AI-Driven Cardiac Syndrome X Diagnosis: Expert Fusion at its Best

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INTRODUCTION

Cardiac Syndrome X (CSX), a condition first introduced by Harvey Kemp, represents a perplexing challenge within the realm of cardiovascular diseases (CVDs). It is a condition that baffles medical professionals due to its unique characteristics. Despite showing typical anginal chest pain and positive exercise tolerance test results, CSX patients exhibit normal or near-normal findings in coronary angiographies (CAG). This condition is not only enigmatic but also has significant implications for both patient care and healthcare resources. In this context, the study of CSX becomes vital, as it sheds light on the need for innovative approaches in CVD diagnosis and management, especially in cases where traditional diagnostic methods may not be adequate.

AIM

Develop a highly accurate diagnostic tool for CSX using a novel machine learning model incorporating with a novel uncertainty quantification technique and aims to improve CSX diagnosis and clinical trustworthiness.

SETTING

This study utilized data from the Tehran Heart Center, Tehran University of Medical Sciences in Iran. Information from over 200 variables, including patient demographics, medical history, diagnostic tests, and more, was collected. The focus was on patients with typical angina who underwent coronary angiography between 2004 and 2014. Exclusions included emergency cases and prior cardiac interventions. Patients with significant coronary stenosis were classified with coronary artery disease (CAD), while those with milder conditions or normal arteries were identified as CSX cases. A total of 2,530 patients from the registry, who had angiography between September 2016 and June 2018, were included in this study.

METHOD

- Proposed a new, simple, yet very efficient Binarized Multi-Gate Mixture of Bayesian Experts (MoBE), which includes a multi-level gating network.
- The proposed binarized multi-gate MoBE is a probabilistic model that is used for classification tasks.
- Used the Bayesian Neural Networks (BNNs) [2], which provide a rigorous framework to analyze and train uncertainty-aware neural networks allowing us to account for uncertainty.

REFERENCES

1. Abdar, M., Mehrzadi, A., Goudarzi, M., Masoudkabir, F., Rundo, L., Mamouei, M., ... & Nahavandi, S. (2023). Binarized multi-gate mixture of Bayesian experts for cardiac syndrome X diagnosis: A clinician-in-the-loop scenario with a belief-uncertainty fusion paradigm. *Information Fusion*, *97*, 101813.

2. Sebastian, A., Pendurthi, R., Kozhakhmetov, A., Trainor, N., Robinson, J. A., Redwing, J. M., & Das, S. (2022). Two-dimensional materials-based probabilistic synapses and reconfigurable neurons for measuring inference uncertainty using Bayesian neural networks. *Nature communications*, *13*(1), 6139.

