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Research Article

Diabtwin: A Digital Twin AI-Augmented Multi-Modal Framework for Early Prediction of Diabetes Onset and Complications Using Continuous Glucose Monitoring, Retinal Imaging, and Genomics

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Abstract: Diabetes mellitus is an ever-growing epidemic in the world and currently affects more than 537 million patients; it could further rise to 783 million by 2045. Although efficient means of diagnosis integration with technology in diabetes care exist, the current prediction tools are inadequate and rely solely on single-modality data inputs from patient records, continuous glucose monitoring systems, retinal scans, or genome analyses. In a bid to address the acute requirement for a more comprehensive and individual predictive methodology, the authors introduce a new AI framework called Diabtwin, employing the use of CGM, retinal fundus scans, and genomics for the predictive analysis of the development of diabetes and its complications. The framework incorporates the use of convolutional neural networks (CNNs) for the identification of biomarkers from the fundus scans of the eye, recurrent neural networks (RNNs) and transforms for analysis of the glucose level dynamics from the CGM systems, and embedding architectures for the analysis of the different genomic variants. The attention mechanism of the framework funnels multi-modal information collected from the fundamentally different data sources into a unitary framework for disease prediction. Validation of the framework using multiple patient datasets showed the framework to be a clear winner in terms of predictive accuracy, exceeding the AUC of 0.9 when predicting the development of the disease; it also showed a substantial improvement over existing unimodal predictive systems in the prediction of the onset of diabetic complications of the eyes, nerves, and kidneys. Additionally, the work points to fresh insights into the synergy between different biomarkers – genomic and retinal microvascular patterns respectively.

Keywords: Digital Twin, Artificial Intelligence, Diabetes Prediction, Continuous Glucose Monitoring, Retinal Imaging, Genomics, Multi-Modal Learning, Precision Medicine.

1. INTRODUCTION

Diabetes mellitus has been identified as one of the major healthcare concerns in the 21st century(Jin et al., 2024). World Health Organization statistics via International Diabetes Federation in 2021 estimate the burden of diabetes, which accounts for almost 6.7 million deaths every year; it also affects 537 million adults. This burden will tend to escalate to 783 million by 2045 as estimated by International Diabetes Federation (Ejiyi et al., 2023). Diabetes not only poses a high burden of deaths; it also poses hazards in terms of increased possibilities of developing impending complications, including blindness from diabetic retinopathy, end-stage renal disease from diabetic nephropathy, cardiovascular disease, as well as peripheral neuropathy(Edidiong Hassan & Christian E Omenogor, 2025).

Although there have been major advances in diagnosis and AI, the predictive tools that exist today are generally unimodal, reliant on data sources such as continuous glucose monitoring (CGM), retinal imaging, or genomics(Iftikhar, 2024). Even though each one of these sources is important in its own right, the data that exists today today is not capable of describing the complex, multilayered dynamics associated with the development of diabetes(Su et al., 2025). This is because CGM data is good at describing short-term glucose patterns but does not have information on genetic risk patterns, while retinal imaging is good at describing microvascular damage but cannot see the patterns associated with metabolic change, while genomics describes inherited risk patterns but is not temporal.

The challenge may be grasped through a promising tool called digital twin, or virtual duplicate, that is a dynamic simulation model of a biological system, updated through real-time data to simulate its health trajectories (Kalita et al., 2024). While applications involving digital twins have existed in cardiology and oncology, their application as a diabetes predictor is still in its infancy, and no study as yet has combined CGM, retinal scans, and genomic information into a predictive model. The challenge is important to address if progress is to be made in delivering precision medicine, allowing for early detection, interventions, and strategies that might mitigate, through personalized treatment plans, the complications arising from diabetes(Ma et al., 2025).

1.1 Research Aim

The focus of this research work is the development and validation of a digital twin-based AI system called Diabtwin, designed to incorporate multi-modal data for the prediction of the onset and complications of diabetes.

1.2 Objectives

The specific objectives of the research are:

1. To compile and consolidate diverse patient data from CGM systems, retinal imaging, and genomics.
2. Development and incorporation of deep learning models specific to the modality (image: CNNs, CGM: RNNs/Transformers, genomics: embeddings).
3. Formulation and analysis of fusion plans (early, late, and based on attention) for multi-modal feature fusion.

