2023 IEEE International Conference on Data Mining Workshops (ICDMW) | 979-8-3503-8164-1/23/$31.00 ©2023 IEEE | DOI: 10.1109/ICDMW60847.2023.00051

Dual trustworthy mechanism for illness classification with multi-modality data

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***Abstract*—Multi-modality classification has flourished in recent years. Traditional methods mainly focus on advancing deep neural networks (DNN) to meet high performance. However, the interpretability of these methods remains blind due to the complexity and ambiguity of DNN, which also causes distrust. This problem is enlarged in sensitive areas, such as biomedical computing. Hence, we propose a novel dual trustworthy mechanism for multi-modality classification (DTMC), which can make the process and results of DNN more credible and interpretable while increasing performance. Specifically, a confidence attention mechanism is performed from local and global views to improve the process' confidence by evaluating the attention scores and distinguishing the abnormal information. A confidence probability mechanism from local and global perspectives is conducted in the prediction stage to enhance the results' confidence. Extensive experiments on multi-modality medical classification datasets show superior performance with the interpretability of the proposed method compared to the state-of-the-art (SOTA) methods. Our resources are open at https://github.com/ghh1125/data.**

***Index Terms*—Multi-modality learning, Trustworthiness and Interpretability learning, Illness classification**

I. Introduction

The explosion of multi-modality data has increased the research interests in multi-modality classification [1], [2]. Multi-modality classification requires mining-related information from heterogeneous data to assign labels to samples. For instance, in biomedical computing, people expect to use different views of DNA features to infer diseases. The deep learning (DL) based methods like [3], [4], [5], [6], [7], [8] are wide use and show incredible performance. However, like a black box, the process of most DL methods remains unknown, making it difficult to persuade the public, especially when facing safety-related tasks.

Due to the component heterogeneity of different modalities, the fusion of modalities is tricky. Previous DL methods like CF [9] use simple concatenation for complex multi-modality information, and others use weighted summation, feature multiplication, or gating mechanism [10]. These methods need to be more comprehensive to fuse multi-modality information. Because for every single sample, there is an unbalanced informativeness between different modalities and features. HMCAN [11], [12], and [13] introduce a variety of variant attention mechanisms that are expected to obtain better multi-modality fusion capabilities. The attention mechanism can find adequate information from more fine-grained features but can only sometimes run well. Some distinctive features can attract more attention, but it does not mean the informativeness of these features, which we call $sharp-features$. Later work [14] dynamically fuses the feature and modality informativeness to promote accuracy, but the model confidence has yet to be further explored.

Considering the model's credibility in the real scene, [15] use Dirichlet distribution to model a distribution with evidence-level features to provide reliable uncertainty estimations. Dynamics [16] transfer the concept of True class probability from ConfidNet [17] to enhance the trust. However, it still needs further exploration to reach public acceptance. This work is devoted to increasing the trustworthiness and interpretability of illness classification with multi-modality data. The proposed method, called DTMC, designed two trustworthy mechanisms, the confidence attention module (CAM) and the confidence probability module (CPM), to make the process and results of DNN more credible. Additionally, we notice that high attention scores of multi-modality features ($sharp-features$) do not represent high informativeness and alleviate this phenomenon by a penalty term.

II. Related Work

Recently, multi-modality learning has become a research hotspot with the increase of multi-modality data such as advertisements and publications [18]. Generally speaking, multi-modality data refers to heterogeneous data such as text, pic-

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DOI 10.1109/ICDMW60847.2023.00051

tures, and audio, but there is still no standard definition. For example, in disease classification, mRNA, DNA methylation, and miRNA expression data are considered three modalities. Tasks in multi-modality learning mainly comprise finding some unified representation of multi-modality information (representation), mapping a modality to another (translation), finding relationships between modality sub-components (alignment), integrating information (fusion), assisting scarce modalities by leveraging the knowledge of plentiful modalities (co-learning). Earlier work likes [19], [1] et al., using simple concatenate strategies for fusion. Other approaches use decision-making and dynamic fusion methods. With the popularity of the Attention mechanism [20], more and more methods tend to use the attention mechanism to integrate multi-modality data better. However, these methods cannot deal with the trustworthy problem of DNN.

