MATIIGEN: Model-Driven Software Engineering Meets Precision Medicine for Improving Woman Healthcare

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Abstract. *Software engineering is a fundamental pillar for developing quality healthcare systems, with speciall atention in the Precision Medicine field, which tailors treatment based on individual genetic, environmental, and lifestyle variability. In this context, the MATIIGEN project aims to transition an intelligent software system for automated DNA variant interpretation from laboratory validation (TRL4) to operational clinical settings (TRL6). MATIIGEN is centered on Lipedema early detection, a chronic and widely under-researched disease primarily affecting women. Despite its high prevalence and significant physical and psychological impact, Lipedema was only recognized by the WHO in 2018, leaving its genetic basis largely unexplored. By applying a Model-Driven Software Engineering approach to the Lipedema use case, MATIIGEN will demonstrate how bridge the gap between management of complex clinical data and the descovery of actionable clinical insights, ultimately providing a systematic framework for developing high-quality systems in precision medicine.*

1. Introduction

Precision medicine is a medical approach to disease treatment and prevention that considers individual differences in DNA (i.e., DNA variants), environment, and lifestyle [Zeggini et al. 2019]. For the past decade, the PROS research group at the Universitat Politècnica de València has focused on the intersection of advanced software engineering and precision medicine, aiming to manage complex clinical data and generate actionable medical insights. In this context, the MATIIGEN project, funded by the *Instituto de Salud Carlos III* under the Health Technology Development program, aims to advance the technological maturity of a prototype for the automated clinical interpretation of DNA variants [Palacio et al. 2024], progressing from a laboratory environment (TRL4) to operational validation in real clinical settings (TRL6). The project is framed as applied R&D, integrating model-driven software engineering methods, cloud-based architectures, and validation with end users in healthcare environments.

The project focuses on the early diagnosis of Lipedema, a chronic and progressive disorder that predominantly affects women. It is characterised by painful, disproportionate fat accumulation and a significant psychological burden, yet it remains a largely under-recognised disease. Despite an estimated prevalence of up to 11% Lipedema was only officially recognised by the World Health Organization in 2018. Consequently, many patients undergo a 'diagnostic odyssey' because they are misidentified as obese or merely having an aesthetic problem. While a hereditary component is strongly suspected, the exact genetic drivers remain largely unexplored [Kruppa et al. 2026]. In this context, an automated clinical interpretation tool for

DNA variants, such as that proposed by MATIIGEN, allows for an earlier, objective, and more effective diagnosis and intervention.

From a software engineering perspective, the project is organized into four key areas. First, the DNA data to be analyzed is based on an adapted conceptual model of the human genome that has been validated in other clinical domains, such as oncology and cardiology. Therefore, the specification of relevant DNA variants and the connection of evidence to demonstrate their clinical significance in the MATIIGEN project are driven by a model-driven approach. Second, the model-driven approach also drives the architectural specifications. It incorporates requirements elicited from clinical experts using validated Model-Driven Development (MDD) approaches [Giachetti et al. 2012] for user experience (UX), web-based development, and deployment on cloud infrastructure. Third, real-world validation with Lipedema patients and clinicians will be conducted to assess the quality of the generated outputs and the system's integration into clinical workflows. Finally, the project defines software protection and licensing strategies for academic and commercial contexts, enabling technology transfer and exploitation. This includes market analysis and a preliminary regulatory roadmap.

The project will result a validated software prototype supporting the genetic diagnosis of Lipedema, contributing to the transfer of model-driven software engineering research into clinical practice and demonstrating the applicability of mature MDD techniques for developing quality systems in precision medicine.

2. MATIIGEN Objectives

The main objective of MATIIGEN is to mature and validate the technology of a software prototype currently at TRL4, developed using MDD and Explainable Artificial Intelligence (XAI) techniques to automate the interpretation of genetic variants. Through MATIIGEN, the technology will be advanced to TRL6, demonstrating its applicability in real clinical environments, using Lipedema as a representative use case.

To achieve this goal, the project will pursue the following specific objectives:

1. Adapt conceptual representations and Model-Driven solutions implemented to the Lipedema context. The conceptual model of the genome [Bernasconi et al. 2022, García S. et al. 2020] must be refined and instantiated to support clinical professionals involved in Lipedema diagnosis. The different MDD techniques used to generate variation reports and traceability with reference to clinical evidence will also be applied to capture the requirements and pipelines from Lipedema experts and users. This will include redesigning web-based interfaces, integrating interactive visualizations for interpreting genomic data, and implementing a secure, scalable, GDPR-compliant cloud architecture. This architecture will feature role-based access control, data encryption, and performance testing. These changes are intended to improve user experience, workflow efficiency, and data visualization.
2. Validate the MATIIGEN platform in real clinical settings using Lipedema patient cohorts. The platform will be validated in collaboration with reference hospitals and clinics through its application to real Lipedema cases. This validation will assess the system's capability to prioritize genetic variants potentially associated with Lipedema and will evaluate diagnostic precision and efficiency using quantitative metrics such as concordance with expert interpretation and reduction in analysis time, demonstrating effective integration into real clinical workflows.