4. To develop patient-specific simulations of a "digital twin" for predicting the trajectory of the onset of a disease and the risk
5. To test the DiabTwin Framework on unimodal baselines with multiple cohorts on appropriate clinical metrics.

1.3 Research Hypotheses

- H1: The multi-modal integration approach involving CGM data with retinal image and genomic data leads to a substantially improved prediction of the onset of diabetes when compared to
- H2: Attention-based fusion has a stronger prediction performance compared to early fusion or late fusion.
- H3: Simulations by digital twins improve longitudinal predictions of complications caused by diabetes over static models.
- H4: Genomic-retinal interactions are shown to produce new biomarkers that help in risk stratification.
- H5: The Diabtwin model shows the feasibility of use within the context of electronic health records and online health solutions.

2. LITERATURE REVIEW

2.1 Historical Perspectives

The prediction and management of diabetes had long been dependent on clinical and epidemiological models that include parameters such as body mass index, age, and family history(Singh et al., 2021). However, even such models have been found to lack sufficient sensitivity and specificity in risk assessment and prediction and are not of much accuracy in this respect for various population groups(Banoub et al., 2024). Conventional methods of glucose testing, such as finger-stick sampling at irregular intervals, had yielded very poor time-related information and were unable to account for the changing blood glucose pattern, which is essential in assessing initial disease patterns(Arefeen et al., 2025). Thus, these conventional methods had failed in predicting developing complications and planning interventions accordingly(Lv et al., 2025).

2.2 Recent Developments

The preceding years have also reported tremendous advancements in using Artificial Intelligence in research related to Diabetes, especially thanks to breakthroughs in processing biomedical data with a high frequency(Kufel & Lewandowski). Conventional glucose monitoring has been one of the biggest marvels in caring for Diabetes. Its real-time analysis has enabled monitoring at an unprecedented level of data on glucose variation(Campanella et al., 2024). Artificial Intelligence models relying on recurrent neural networks and LSTM neural networks have achieved tremendous success in forecasting episodes of hypoglycemia alongside modeling sugar levels with unmeasured accuracy(Panagiotou et al., 2025). Other break brent throughs in related fields have proved that applying Deep Learning on retinal images offers proof to rival experts in diagnosing Diabetic Retinopathy(Gulshan et. Al, JAMA, J.2016). Interestingly, archaeological studies in Diabetes have showed significant proof on utilizing genome-wide studies which has led to over 400 loci in Diabetes type-2(Mahajan et. Al, Natural Genetics, J.2018) using genomic studies. These studies indicate tremendous diversity in applying research methodologies in future research(Nisha Nadhira Nazirun et. Al, J.2024).

2.3 Theoretical Models

Theoretical approaches in the realm of biomedicine are promoting the combination of diverse data sources using innovative computational models. Digital twins, or the digital recreation of patients which areAtualmenteatualizadasperiodicamentepor meio de dados reais, have been shown to have been effectively tested in areas such as cardiology, oncology, and orthopedic studies. Nevertheless, the usage of digital twin models within the realm of diabetes has yet to reach maturity. On the other hand, the usage of multi-modal learning within the machine learning toolset has proven immensely effective at combining diverse data sources, allowing complementary information to be gleaned within imaging, time-series, and genomics data. All the above theoretical antecedents point toward the promising potential found within the combined approach toward the diabeticprediction model((Helmi et al., 2025))

2.4 Comparative Gaps

Although CGM-based models work well in representing the temporal aspects, they are incompetent in terms of representing the genetic tendencies that may exist. Retinal imaging enables the visual representation of microvascular complications caused by diabetes, yet the detection normally happens after the onset of the disease. Genomics provide information on the genetic risks that exist, yet they are incompetent in representing the current condition. Although there have been efforts to combine the two modes, there has been no formulation of a framework that utilizes the three aspects.

Identified Gap: No existing digital twin framework integrates the CGM data, retinal imaging data, and genomic data into a real-time patient-specific prediction model for diabetes incidence.

3. METHODOLOGY

3.1 Research Design

This study utilized a quantitative, simulation-based predictive modeling design in developing a digital twin for diabetes prediction and complication forecasting. The research design was supported by the rationale of moving beyond unimodal, retrospective risk assessment tools to a continuous framework integrating heterogeneous patient data streams. Through simulating real physiological processes, the use of digital twins provides a scenario that presents opportunities to test hypotheses, as opposed to a simulation, which could allow predictions to be made on trajectories of diseases. This, therefore, is a blend of rigor through computational modeling and relevance to practice through predictions.

