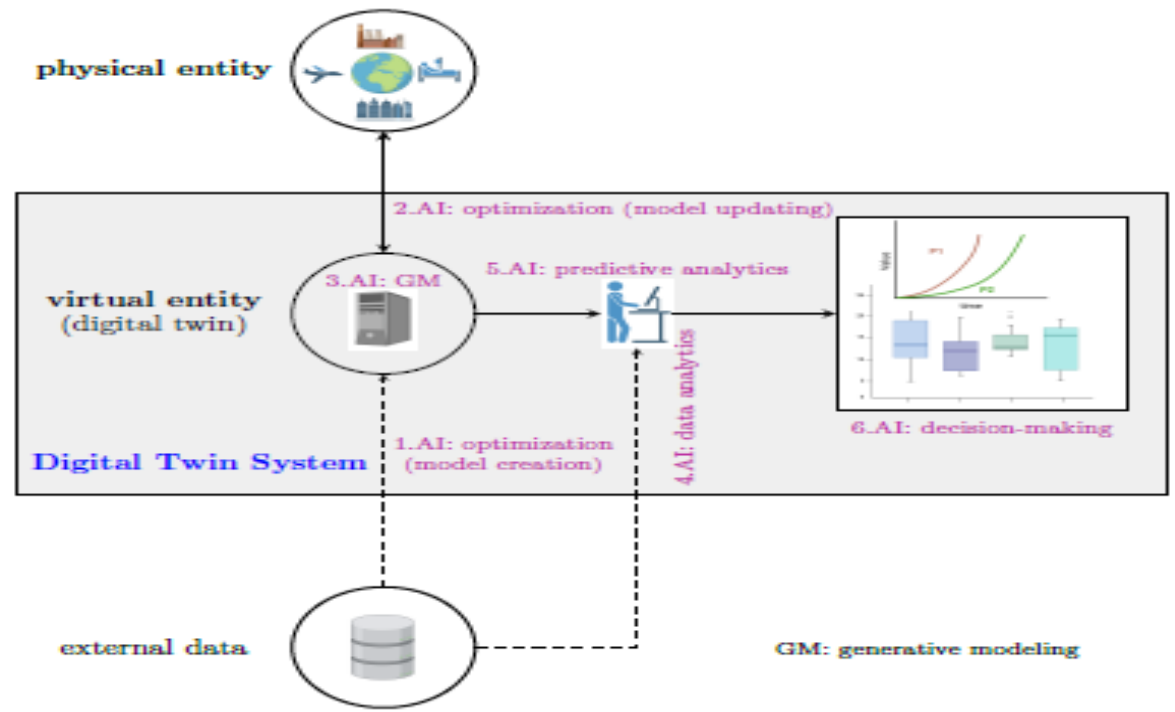
The fourth level is explanation. In clinical medicine, prediction without explanation is insufficient. Clinicians need to know why a model raises concern. Patients need to understand the recommendation. Regulators need to evaluate safety. Therefore, the future is not black-box AI alone. It is explainable, hybrid, and clinically auditable AI.

AI 2023, 4, 721–728. https://doi.org/10.3390/ai4030038 https://www.mdpi.com/journal/ai

Predictive Society and Data Analytics Lab, Faculty of Information Technology and Communication Sciences, Tampere University, 33100 Tampere, Finland; v@bio-complexity.com

Abstract: The concept of a digital twin is intriguing as it presents an innovative approach to solving numerous real-world challenges. Initially emerging from the domains of manufacturing and engineering, digital twin research has transcended its origins and now finds applications across a wide range of disciplines. This multidisciplinary expansion has impressively demonstrated the potential of digital twin research. While the simulation aspect of a digital twin is often emphasized, the role of artificial intelligence (AI) and machine learning (ML) is severely understudied. For this reason, in this paper, we highlight the pivotal role of AI and ML for digital twin research. By recognizing that a digital twin is a component of a broader Digital Twin System (DTS), we can fully grasp the diverse applications of AI and ML. In this paper, we explore six AI techniques—(1) optimization (model creation), (2) optimization (model updating), (3) generative modeling, (4) data analytics, (5) predictive analytics and (6) decision making—and their potential to advance applications in health, climate science, and sustainability.

Keywords: digital twin; artificial intelligence; data science; machine learning; sustainability; climate science



Validation, governance, and limitations

For a scientific audience, it is essential to emphasize that digital twins are not magic. They are models. And all models are simplifications.

The future of STRATIF-AI depends on rigorous validation. We need internal validation, external validation, prospective validation, and clinical utility studies. Accuracy alone is not enough. We need calibration, robustness across hospitals, subgroup fairness, resistance to dataset shift, interpretability, and evidence that the model improves outcomes or workflow.