Research on trustworthy learning for DNN [21], [22], [23] [24] have always been prosperous. [21] give a complete theoretical treatment of the link between Gaussian processes and dropout and develop the tools necessary to represent uncertainty in deep learning. [25] pointed out that the confidence of most deep learning models has yet to be perfectly corrected, and the overall tendency is overconfident, which means the average confidence of the prediction is higher than the average accuracy of the prediction. [17] proposed the True Class Probability (TCP) concept, effectively enhancing the model's confidence. Applications to trustworthy learning have also emerged in work such as [26] and [27]. [26] adopts normalized cross-entropy (NCE) loss to measure the quality of confidence score, while [27] uses a bi-directional approach for lattices (BiLatRNN) for confidence estimation. [28] noted that the common attention mechanism could not achieve credibility and proposed saliency-based explanations to achieve success. It will be helpful to transfer these methods to our topic.

III. Proposed Method

A. Datasets

This study adopts several multi-modality datasets from biomedical computing, which is safety-related for experiments in the credible and interpretable fusion and representation of heterogeneous data features. Four popular common datasets, ROSMAP, LGG, KIPAN, and BRCA, are tested. They all contain mRNA expression data, miRNA expression data, and DNA methylation data (meth). The ROSMAP dataset is used to classify Alzheimer's disease patients from normal control patients, including 200 mRNA, 200 miRNA, and 200 meth features. The LGG dataset is for classifying low-grade gliomas (LGG), containing 2000 mRNA, 2000 miRNA, and 548 meth features. The KIPAN dataset is used for kidney cancer type classification with 2000 mRNA, 2000 miRNA, and 445 meth features. The BRCA dataset is about breast cancer (BRCA) PAM50 subtype classification, embracing 1000 mRNA, 1000 miRNA, and 503 meth features. The specific information can refer to the TABLE I.

TABLE I
DETAILS OF THE FOUR DATASETS.

Datasets	Samples	Classes	Modalities
BRCA	875	5	3
KIPAN	658	3	3
LGG	510	2	3
ROSMAP	351	2	3

B. Preliminaries

Suppose a dataset D with N samples in multi-modality classification is expressed as $D = \{X_n, Y_n\}_{n=1}^{N}$, for each sample X with M ($M > 1$) modalities can be expressed as $X = \{x_m\}_{m=1}^{M}$, where each x represents features of a modality, which generally be high-dimensional. The corresponding Y should be a binary or multivariate vector, depending on the number of classification labels. The multi-modality classification task aims to find a function f to map X and Y. Generally, f can be written as $f : X- > Y$.

Before the process of CAM, the raw data needs to be preprocessed by the feature extractor E and then get the w as the input of DTMC. For simplicity, E is a fully connected layer. In multi-modality classification, each modality x_m has a corresponding feature extractor, which can be expressed as the following formula:

$$w_m = \sigma(E_m(x_m)), \tag{1}$$

where σ is the activation function and E_m is the feature extractor.

C. Confidence Attention Module

Traditional attention mechanisms fail to realize that high attention does not always represent informativeness, which means the excessive participation of some invalid or harmful information, threatening the downstream network. It is, therefore, essential to improve the credibility of the attention mechanism. The CAM mainly includes Local Confidence Attention (LCA) and Global Confidence Attention (GCA) to learn multi-modality information from local and global perspectives with a confidence evaluation to enhance the reliability of the attention mechanism.

a) Local Confidence Attention: The input of every modality often contains some noise or useless features. The attention mechanism is expected to filter out the noise and reduce attention to uninformative features. However, when abnormal features appear, the traditional attention mechanism is not well adapted to this goal. Thus, reevaluating the attention scores can effectively improve the accuracy and credibility of the attention mechanism [26].

For LCA, the attention branch's Q, K, and V inputs are the same: a single-modality feature. Then, a regular attention score $Score_{LCA}$ and weight output $Weight_{LCA}$ are obtained after single-modality attention processing. The input of the confidence branch is the same, and the output gets a Confidence attention score $ConfScore_{LCA}$ to correct the original