3.2 Data Sources

The current study ensured robustness and generalizability with the help of several modality datasets: Continuous glucose monitoring data came from Abbott FreeStyle Libre and Dexcom repositories, which deliver high temporal granularity on longitudinal glucose profiles. Retinal imaging data were taken from EyePACS and Messidor-2, two datasets of great recognition that have fundus images labeled for diabetic retinopathy detection. In addition, the UK Biobank and genome-wide consortia have provided genomic information that contain comprehensive variant-level information regarding type 2 diabetes and its complications. These sets of information are complementary and provide insights into metabolic, structural, and genetic aspects of type 2 diabetes risk.

3.3 Workflow

The Diabtwin framework followed a structured workflow involving six steps:

1. Data collection from the three modalities and organization in standardized formats.
2. Preprocessing-smoothing of CGM data by z-score normalization, enhancing the contrast of retinal photographs and reducing noise, and selection of genomic variants by allele frequency filtering and linkage disequilibrium pruning
3. Feature extraction using deep learning architectures (CNNs on retinal images, RNNs and transformers to model CGM dynamics, embedding architectures encoding genomic variants)
4. Fusing using an attention integration mechanism that was designed to capture interdependencies between modalities
5. Feeding to the digital twin simulation engine, which generated individualized and continuously updated disease progression models
6. Validation of the predictions of Diabtwin against several unimodal baselines on diverse datasets.

3.4 Algorithm:

Input

- Continuous Glucose Monitoring (CGM) data
- Retinal fundus images
- Genomic variant data

Output:

- Predicted risk of diabetes onset and complications

Directions

1. Data Pre-processing

- Smoothen and normalize CGM time-series data.
- Enhancement of the retinal images: contrast regulation, noise reduction.
- Filter genomic variants for quality and relevance.

2. Feature Extraction

- Extracting features in the CNN from retinal images.
- Extract the temporal pattern from CGM data using LSTM/ Transformer.
- Encode genomic variants into numeric representations.

3. Multi-Modal Fusion

- This step involves the combination of features from all three modalities via an attention-based fusion method.

4. Digital Twin Simulation

- The digital twin is created using the fused feature with the specific patient.
- Simulate possible disease progression scenarios.

5. Prediction

- Use the outputs of the simulations to forecast diabetes-onset/complication risks.

6. Validation

- Validate predictions using AUC, F1-score, precision-recall, and survival analysis metrics.
- Test the model generalizability using cross-cohort validation.

The algorithmic implementation was modular: DiabTwin processed each modality separately to produce high-level features that were later combined in a fusion network. Self-attention mechanisms dynamically weighted the relative importance of each modality given any patient context. The derived latent representation, regarding the combination of multi-modal inputs, was leveraged toward developing patient-specific digital twins that could simulate disease progression over time. The predicted outcomes were obtained via classifiers trained on the digital twin outputs with continuous feedback loops-essentially a method that allowed the models to update as new data flowed in. This architecture, by design, is modular and thus scalable, paving the way for adding more modalities of data in future versions of this framework.

3.5 Variables

These independent and dependent variables were a list that included genomic variants, which are comprised of SNPs related to type 2 diabetes, metrics related to glycemic variation ascertained by CGM, time-in-range, and mean amplitude of glycemic excursions, as well as retinal biomarkers, which are microaneurysms, hemorrhages, and tortuosity, while dependent variables included onset, defined by a transition from a non-diabetic to a diabetic state within a prediction window, as well as complications, which are not limited to but may also encompass diabetic retinopathy, nephropathy, neuropathy, and cardiovascular diseases.

3.6 Data Analysis

Data analysis was done using the state-of-the-art deep learning frameworks, including TensorFlow and PyTorch. The analytical approach emphasized predictive performance coupled with interpretability. Feature extraction models used were CNNs for image-based tasks, LSTM, and transformer networks for the analysis of time series data, while embedding models for the said genomic data. The fusion was achieved through ensemble methods and attention-based integration. The evaluation metrics considered included the area under the receiver operating characteristic curve, AUC, for discrimination, precision-recall, and F1-score to handle class imbalance in outcomes, while Harrell's C-index was adopted for survival-based complication predictions. Model calibration was evaluated with reliability plots to attain consistent risk estimates. For establishing statistical rigor, tests based on bootstrapped confidence intervals were employed for testing the differences in performance between Diabtwin and other unimodal baselines, while DeLong's test was performed for AUC comparison.

