

# DEEP SPATIO-TEMPORAL MULTIPLEX GRAPH LEARNING FOR CARDIAC IMAGING CLASSIFICATION

Jaume Banus\*, Augustin Ogier\*, Roger Hullin †, Philippe Meyer ‡, Ruud B. van Heeswijk\*, Jonas Richiardi\*

\* Department of Radiology, Lausanne University Hospital and University of Lausanne, Switzerland

† Department of Cardiology, Lausanne University Hospital and University of Lausanne, Switzerland

‡ Department of Medicine, Geneva University Hospital and University of Geneva, Switzerland

## ABSTRACT

Cardiovascular diseases are the leading cause of mortality worldwide. Cardiac imaging is critical for precise characterization of cardiac structure and function, and is key in diagnosis, therapeutic management, and prognosis. In this work, we propose a novel representation of spatio-temporal cardiac data as a multiplex graph and develop a multi-level message passing neural network to classify clinical groups corresponding to different cardiovascular diseases. Using open data from the Automated Cardiac Diagnosis Challenge (N=150), our results show that the multiplex representation extracts discriminative features from the data (up to 94% accuracy compared to up to 80% for well-tuned baselines such as XGboost and MLP). Ablation studies show the bias induced by the graph's spatio-temporal structure improves generalization.

**Index Terms**— Message passing, Graph neural networks, Cardiac imaging, Multiplex graphs.

## 1. INTRODUCTION

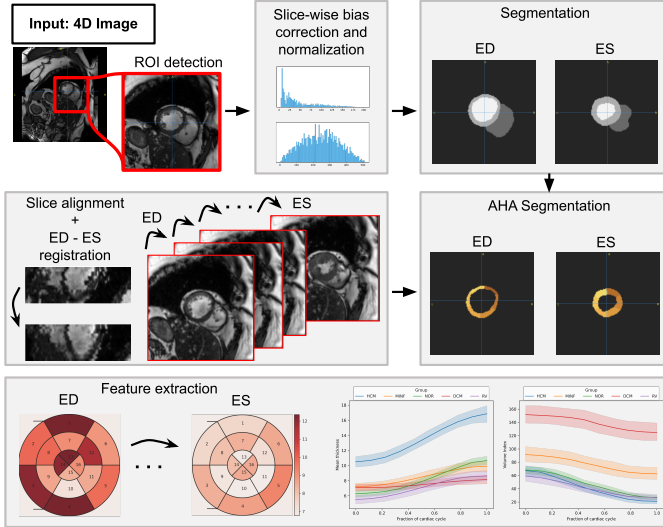
Cardiovascular diseases (CVDs) are the leading cause of mortality globally, with an estimated prevalence of around 6'000/100'000 [1]. In this context, the analysis of the cardiac function is key for patient management, diagnosis and risk evaluation. Image-derived features are increasingly used in clinical routine. Most features, including stroke volume or ejection fraction (EF), are derived from automated segmentations obtained from algorithms such as convolutional neural networks (CNNs) [2]. Nevertheless, in the clinical environment there is a large data heterogeneity stemming from hardware and sequence differences, generating images with a variable resolution, contrast, and signal-to-noise ratio [3]. These differences impair generalization and result in variable performance when applied to unseen data. While data pre-processing and bias correction [4] are used to minimize these effects, processing pipelines themselves add another source of variability. Therefore, introducing domain knowledge as priors in those algorithms could help to mitigate measurement differences. Graph neural networks (GNNs) offer a possibility to include prior knowledge, e.g. by encoding the position