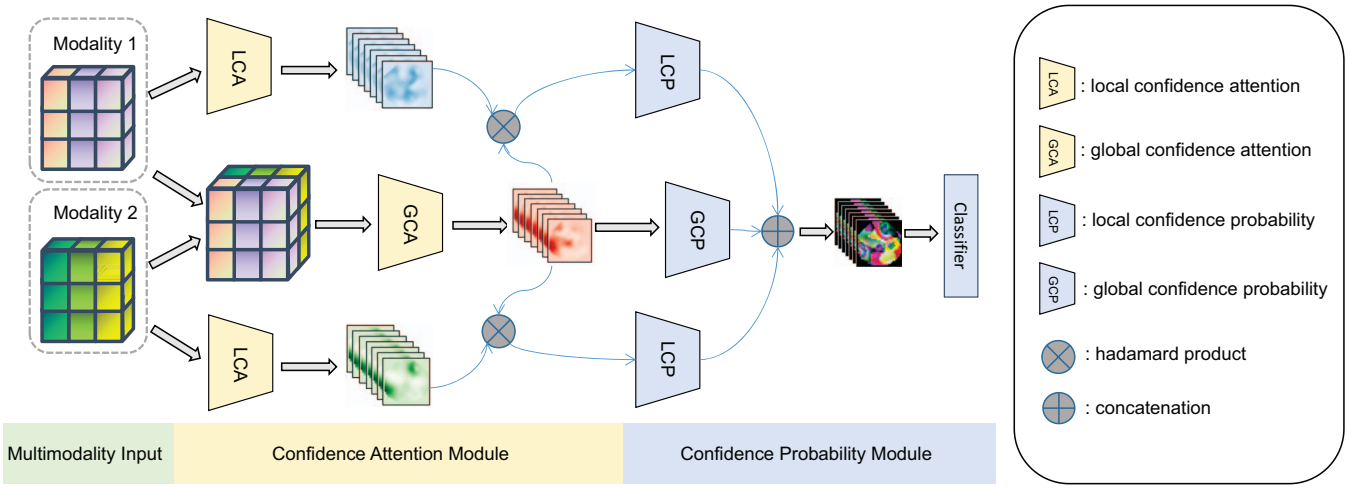

Fig. 1. The proposed method (two modalities example).

attention score. Due to the data of different domains having heterogeneity in content, a projection layer is responsible for mapping the domain-specific features to a common latent space. So, the final V for single-modality attention is the output of the projection layer. Inspired by [16], most features are uninformative. DTMC adds a condition that conforms to a Gaussian distribution to the loss function. LCA generates the local confidence attention loss for optimizing expressed in equation 2.

$$L_{LCA} = \sum_{n=1}^{N}\sum_{l=1}^{L}\left\|\text{atten}_{nl}^{sa} - \text{atten}_{nl}^{lconf}\right\|_1 + \left\|\text{Sk}^2 + (\text{Ku-3})^2\right\|_1, \tag{2}$$

where $atten_{nl}^{sa}$ produced by single-modality attention and $atten_{nl}^{lconf}$ caused by local confidence evaluation. L represents the number of features. Ku and Sk represent the kurtosis and skewness of a certain distribution, respectively. If the distribution is closer to the Gaussian distribution, Ku and Sk tend to be 3 and 0.

b) Global Confidence Attention: Different modalities have different construction forms, leading to composition heterogeneity. We proposed the GCA to capture multi-modality information from a global perspective to fuse them better. In the same role as LCA, GCA can evaluate the cross-modality attention score. Additionally, because the modality importance varies between samples, a gated network from the sample level captures features before the fusion. Similar to LCA, global confidence attention generates the global attention confidence loss as follows:

$$L_{GCA} = \sum_{n=1}^{N}\sum_{l=1}^{L}\left\|\text{atten}_{nl}^{ca} - \text{atten}_{nl}^{gconf}\right\|_1 + \left\|\text{Sk}^2 + (\text{Ku-3})^2\right\|_1, \tag{3}$$

where the $atten_{nl}^{ca}$ produced by cross-modality attention and $atten_{nl}^{gconf}$ caused by global confidence evaluation. Same as equation 2, Ku and Sk represent the kurtosis and skewness of a certain distribution, respectively.