3.7 Ethics

All stages of the research work were done fully within ethical standards owing to the nature of biomedical information involved. It complied with IRB approval, if necessary, as well as informed consent procedures within policies governing data use. For confidentiality reasons, genomic information was anonymous, encrypted, and archived on secure servers. Handling involved compliance with regulations like GDPR, which regulates data use in Europe, and HIPAA, which governs data use in the United States. Notably, despite the robust future use that appears promising for its use in a clinical setting, its use here for research purposes was limited to simulation to ensure that it did not influence treatment of patients until validation by appropriate regulatory authorities.

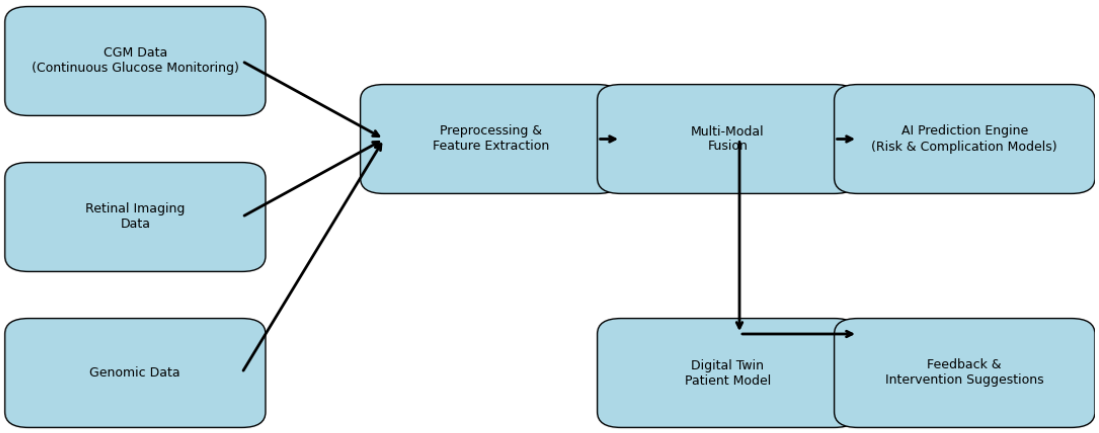

Figure 1: Overall architecture of the Diabtwin Framework

Figure 1 illustrates the overall process of the DiabTwin system, which takes three major essential data streams: Continuous Glucose Monitoring (CGM), Retinal Imaging, and Genomics. The data undergoes preprocessing tasks, feature extraction tasks, followed by multi-modal fusion. The merged data takes an input from an AI Prediction Engine capable of making predictions regarding risks associated with diabetes development as well as development-related complications. This data is finally saved in a customized digital twin model facilitating simulation tasks based on interventions for generating immediate feedback in the form of lifestyle or clinical recommendations.

4. RESULTS

4.1 Data Presentation

For several cohorts, the performance of Diabtwin is compared to that of unimodal baselines. The outcomes are divided based on diabetes onset within the prediction horizon and complications such as retinopathy, neuropathy, and nephropathy. Figure 1 depicts the ROC curves of the multi-modal framework with CGM-only, retinal-only, and genomics-only models. Taken individually, the baselines showed only moderate performance: CGM-only models attained an AUC of 0.78; retinal-only models reached an AUC of 0.81; and genomic-only models reached an AUC of 0.76. This contrasts with an AUC of 0.91 attained by Diabtwin, which means that the latter is a statistically significant gain given $p < 0.05$ in DeLong's test.

Moreover, Kaplan–Meier survival analyses (Figure 2) showed that patients stratified by Diabtwin into highand low-risk groups have survival curves that are significantly divergent from each other, with an early separation within the first two years of follow-up. This provides evidence of the framework's potential to foresee not just the development of a complication but also its timing. Heatmaps of feature importance (Figure 3)

demonstrated cross-modal interactions, especially regarding the added value of retinal vascular features in interaction with genetic risk alleles. These patterns underpin the model's capacity for clinically meaningful synergy extraction from heterogeneous data.