3. Define and implement an intellectual property protection strategy for software exploitation. An appropriate intellectual property protection strategy will be defined and implemented, including patentability assessment, software copyright registration, and the establishment of differentiated licensing schemes for academic and commercial exploitation.
4. Develop a technology transfer and commercialization strategy for the genomic diagnostics domain, including market analysis, identification of early adopters, pilot deployments in real environments, and the definition of a preliminary regulatory roadmap.

3. MATIIGEN Timeline

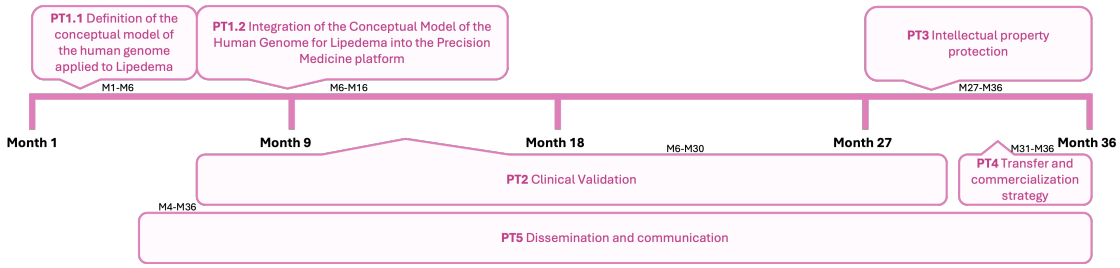

Figure 1. MATIIGEN Project timeline until Dic 2028

At the time of submission, the MATIIGEN project is in its initial execution phase, corresponding to the first months of the work plan (see Figure 1). Ongoing activities are focused on the early stages of PT1 (Platform usability improvement and development), specifically PT1.1 (conceptual model definition) and PT1.2 (conceptual model integration), as well as on the preparatory work of PT2 (Clinical validation), which are key to supporting the planned technological maturation from TRL4 to TRL6.

During this initial phase, the project is conducting requirements analysis and user-centered design activities through structured interactions with medical specialists in Lipedema, clinical geneticists, and other healthcare professionals. Additionally, collaboration with Lipedema patient associations has been initiated, incorporating a patient-centered perspective. These activities enable the definition of usage scenarios and requirements that will guide the system redesign from a software engineering perspective. In parallel, the initial user experience (UX) design and interface conceptualization tasks are being carried out, including the development of mockups and interaction flows for genomic data upload, analysis, and visualization.

The reference genome model is being adapted to consider genomic variants and the analysis protocols to be used in validation studies. This ensures compatibility between the data generation processes and the software analysis workflow.

4. Relevance for the CIBSE Community

1. Demonstrating Model-Driven Engineering (MDE) at high technology readiness levels (TRLs) in healthcare. The project applies MDD techniques from the research stage (TRL4) to operational clinical validation (TRL6). This provides empirical evidence of how mature MDD approaches can be scaled up for use in real healthcare environments.
2. Conceptualisation of genomic knowledge. MATIIGEN advances domain modelling for precision medicine by adapting and reusing a conceptual model of the human genome that has been previously validated in oncology and cardiology..

3. Model-driven engineering support for under-researched and complex domains. By targeting Lipedema, a disease for which there are few supportive tools, the project demonstrates how software engineering methods can facilitate technological innovation even when domain knowledge is limited.
4. Reference empirical studies for precision medicine software engineering. MATIIGEN serves as a reference empirical case study for the CiBSE community, demonstrating the application of model-driven engineering to the development of precision medicine software systems.
5. Collaborate with different research teams to develop new studies that expand knowledge about software engineering in the healthcare domain.

5. Conclusions

MATIIGEN aims to provide robust, precision-medicine technology to support the early detection of Lipedema by integrating model-driven software engineering principles with XAI. This integration will support the creation of an intelligent system to address a long-standing gender gap in recognition and treatment, promote more personalized management, and ultimately contribute to more equitable and effective healthcare for women.

6. Acknowledgement

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