of anatomical structures or functional connectivity [5, 6]. Their flexibility to handle structured and non-structured data with different relationships makes them a promising tool in medical diagnosis [7]. GNNs exploit spatial dependencies between entities under the main assumption that the state of a node relates to the state of its neighbors. Most of the work done in GNNs focused on message passing (MP) [8] and graph convolutional networks (GCNs) [9]. These approaches learn a latent feature representation on each node by aggregating information of a node and its neighbors, and proved to be an efficient solution for a variety of tasks including classification and regression at multiple hierarchical levels (nodes, edge and graph) and in different settings, such as supervised, unsupervised and semi-supervised learning [10]. Recently, GNNs have been extended to heterogeneous graphs, with multiple types of nodes and edges [11]. We propose to represent the heart as a multiplex graph whose nodes correspond to cardiac regions connected among them based on their anatomical location. Each node has a set of image-derived features, e.g. thickness or volume. Heterogeneous edges connect these nodes carrying information relative to the differences between cardiac regions. Moreover, cardiac images capture a temporal sequence that spans from end-diastole (ED) to end-systole (ES), adding a temporal dimension to the graph. Our goal is to use the multiplex graph representation to derive latent representations that capture the dynamics of the underlying system, in this case the heart contraction, and assess the influence of the added bias by the graph structure in the classification of clinical groups in the ACDC challenge [2] compared to classical approaches.

## 2. METHODS

### 2.1. Data processing and feature extraction

We used open data from the ACDC challenge [2], consisting of 150 patients divided into 5 evenly distributed subgroups: 1 normal control group (NOR) and 4 pathological groups which encompass myocardial infarction (MINF), dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM) and abnormal right ventricle (RV). The diagnostic criteria for each disease can be found in the challenge article [2]. The dataset



**Fig. 1.** Data processing pipeline. The input is a 4D image composed of 2D short-axis slices. We perform slice-wise bias-field correction and normalization, and use [12] to obtain the segmentation of the whole 4D volume. Next, we align the slices of the 4D volume to correct breath-motion artifacts and obtain the diffeomorphism from ED to ES. The LV myocardium at ED is divided in 16 AHA segments and the ED-ES diffeomorphism is used to map the AHA labels at each time frame from ED to ES. For each segment we extract features associated to its thickness, volume and intensity distribution.

was split in a balanced way in a training set of 100 subjects and a blind test set of 50 used to evaluate algorithms in the challenge. Each patient has a series of short-axis slices stacked in a 4D ( $x$ - $y$ - $z$ - $t$ ) volume covering the base to the apex, with a variable in-slice resolution around  $1.5mm^2$  and a slice thickness from 5 to  $10mm$ . The entire dataset was acquired in clinical routine, resulting in an heterogeneous image quality. As illustrated in Figure 1, we processed the 4D images by performing slice-wise bias-field correction and normalization, and defined a region of interest (ROI) covering the whole heart. To segment the images we fine-tuned the model presented in [12] using the ED and ES ground-truth segmentation maps available in the training set. From the segmentation maps we computed the volumes of left ventricle (LV), right ventricle (RV), and the LV myocardium mass, as well as the ejection fraction (EF) for each region. We used the average center of mass of the LV at mid-cavity slices to re-align the 2D slices and correct the slice breath-motion misalignment. We divided the LV myocardium at ED in 16 segments according to the American Heart Association (AHA) model [13] and computed the volume and thickness of each segment. The apex region was not included given that for some subjects it is not in the field of view of the image. The division was done at ED since it represents the end of the filling phase, the instant at which the ventricles are expanded and filled with blood.

From the thickness and intensity measurements of each region we extracted the mean, median, interquartile, lower quartile and upper quartile values. Following, we disassembled the 4D images and registered the consecutive frames from ES to ED using the symmetric normalization (SyN) registration algorithm, available in the advanced normalization tools (ANTs) package [14]. We obtained the diffeomorphism from ED to ES through the composition of the consecutive frames deformations. This allowed us to transfer the AHA labels to ES, and extract the volumes and thickness measurements at each frame up-to ES. Height and weight were used to compute the body surface area (BSA) according to Mosteller’s formula [15]:  $BSA = \left(\frac{Weight[kg]*Height[cm]}{3600}\right)^{\frac{1}{2}}$ , and used it to normalize the volumes of each region. Finally, we computed the Wasserstein distance between the distribution of voxel intensities of each region at each frame and between frames, as well as the distance between the centers of mass of each region. These distances are used as edge features in our multiplex graph to encode relative motion. Height, weight, BSA, and EF of the LV, RV and LV myocardium as well as stroke volume index were used as global features independent of the graph structure. Table 1 shows all features, their anatomical location, and whether they are node or edge attributes.