D. Confidence Probability Module

The CPM includes Local Confidence Probability (LCP) and Global Confidence Probability (GCP) to improve the credibility of the results from a global and local perspective. LCP will evaluate the probability of each modality feature output by the softmax function. For C classification problems, LCP will select the corresponding prediction scores of C classes and treat them equally through the confidence layer to output a confidence score. GCP, on the other hand, focuses on evaluating the confidence of multi-modality fusion features. The different modality information contained in different samples is different, and the proportion of informativeness varies for different modalities. So, using local and global attention can better capture adequate information. Equations 4 and 5 are the expressions of the LCP and GCP losses.

$$L_{LCP} = \sum_{n=1}^{N}\sum_{c=1}^{C}\left\|\text{prob}_{nc}^{lsof} - \text{prob}_{nc}^{lconf}\right\|_1, \tag{4}$$

$$L_{GCP} = \sum_{n=1}^{N}\sum_{c=1}^{C}\left\|\text{prob}_{nc}^{gsof} - \text{prob}_{nc}^{gconf}\right\|_1, \tag{5}$$

where $prob_{nc}^{lsof}$ and $prob_{nc}^{lconf}$ are the raw probabilities and the confidence probabilities in single-modality features. $prob_{nc}^{gsof}$ and $prob_{nc}^{gconf}$ are the raw probabilities and the confidence probabilities in multi-modality features.

The optimization goal of DTMC is to minimize the value of equation 6, which consists of four parts in total.

$$L_{\text{OVERALL}} = L_{CLS} + \lambda_1 L_{CA} + \lambda_2 L_{CP} + \lambda_3 L_{SF}, \tag{6}$$

where L_{CLS} is the classification loss, L_{CA} is the attention loss, L_{CP} is the probability loss, and L_{SF} is the penalty term

for $sharp - features$. λ_1, λ_2, λ_3 are hyperparameters that control the influence of L_{CA}, L_{CP}, and L_{SF}, respectively.

IV. Experiments and Results

A. Experimental Settings

For multi-class datasets (BRCA, KIPAN), three evaluation metrics are ACC, WeightedF1, and MacroF1, and for two-class datasets (LGG, ROSMAP), ACC, F1, and AUC are used. Experiments were performed on Linux (Ubuntu 20.04.1) with four Nvidia GeForce RTX 3090 GPUs and Intel(R) Xeon(R) Gold 6254 CPU @ 3.10GHz to do calculations. Experiments were repeated five times. The results shown in this paper are the average of these experiments.

Five methods were compared: MOGONET [29], TMC [15], CF [9], GMU [10], and Dynamics [16]. MOGONET through Graph Convolution Network and View Correlation Discovery Network to explore multi-omics relation for classification. TMC conducts decision fusion based on the confidence of different modalities. CF integrates multiple modalities by concatenating late-stage multi-modality representations. GMU establishes an intermediate multi-modality representation based on a combination of data. Dynamics dynamically evaluates the feature-level and modality-level information for integrating multi-modality.

B. Experimental Results and Discussions

The main experimental results for the BRCA, KIPAN, LGG, and ROSMAP datasets are shown in TABLE II. Experimental results show that DTMC achieves SOTA performance on four biomedical computing datasets. All indicators have improved, except for the ACC in the KIPAN dataset, which has decreased by 0.1%. The improvement of the effect is due to the advancement of the feature representation by CAM, the improvement of confidence in the decision by the CPM, and the introduction of the penalty term.

In the ablation experiment, we tested the performance of models without CAM, CPM, and without both, respectively. The detailed results are shown in TABLE III. The results of the ablation experiments verify the effectiveness of the CAM and CPM. DTMC has the best performance only when using CAM and CPM simultaneously. The experimental results also show that CAM's importance is more significant than CPM's. This may be because using single-modality attention for feature extraction and cross-modality attention for modality fusion representation is more critical because it lies upstream. A good feature representation can significantly reduce the interference of invalid information on the final classification. Another ablation experiment is to test the confidence evaluation of the classification results of the model. The experimental results can be seen in Fig. 2. Similar to [25], if the model obtains a more reliable prediction result, its polyline will fit more with the diagonal. It can be concluded from Fig. 2 that DTMC is closer to the diagonal line under the blessing of the dual-trust mechanism, which also means that the model confidence of DTMC is increased.