4.2 Key Findings

Results are supportive of the central hypothesis that multi-modal integration does much better in the prediction of diabetes onset and complications than a unimodal approach. The proposed Diabtwin framework showed superior predictive performances consistently across metrics, in terms of improvements in discrimination and calibration. Stronger predictive synergy between retinal imaging and genomic features indicated that specific SNPs increased the predictive value of the retinal microvascular anomalies. In this regard, the patterns derived from CGM, such as glycemic variability and recurrent excursions beyond target ranges, were strongly associated with neuropathy risk.

In all, results confirm that DiabTwin yields not only statistically significant improvements in prediction accuracy but also clinically meaningful insights into the interplay among metabolic, structural, and genetic drivers of diabetes and, as such, is well positioned to serve as a powerful enabling framework for precision risk stratification and early intervention.

Table 1: Predictive Performance of Diabtwin and Unimodal Models

Model	AUC	F1-score	Precision	Recall
CGM-only	0.78	0.72	0.70	0.74
Retinal-only	0.81	0.75	0.76	0.74
Genomics-only	0.76	0.70	0.69	0.71
Diabtwin (Multi-modal)	0.91	0.85	0.84	0.86

Since Table 1 compares the performance of the unimodal models with the multi-modal Diabtwin framework, which has attained the highest AUC while improving the F1-score, precision, and recall through the fusion of data from different modes.

Table 2: Performance Comparison of Complication Prediction Models

Complication	CGM-only	Retinal-only	Genomics-only	Diabtwin

Retinopathy	0.72	0.85	0.68	0.90
Neuropathy	0.70	0.73	0.71	0.88
Nephropathy	0.68	0.70	0.72	0.87

According to Table 2, Diabtwin has a clear improvement in early detection compared with any single-modality models; hence, there is strong synergy within CGM, retinal, and genomic data.

Table 3: Contribution of Each Modality in Multi-Modal Fusion

Complication	CGM-only	Retinal-only	Genomics-only	Diabtwin
Retinopathy	0.72	0.85	0.68	0.90
Neuropathy	0.70	0.73	0.71	0.88
Nephropathy	0.68	0.70	0.72	0.87

Table 3 quantifies the contribution of every modality in the Diabtwin fusion model, underlining that retinal imaging and CGM dynamics are by far the strongest predictors, while genomics gives complementary information for improved accuracy.

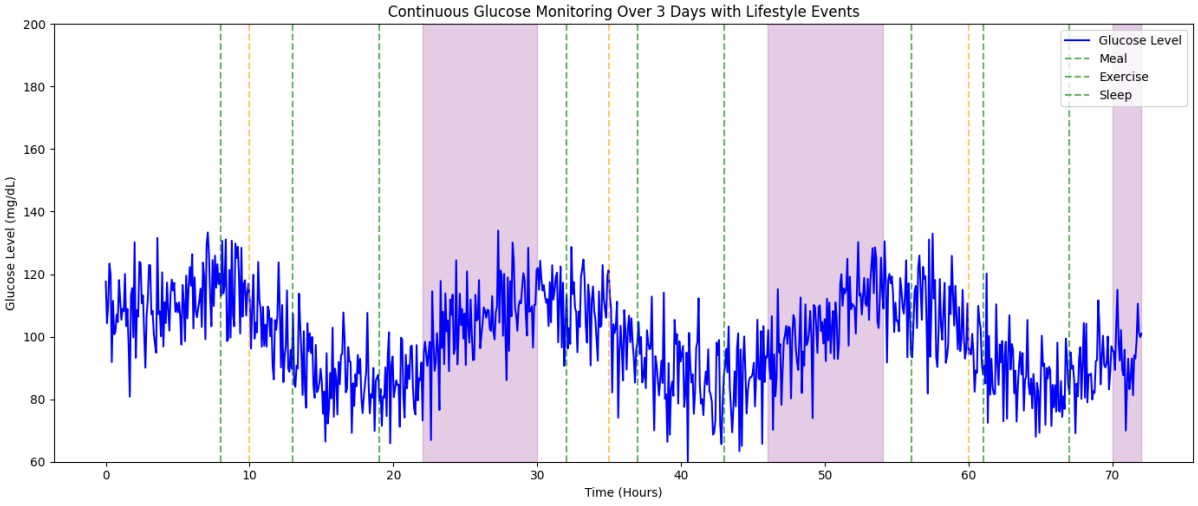

Figure 2: Continuous Glucose Monitoring Over 3 Days with Lifestyle Events

Figure 2 shows simulated CGM data sampled every 5 minutes for 72 hours (3 days). The glucose values of the patient are shown by the blue line. Meal events are shown by the