**Table 1.** Edge and node features. For the voxel intensity and thickness we extracted mean, median, lower quartile, upper quartile and interquartile values. Center of mass (CM), myocardium (Myo), left ventricle (LV), right ventricle (RV).

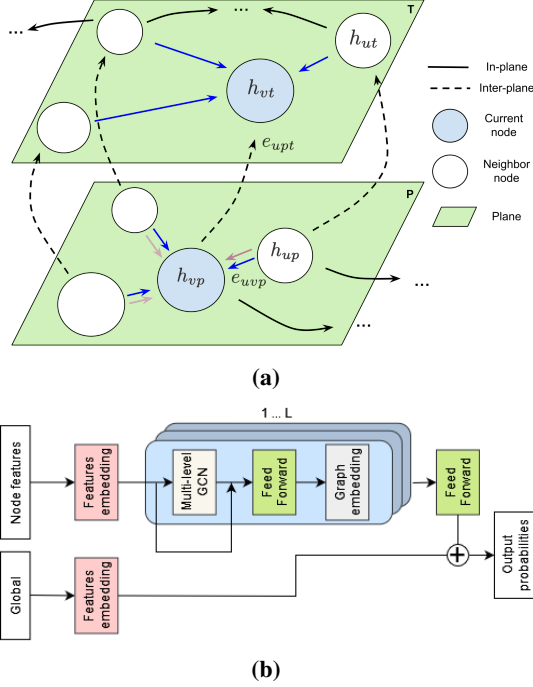
Feature	LV	RV	LV Myo	AHA	Type
Volume	✓	✓	✓	✓	Nodes
Voxel intensity	✓	✓	✓	✓	Nodes
Position (CM)	✓	✓	✓	✓	Nodes
Thickness			✓	✓	Nodes
Wasserstein distance	✓	✓	✓	✓	Edges
CM Distances	✓	✓	✓	✓	Edges

## 2.2. Graph representation

We represent the heart as a spatio-temporal multiplex (multilayer) graph, with the idea to exploit the interdependence between the different features and their spatio-temporal trajectory. In this context, each image frame can be viewed as a plane ( $\mathcal{P}$ ) in the multiplex graph. In each plane there are multiple edges ( $\mathcal{E}$ ) that connect the heart regions, mapped one-to-one to a set of vertices (or nodes) ( $\mathcal{V}$ ). At the same time, the planes are connected between them through multiple edges ( $\mathcal{T}$ ) encoding frame to frame differences in time. We formally represent the multiplex graph as  $\mathcal{G} = (\mathcal{V}, \mathcal{E}, \mathcal{P}, \mathcal{T})$ . We considered as nodes the different AHA segments, as well as the LV myocardium, LV and RV blood pool regions. Typically, the adjacency matrix is based on a defined similarity between pairs of nodes. However, to include a spatial prior, we decided to connect each AHA segment to his adjacent segments. In turn, all the AHA segments are connected to the LV

myocardium and to the RV and LV blood pools.

### 2.3. GNN implementation



**Fig. 2.** a) GCN layer blocks. Planes represent cardiac frames from the 4D image. Arrow colors indicate different edge features, dashed arrows show inter-plane edges, solid arrows show in-plane edges. b) End-to-end network architecture.