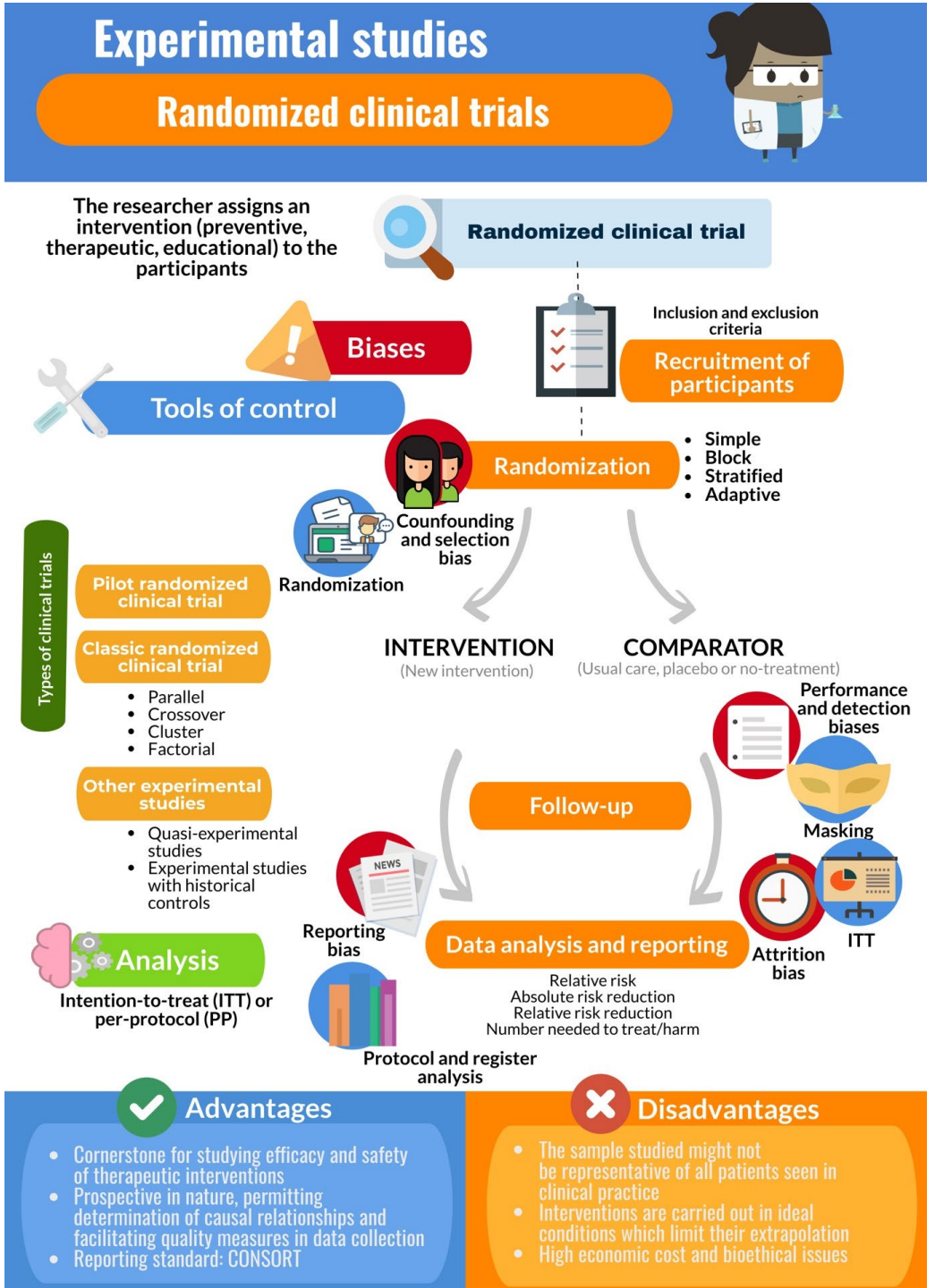
There are also technical limitations. Data can be incomplete, biased, delayed, noisy, or non-interoperable. Wearable signals may be inconsistent. Imaging protocols differ across centers. Rehabilitation outcomes may be measured with different scales. Patient-generated data may reflect digital literacy as much as health status.

There are ethical and governance challenges as well. A patient-specific digital twin requires sensitive longitudinal data. Patients must understand what data are collected, who controls them, how they are used, and how recommendations are generated. STRATIF-AI's Personal Data Vault concept is important because it explicitly places patient control at the center of the data architecture.

Finally, we must avoid therapeutic overclaiming. A digital twin should augment clinicians, not replace them. It should reduce uncertainty, not create false certainty.