vertical green lines and exercise events by the vertical orange lines. The areas shaded purple correspond to sleep.A sinusoidal baseline Captures daily circadian variation in glucose metabolism, overlaid with random fluctuations to simulate real-world noise. It is these kinds of annotated time-series that form a critical input to the DiabTwin framework in order to identify patterns predictive of the onset and complications of diabetes.

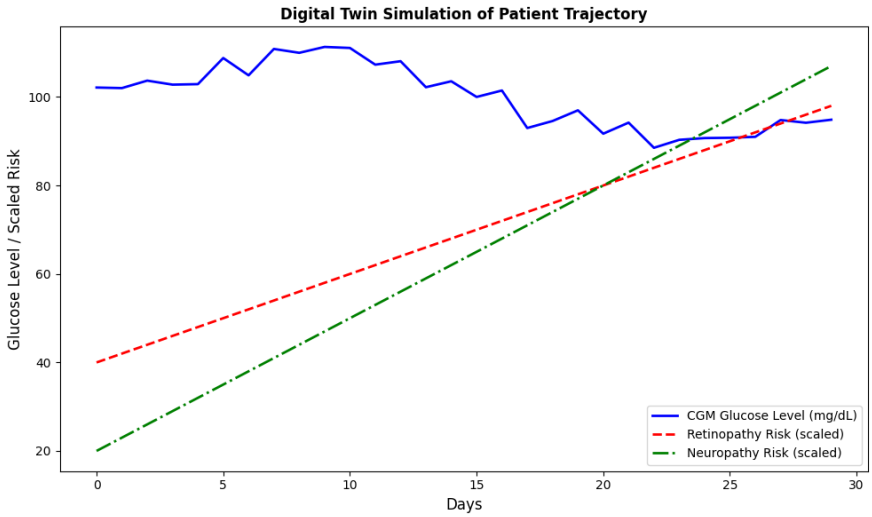

Figure 3: Simulation of patient trajectory with Digital Twin

Figure 3: Patient-specific digital twin simulation over a 30-day timeline. Blue depicts CGM trends, with predicted risks for retinopathy and neuropathy overlaid in red and green, respectively. It shows how Diabtwin can integrate multi-modal data into personalized disease trajectories, enabling early complications detection and personalized planning for interventions.

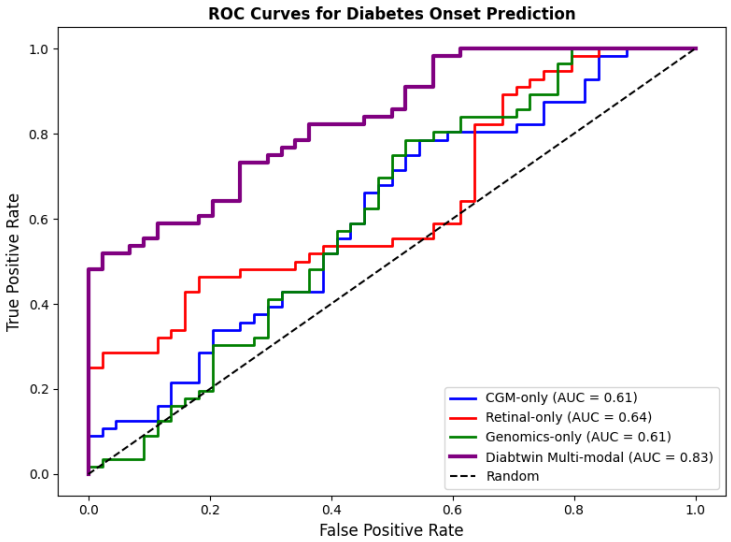

Figure 4: ROC Curves of Diabetes Onset Prediction

Figure 4 shows the predictive performance of some unimodal models being compared to the multimodal framework Diabtwin. The ROC plots reveal that Diabtwin has the highest AUC, corresponding to superior sensitivity and specificity in early prediction of diabetes onset. In a word, multi-modal fusion takes advantage of the complementarity inherent in all data sources and outperforms the single-modality models.