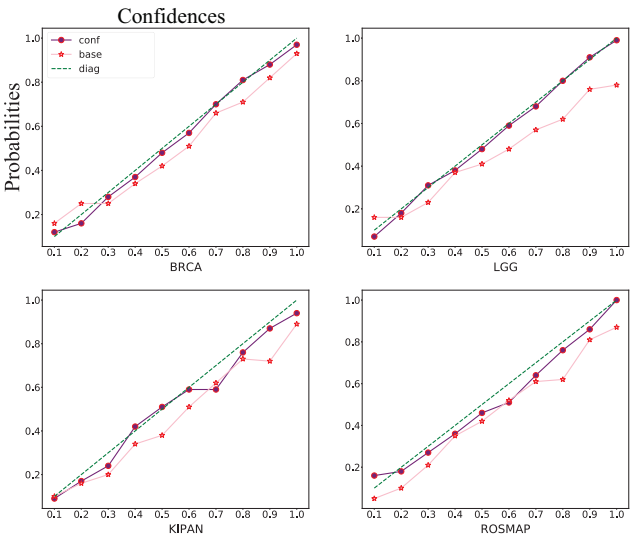

Fig. 2. Comparison of results with and without confidence mechanisms. $conf$ indicates the result of using the confidence mechanism, $base$ indicates the result of not applying the confidence mechanism, and $diag$ indicates the diagonal.

To explore the sensitivity of DTMC to parameters, we performed a parametric analysis. The first term analyzes a set of hyperparameters λ_1, λ_2, and λ_3 controlling for loss effects. Four sets of settings for three hyperparameters were carried out in the experiment. The specific experimental results are shown in Fig. 3. It can be found that the first group of parameters (balanced weights) performs best, the last group of parameters takes second place, and the third and fourth groups rank last. Overall, the difference between different experimental results is trivial.

The second experiment investigates the effect of the parameter R in the $sharp-features$ penalty. R is a hyperparameter indicating the number of $sharp - features$ expected to be penalized. Considering that different datasets use different numbers of features for training, the sensitivity validation to the number of R will be different. We select the 10%, 30%, and 50% of all found $sharp - features$ to be punished. The experimental results are shown in TABLE IV. Overall, selecting 30% of the $sharp-features$ for punishment is the most beneficial to DTMC. This may be due to the fact that too few $sharp - features$ do not affect the model enough, while too many $sharp - features$ may make less obvious $sharp - features$ be over-smoothed.

C. Detail Study of Biomarkers

To further validate the effectiveness of the model and give its interpretability. We conducted additional experiments to verify the details. The visualized results will demonstrate DTMC's performance and provide convincing reasons to reduce people's bias and distrust towards deep learning, especially in these two sensitive areas. In biomedical computing, representative and essential applications of multi-modality analysis are identifying biomarkers. Some features (biomarkers) of

TABLE II

IN FOUR BIOMEDICAL COMPUTING DATASETS, THE PRELIMINARY EXPERIMENTAL RESULTS OF DTMC COMPARED FIVE SOTA METHODS ON THREE METRICS. THE PERFORMANCE DATA OF THESE FIVE METHODS COMES FROM THEIR ORIGINAL PAPERS AND OTHER PUBLICATIONS.

Dataset	Metrics	MOGONET [29]	TMC [15]	CF [9]	GMU [10]	Dynamics [16]	DTMC (ours)	%Improv.
BRCA	ACC	82.9±1.8	84.2±0.5	81.5±0.8	80.0±3.9	87.7±0.3	**89.6±0.4**	2.2% ↑
	WeightedF1	82.5±1.7	84.4±0.9	81.5±0.9	79.8±5.8	88.0±0.5	**90.1±0.4**	2.4% ↑
	MacroF1	77.4±1.7	80.6±0.9	77.1±0.9	74.6±5.8	84.5±0.5	**88.3±0.5**	4.5% ↑
KIPAN	ACC	**99.9±0.2**	99.7±0.3	99.2±0.5	97.7±1.6	**99.9±0.2**	99.8±0.3	-0.1% ↓
	WeightedF1	**99.9±0.2**	99.7±0.3	99.2±0.5	97.6±1.7	**99.9±0.2**	**99.9±0.2**	-
	MacroF1	**99.9±0.2**	99.4±0.5	98.8±0.9	95.8±3.2	**99.9±0.3**	**99.9±0.2**	-
LGG	ACC	81.6±1.6	81.9±0.8	81.1±1.2	80.3±1.5	83.3±1.0	**83.9±0.6**	0.7% ↑
	F1	81.4±2.7	81.5±0.4	82.2±0.4	80.8±1.2	83.7±0.4	**85.6±0.7**	2.3% ↑
	AUC	84.0±2.7	87.1±0.4	88.1±0.4	88.6±1.2	88.5±0.4	**89.8±0.5**	1.4% ↑
ROSMAP	ACC	81.5±2.3	82.5±0.9	78.4±1.1	77.6±2.5	84.2±1.3	**86.0±1.0**	2.1% ↑
	F1	82.1±1.2	82.3±0.6	78.8±0.5	78.4±1.6	84.6±0.7	**86.7±0.8**	2.5% ↑
	AUC	87.4±1.2	88.5±0.6	88.0±0.5	86.9±1.6	91.2±0.7	**91.7±0.7**	0.6% ↑