Our approach is mainly inspired by graph isomorphism networks (GIN) [16] and approaches based on MP neural networks [8]. In these approaches, the node representations are obtained by aggregating the neighbours' representations and combining them with the current node representation. Moreover, they can be extended to work with heterogeneous GNNs, as in [11] where each node process the messages of the different neighbors types independently and mixes them. In our case, we have a single node type, heart regions, but multiple messages. At each neural layer we have two messages that travel simultaneously through the graph in orthogonal directions, space and time. In particular, we have a spatial message ( $m_p$ ) at each plane of the graph, and an additional temporal message ( $m_{pt}$ ) that travels alongside the directed edges connecting consecutive graph planes ( $p$  and  $t = p + 1$ ). This split of the MP introduces the notion of time in the network. The input to our layer ( $l$ ) is a set of node features for each plane,  $h_p^{l-1} = (h_1, h_2, \dots, h_{v_p}), h_{ip}^{l-1} \in \mathbb{R}^D$ , where  $D$  is the number of features and  $v_p$  the number of nodes at the plane  $p$ . The layer produces a new set of node features per plane ( $D'$ ),  $h_p' = (h'_1, h'_2, \dots, h'_{v_p}), h'_{ip} \in \mathbb{R}^{D'}$ . The set of edges at each plane is denoted  $\mathcal{E}_{pt} = (e_1, e_2, \dots, e_{E_{pt}}), e_i \in \mathbb{R}^{F_e}$ , where  $F_e$

is the number of edge features and  $E_{pt}$  indicates the number of edges in the set, the set  $\mathcal{E}_{pp}$  represents the in-plane edges. At layer  $l$ , the message at node  $v$  and plane  $p$  is defined as:

$$m_{vp}^l = \max_{u \in \mathcal{N}_p(v)} \left( \sum_f^{F_e} \frac{h_{up}^l \cdot e_{uvpp}^f}{c_{uvpp}} \right) + m_{vpt}^l, \quad (1)$$

where  $m_{vpt}^l$  is defined as

$$m_{vpt}^l = \max_{u \in \mathcal{N}_{pt}(v)} \left( \sum_f^{F_e} \frac{(h_{ut}^l - h_{vp}^l) \cdot e_{uvpt}^f}{c_{uvpt}} \right), \quad (2)$$

where  $\mathcal{N}_p(v)$  denotes the neighbourhood of node  $v$  at plane  $p$ ,  $c_{uvpt}$  represents the normalization coefficient based on the in-node degree, and  $f$  iterates over the edge features. The received messages are combined to update the node representation as  $h_{vp}^l = \phi^l((1 + \epsilon) \cdot h_{vp}^{l-1} + m_{vp}^l)$ , where  $\phi^l$  is a 2-layer MLP with  $H$ -dimensional input and  $H$ -dimensional output and  $\epsilon$  is a learnable parameter. For each neural network layer ( $l$ ), a graph embedding is obtained based on the node embeddings as  $g^l = \psi_G(\psi^l(h^l))$ , where  $\psi^l$  is parameterized as a 2-layer MLP with a  $H$ -dimensional output and a  $H \cdot N$ -dimensional input, and  $\psi_G$  is a 2-layer MLP shared across the neural network layers with  $H$ -dimensional input and 5-dimensional output. The final graph embedding is obtained as the addition of the average latent representations of the total number of neural network layers ( $L$ ) and the global features embedding ( $h_{ext}$ ), as  $G_h = \frac{1}{L} \left( \sum_{l=1}^L g^l \right) + h_{ext}$ ; where  $h_{ext}$  is obtained using a 2-layer MLP with  $H_g$  hidden dimensions and 5-dimensional output. Initial node features and global features were z-score normalised with respect to the healthy group. The graph embedding,  $G_h$ , is used to classify each graph into the 5 different groups using a softmax non-linearity to optimize a multi-class cross-entropy loss. The GNN was implemented using deep graph library (DGL) [17] with Pytorch [18] backend and optimized with Adam [19].