Collaborations and Future Research Opportunities

- Successful implementation of Digital Twins in medicine requires interdisciplinary collaboration among healthcare providers, data scientists, engineers, and regulatory agencies.
- Partnerships with academic institutions can facilitate the development of advanced DT algorithms and validate them through clinical trials, while collaborations with technology companies can improve data capture and sensor integration.
- Future research opportunities include hybrid DT models that combine patient-level and population-level data, AI-driven analytics to enhance predictive accuracy, and experimental studies to explore DT applications beyond physical therapies, such as mental health.
- These partnerships and research directions are essential for ensuring that DT-driven rehabilitation evolves as a rigorously validated, highly effective clinical practice.



Conclusions

The future perspective is that stroke care can become a continuously learning, patient-specific, multi-scale process.

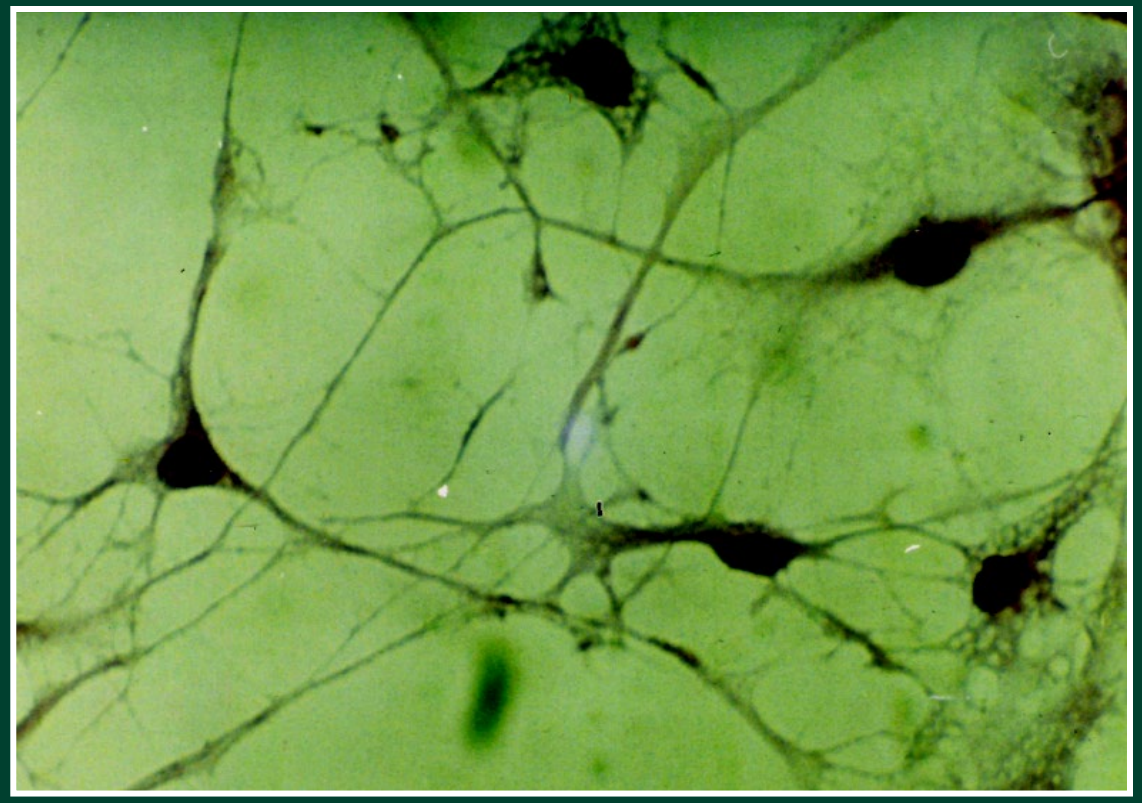
In prevention, digital twins may identify instability before stroke occurs. In the acute phase, they may help integrate imaging, physiology, and comorbidity under time pressure. In hospital monitoring, they may detect deterioration earlier. In rehabilitation, they may personalize therapy intensity and modality. In chronic follow-up, they may support adherence, lifestyle change, recurrence prevention, and long-term functional independence.

STRATIF-AI is important because it does not treat these as isolated applications. It proposes a connected architecture in which the same patient-specific model can accompany the patient across the full pathway, from prevention to acute treatment and rehabilitation.

The final message is this: continuous stratification is the clinical translation of the digital twin concept. It transforms data into trajectories, trajectories into predictions, predictions into decisions, and decisions into measurable outcomes.

For stroke patients, this means moving from reactive care to anticipatory care; from population averages to individualized simulation; from fragmented episodes to a coherent pathway; and from static risk scores to living models of recovery and risk.

The challenge ahead is not only technological. It is clinical, ethical, regulatory, and organizational. But if implemented rigorously, STRATIF-AI can help define a new generation of stroke medicine: predictive, preventive, personalized, participatory, and continuously adaptive.



Thank you!

Romanian Association of Balneology



www.bioclima.ro
Email: office@bioclima.ro

Mobile: +4/0723.138.339

UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE
GRIGORE T. POPA IAȘI

Assoc. Prof. dr. biol. Constantin Munteanu