TABLE III

ABLATION EXPERIMENTAL RESULTS ON FOUR BIOMEDICAL COMPUTING DATASETS. w/o MEANS *without*. ACC, F1, AND AUC WERE TESTED FOR LGG AND ROSMAP. BRCA AND KIPAN TESTED ACC, WEIGHTEDF1, AND MACROF1.

Datasets	Methods	ACC	WeightedF1	MacroF1
BRCA	w/o both	87.1±0.4	87.4±0.3	83.7±0.5
	w/o CAM	87.7±0.4	87.2±0.5	86.8±0.5
	w/o CPM	88.1±0.3	89.1±0.4	87.2±0.3
	Proposed	**89.6±0.4**	**90.1±0.4**	**88.3±0.5**
KIPAN	w/o both	99.7±0.3	99.9±0.3	99.8±0.2
	w/o CAM	99.8±0.3	99.9±0.2	99.9±0.2
	w/o CPM	99.8±0.3	99.9±0.2	99.9±0.3
	Proposed	**99.8±0.3**	**99.9±0.2**	**99.9±0.2**

Datasets	Methods	ACC	F1	AUC
LGG	w/o both	80.6±0.5	81.7±0.6	85.6±0.5
	w/o CAM	81.0±0.6	82.4±0.6	86.9±0.3
	w/o CPM	82.9±0.4	83.7±0.7	87.7±0.8
	Proposed	**83.9±0.6**	**85.6±0.7**	**89.8±0.5**
ROSMAP	w/o both	82.1±0.9	82.6±1.0	89.5±0.7
	w/o CAM	84.7±0.8	82.8±0.9	90.0±0.6
	w/o CPM	85.0±0.8	84.1±0.9	91.4±0.7
	Proposed	**86.0±1.0**	**86.7±0.8**	**91.7±0.7**

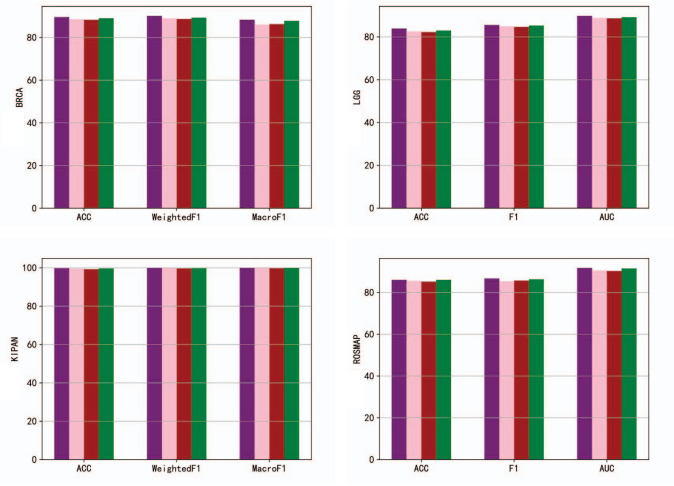

Fig. 3. Sensitivity experiment results for the parameter set λ. A total of four sets of parameters were tested. The purple bars indicate the first set (1/3, 1/3, 1/3), the pink bars indicate the second set (1/2, 1/4, 1/4), and the brown and green bars indicate the third (1/4, 1/2, 1/4) and fourth (1/4, 1 /4, 1/2) set of parameters.

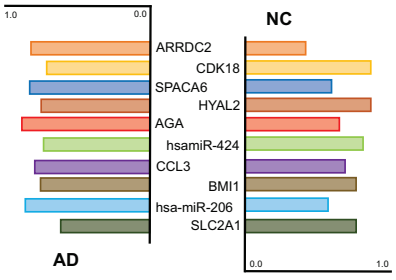

Fig. 4. The top 5 biomarkers for attention scores for each class on the ROSMAP dataset. It also shows the attention score obtained by the 5 biomarkers in another class.