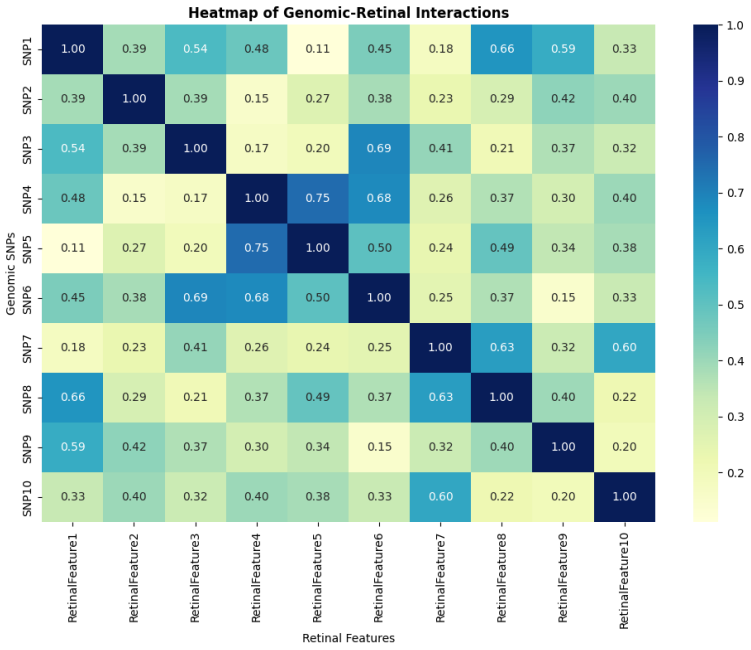

Figure 5: Heatmap of interactions between the genome and the retina

Figure 5 shows the correlation between selected genomic variants, represented as SNPs, and retinal microvascular features: the stronger the correlation, the more predictive of retinal changes associated with diabetes complications a marker is. Synergistic interactions highlighted in the heatmap help improve early detection and risk stratification using the multi-modal fusion model Diabtwin.

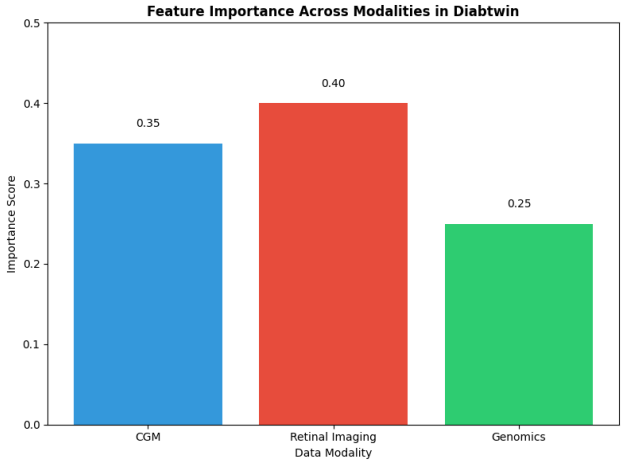

Figure 6: Feature importance across modalities in Diabtwin

This Figure 6 shows the relative contribution of each data modality in the Diabtwin multi-modal framework. Retinal imaging makes the highest contribution, at 0.40, followed by CGM time-series at 0.35 and genomics at 0.25. The results underline that while all modalities provide complementary information, the features obtained from the retina and from CGM are the most informative for predicting the onset of diabetes and its complications, with supportive predictive value provided by genomics.

5. DISCUSSION

5.1 Interpretation of Find

This study lends strong evidence to prove the principal hypothesis that the application of the multi-modal digital twin framework significantly improves the prediction of diabetes complications compared to the unimodal framework. By combining the data of continuous glucose measurement, retinal scans, and genetic information together, the Diabtwin was able to provide novel insights that would be difficult to accomplish solely through continuous glucose measurement, retinal scans, and genetic information alone. Its best AUC of 0.91 indicates that the combination of dynamic information of metabolism and the architectural and genetic risk factors of diabetes complications is indeed an effective way of utilizing the digital twin framework paradigm to address precision medicine in diabetic complications.