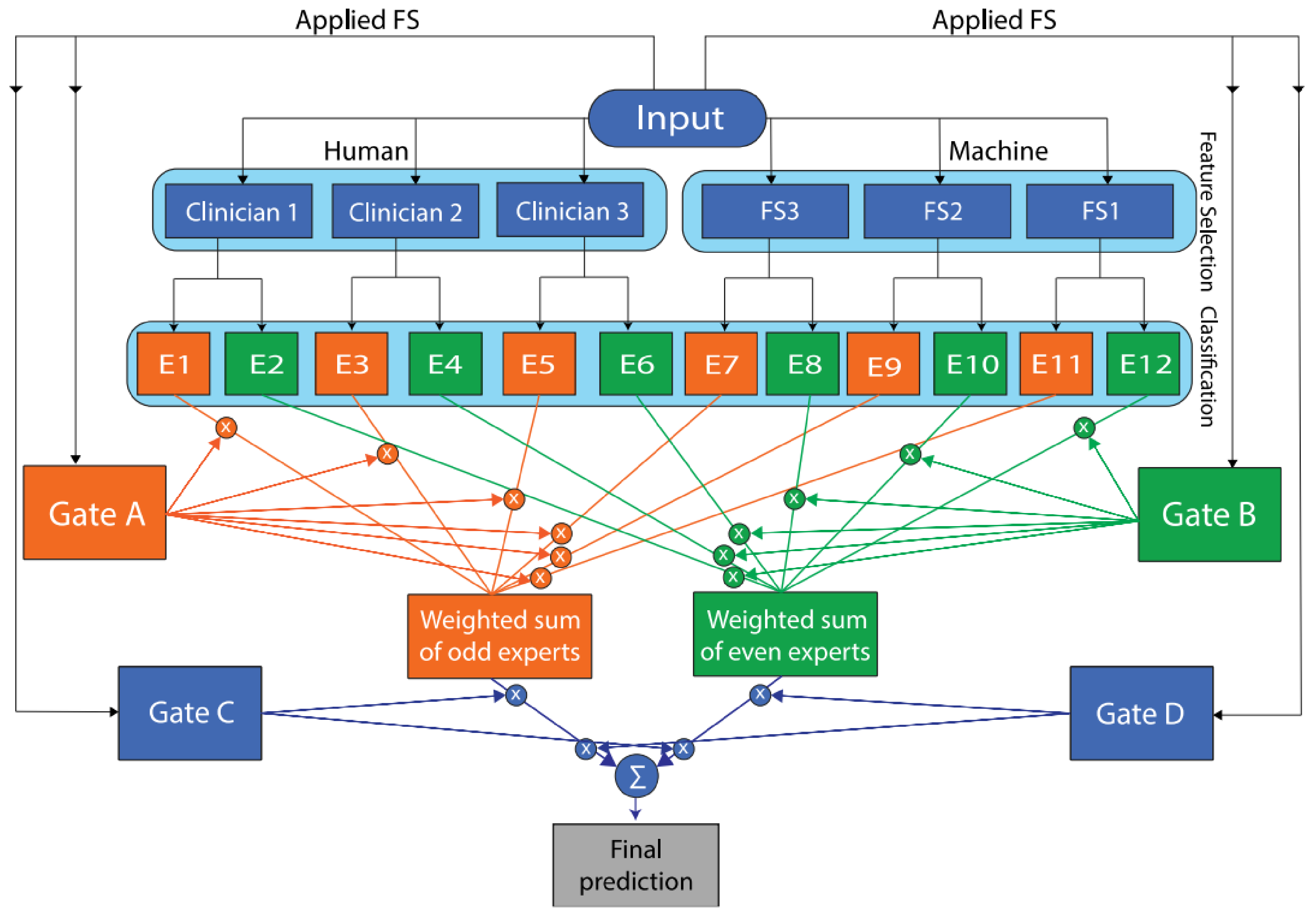

Figure 1. Overview of the proposed binarized multi-gate MoBE.

RESULTS

After applying machine- and human-based feature selection techniques, we found out that age and sex are among the most critical selected features by machines and humans. Interestingly, our feature selection findings reveal that all three clinicians and five out of machine-based feature selection techniques believed in the great importance of the $EjectionFraction$ feature for CSX classification. Moreover, we noticed that all clinicians selected $HighlyPositiveETT$ as an important feature for CSX prediction. At the same time, four out of six applied machine-based feature selection techniques had the same belief.

Table 1

Method	Feature Selection	Accuracy	F1_Weighted	Precision_Weighted	Recall_Weighted
		Mean ± SD	Mean ± SD	Mean ± Mean ± SD	Mean ± SD
BNN	L1-based	0.82 ± 0.0082	0.89 ± 0.0049	0.84 ± 0.0075	0.94 ± 0.0086
	Backward Elimination	0.82 ± 0.0085	0.89 ± 0.0057	0.84 ± 0.0069	0.94 ± 0.0138
	Bidirectional Elimination	0.82 ± 0.0053	0.89 ± 0.0033	0.85 ± 0.0038	0.94 ± 0.0060
	Recursive Feature Elimination	0.83 ± 0.0061	0.90 ± 0.0039	0.84 ± 0.0038	0.95 ± 0.0075
	Univariate	0.83 ± 0.0062	0.90 ± 0.0039	0.85 ± 0.0045	0.95 ± 0.0069
	Low Variance	0.82 ± 0.0064	0.89 ± 0.0042	0.85 ± 0.0047	0.93 ± 0.0087
	Clinician 1	0.81 ± 0.0049	0.89 ± 0.0031	0.83 ± 0.0030	0.95 ± 0.0058
	Clinician 2	0.81 ± 0.0055	0.88 ± 0.0034	0.84 ± 0.0044	0.93 ± 0.0059
	Clinician 3	0.81 ± 0.0063	0.89 ± 0.0039	0.83 ± 0.0045	0.95 ± 0.0070
MC+NN	L1-based	0.81 ± 0.0071	0.88 ± 0.0042	0.83 ± 0.0054	0.95 ± 0.0063
	Backward Elimination	0.82 ± 0.0078	0.89 ± 0.0047	0.84 ± 0.0056	0.95 ± 0.0070
	Bidirectional Elimination	0.81 ± 0.0088	0.89 ± 0.0053	0.84 ± 0.0057	0.94 ± 0.0076
	Recursive Feature Elimination	0.80 ± 0.0076	0.88 ± 0.0045	0.82 ± 0.0051	0.95 ± 0.0070
	Univariate	0.81 ± 0.0077	0.89 ± 0.0045	0.83 ± 0.0059	0.95 ± 0.0061
	Low Variance	0.80 ± 0.0080	0.88 ± 0.0047	0.83 ± 0.0058	0.95 ± 0.0063
	Clinician 1	0.79 ± 0.0080	0.88 ± 0.0048	0.82 ± 0.0051	0.94 ± 0.0076
	Clinician 2	0.80 ± 0.0087	0.88 ± 0.0052	0.83 ± 0.0061	0.94 ± 0.0073
	Clinician 3	0.80 ± 0.0074	0.88 ± 0.0045	0.82 ± 0.0045	0.95 ± 0.0067
Proposed MoBE	–	0.85 ± 0.0069	0.92 ± 0.0040	0.90 ± 0.0042	0.93 ± 0.0064

DISCUSSION & CONCLUSIONS

- **Achieved outstanding performance in the classification task by outperforming not only traditional ML methods but also the most newly introduced ones.**
- **More certainty to the predictions obtained as one can find that the lack of attention to ML and DL methods' uncertainty is an important gap in the field.**
- **Last but not least, the close involvement of humans and machines in predictions for two main reasons: (a) High sensitivity to medical case studies due to its very close dependence on human life, and (b) An excellent approach to deal with uncertainty is as an ensemble technique to decisions.**