ROSMAP and LGG with high attention scores (top 5) for each class are shown in Fig. 4 and Fig. 5. For the BRCA and KIPAN datasets, some features for obtaining high and low attention are listed in TABLE V.

On the ROSMAP dataset, 'AD' and 'NC' represent Alzheimer's Disease patients and normal control subjects. Experiments show that biomarkers such as $SLC2A1$, $CDK18$, $SPACA6$, $hsa-miR-206$, and $CCL3$ are significant for identifying 'AD' and 'NC.' Some clinical studies such as [30], [31] have also given similar arguments. On the LGG

TABLE IV
EXPERIMENTAL RESULTS OF PARAMETER R SENSITIVITY ON FOUR BIOMEDICAL COMPUTING DATASETS.

Datasets	%.(R)	ACC	WeightedF1	MacroF1
BRCA	10%	89.5±0.6	89.7±0.3	87.8±1.0
	30%	**89.6±0.4**	**90.1±0.4**	**88.3±0.5**
	50%	88.7±0.5	89.9±0.5	88.3±0.5
KIPAN	10%	99.8±0.3	98.9±0.3	99.1±0.3
	30%	**99.8±0.3**	**99.9±0.2**	**99.9±0.2**
	50%	98.9±0.5	99.7±0.3	99.6±0.3
Datasets	%.(R)	ACC	F1	AUC
LGG	10%	81.5±0.6	84.7±0.6	87.8±1.0
	30%	**83.9±0.6**	**85.6±0.7**	**89.8±0.5**
	50%	82.7±0.5	84.9±0.5	88.3±0.5
ROSMAP	10%	84.8±0.7	85.9±0.3	90.1±0.6
	30%	**86.0±1.0**	**86.7±0.8**	89.9±0.7
	50%	85.9±0.5	84.7±0.8	**91.7±0.7**

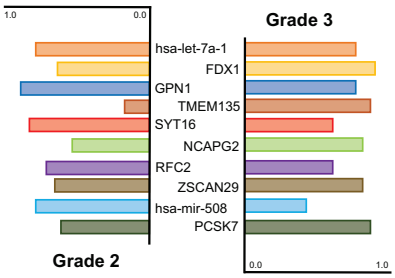

Fig. 5. The top 5 biomarkers for attention scores for each class on the LGG dataset. It also shows the attention score obtained by the 5 biomarkers in another class.

TABLE V
THE BIOMARKERS THAT OBTAINED HIGH AND LOW ATTENTION WERE FOUND IN THE BRCA AND KIPAN DATASETS. THE PINK PART INDICATES HIGH ATTENTION, AND THE CYAN PART INDICATES LOW ATTENTION.

Datasets	Biomarkers	
	High	Low
BRCA	SOX11,KLK8,hsa-mir-452, ZNF671,TMEM207	ACOX2,BBS4,CCKBR, hsa-mir-1254,SCGB3A1
KIPAN	CHD5,ADH5,ARPC3, DVL3,NOD2	GPN1,CCDC121,hsa-mir-29b-1, TMEM232,CCDC121

dataset, 'Grade2' and 'Grade3' represent two grades in low-grade glioma. Experiments show that biomarkers such as $NCAPG2$, $SYT16$, $RFC2$, and $FDX1$ have high attention and significantly affect classification. The correlation between these biomarkers and diseases was also found in some medical literature like [32] and [33]. The selection of these features gives the interpretability and trustworthiness of the model well, which is extremely meaningful for the safety-sensitive biomedical computing field.

V. CONCLUSIONS AND FUTURE WORK

In this work, we proposed DTMC for the problem of untrustworthy and uninterpretable multi-modality learning with DNN models. Extensive experimental results on four biomedical computing datasets prove that DTMC reaches the SOTA level and alleviates the lack of interpretability and confidence in previous DL methods. A penalty trick reduces the influence of $sharp - features$. In the future, we hope to explore the internal logic of deep neural networks from a more fine-grained perspective.

ACKNOWLEDGMENT

This work was supported by the National Natural Science Foundation of China under Grant 62077015.

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