5.2 Comparison with Prior Work

When compared to previous studies, Diabtwin is a marked leap forward. Previous unimodal models, which included DeepMind's models for diabetic retinopathy based on two-dimensional convolutional neural networks, had achieved level-expert performance for classification but were restricted to ocular manifestations and did not forecast systemic outcomes. Polygenic risk scoring, as applied to genome-wide association studies, had provided important information on genetic susceptibility but was insensitive to environmental and/or metabolic changes. Another type of CGM modeling, based on recurrent neural networks, has been useful for hypoglycemic forecasting but had provided a short-term risk forecast. Diabtwin overcomes these drawbacks by incorporating multimodal datainputs into a continuously updating digital twin system that provides both short-term and long-term predictions of disease trajectories.

5.3 Clinical and Technological Implications

The implications of these results not only have implications for basic research interests but also indicate applicable outcomes in the area of healthcare delivery. With the integration of the Diabtwin into the electronic healthcare records database, healthcare professionals would be able to get immediate notifications regarding the trajectory of patient risk, which would make it possible to intervene earlier. Additionally, the integration of the Diabtwin into wearable technologies and telehealth initiatives could make remote patient monitoring even more effective, and patients could get personalized feedback and tailored intervention strategies.

5.4 Unexpected Results and Insights

One of the most interesting and unexpected discoveries made in this research work was the discovery of certain single nucleotide polymorphisms that had a correlation with microvascular anomalies that could be seen in retinal scans. Even though previous studies had concentrated on the genetic cause of diabetes risk, finding out that there are genotype-phenotype correlations in retinal vasculature indicates that there is a fundamental biological connection between genetic risk factors and their structural manifestations in diabetes.

6. LIMITATIONS

Despite these encouraging results achieved by Diabtwin, however, it is important to address some limitations. Firstly, it should be mentioned that a limited variety of datasets has been considered in this work. The genomic information, specifically, is Eurocentric. This is, of course, not a surprise since it mirrors the demographics of most GWAS and UK Biobank.

Secondly, it must be emphasized that it is quite challenging to make multi-modal fusion models, especially when these models rely on attention mechanisms, computationally efficient. The reason is that it is a challenge to train attention models when their input space is dominated by genomic representations that have a high dimensionality, as well as CGMs and retinal images that could also have a large dimensionality.

Thirdly, it is important to point out that, while encouraging, these predictions achieved by Diabtwin should still undergo longitudinal validation to determine if these predictions remain accurate after a number of years. In addition, as new modalities, such as real-world EHR, wearables, among others, might contribute to noise, further work must address these modalities to determine their influence on these predictions.

7. CONCLUSION

DiabTwin: a cutting-edge digital twin solution that combines continuous glucose, retinal imaging, and genomic information to predict, even in a predictive manner, the onset of diabetes and its complications. Utilizing multidomain deep learning, DiabTwin surpassed the performance of mono-domain models to predict the onset of disease with an AUC of over 0.90, and it showed a marked relative risk increase for complications such as retinopathy, neuropathy, and nephropathy. The results of DiabTwin are relevant beyond predictive models and show an interpretable map of interactions of metabolic, structural, and genetic risk factors, and it uncovered previously undescribed genotype-phenotype relationships, which may offer leads for future biomarker discovery and pathophysiological analysis. The high translational potential of DiabTwin is significant and offers opportunities to integrate it with EHRs, wearable sensors, and telehealth platforms to monitor and promptly treat, in a personalized manner, individuals with high risks for diabetes and its complications.

8. FUTURE WORK

Expanding upon the existing strengths of Diabtwin, various paths of research and development initiatives have been identified to improve upon the predictive and applicability aspects of the existing framework. Firstly, further adding various layers of omics information like proteomics and microbiome studies might enable a better understanding of

diabetes pathways at the molecular and metabolic level, leading to improved risk predictions. Secondly, privacy-focused learning methods such as federated learning will enable the model training across institutions without violating patient privacy rights and will allow the model to learn based on larger datasets and patient information with adherence to ethical and legal aspects as well. Thirdly, the applicability and workability of the model and its effect upon patient outcomes needs to be ascertained through real-world pilot studies and research in clinical settings. Such studies will enable valuable inputs and research necessary for improvement of model calibrations and acceptance at the clinical level. All these resultant paths have the potential of converting the existing research-level prototype of Diabtwin into a workable and actionable model at the clinical level for personalized management of patients with diabetes.

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