### 3. EXPERIMENTS AND RESULTS

We compared our method to a fully connected MLP, gradient-boosted decision trees (XGBoost), a random forest and a linear support vector machine (SVM). To obtain the best set of hyperparameters for each algorithm we performed nested cross-validation (CV) with 2 outer folds and 3 inner folds. At each outer fold we split the training set ( $N=100$ ) of the ACDC challenge into 85:15 for training and test, and performed CV in the training set. For our model and the MLP the hyperparameter space was explored using optuna [20]. For the other methods, we relied on the HalvingGridSearch approach implemented in scikit-learn [21]. The set of selected hyperparameters for each classifier is available at Table 3. Finally, we split the training set in 85:15 and used the average of the two

best set of hyperparameters to train the final classifier. Additionally, we performed an ablation study to assess the influence of the edge features and the graph spatial and temporal connectivity. Table 2 reports the mean and standard deviation of the accuracy obtained in CV and the results on the blind test set (N=50).

**Table 2.** Cross-validation (CV) and blind test set accuracy.

Method	CV Acc. ( $\pm$ Std)	Acc. Test	Edges	Global	Spatial	Temporal
Linear SVM	0.72 $\pm$ 0.091	0.76	✓	✓	✓	✓
Random Forest	0.80 $\pm$ 0.066	0.80	✓	✓	✓	✓
XGBoost	0.82 $\pm$ 0.049	0.84	✓	✓	✓	✓
MLP	0.85 $\pm$ 0.033	0.74	✓	✓	✓	✓
Ours and ablation tests						
Multiplex	0.93 $\pm$ 0.044	0.88	✓	✓	✓	✓
	0.91 $\pm$ 0.022	0.86	✓	✓	✓	✗
	0.90 $\pm$ 0.100	0.74	✓	✓	✗	✓
	0.90 $\pm$ 0.056	0.94	✓	✗	✓	✓
	0.85 $\pm$ 0.056	0.80	✗	✓	✗	✗
	0.80 $\pm$ 0.067	0.66	✗	✗	✗	✗

**Table 3.** Hyperparameter ranges and final value. The multiplex GNN and the MLP hyperparameter space were explored using Optuna, others with HalvingGridSearch.

Method	Hyperparameter	Range	Value
Multiplex	Learning rate	[1e-4 1e-2]	0.0038
	Batch size	[20 40]	24
	Num. Layers	[2 6]	3
	Hidden nodes	[15 80]	34
	Hidden global	[15 50]	45
	Dropout rate	[0.1 0.4]	0.317
	L2 weight	[0 0.3]	0.09
	L1 weight	[0 0.3]	0.15
	MLP	Learning rate	[1e-5 1e-2]
Batch size		[20 30]	21
Num. layers		[2 10]	5
Hidden size		[50 250]	190
Dropout rate		[0 0.4]	0.15
L2 weight		[0 0.2]	0.10
L1 weight		[0 0.2]	0.19
Random Forest		Estimators	[501 601]
	Criterion	[Gini Entropy]	Gini
	Class weight	[Balanced Balanced(subsample)]	Balanced(subsample)
XGBoost	Estimators	[501 601]	601
	Alpha	[0 1]	0
	Lambda	[0 1]	0
	Subsample	[0 1]	0.33
Linear SVM	C	[1e-8 1e-3]	1e-3
	Class weight	[None Balanced]	Balanced

#### 4. DISCUSSION

Results presented in Table 2 indicate that our approach outperforms classical methods used to deal with tabular data even when using fewer features. Regarding the ablation tests, we obtained consistently worse results when edges were set to 0. In turn, in-plane spatial connectivity seems to be more important than inter-plane connections. Nevertheless, both temporal and spatial connectivity are needed to achieve the best performance. Moreover, the results suggest that edges have a higher importance than graph external data. Overall, these results highlight that structural information present in the graph helps to generalize to unseen data. To the best of our knowledge, this work is the first to represent the cardiac

cycle as a spatio-temporal multiplex graph. Previous work [22] represented the LV myocardium as point cloud data and used a spatio-temporal GCN [23] to predict the contour position in future frames. However, in the ST-GCN setting, all nodes are connected and edge features are not considered. Moreover, we are using the temporal edge to compute a delta, similar to a discrete step in an Eulerian discretization. The use of directed edges in time encodes the sequence temporal ordering. Therefore, we introduced a novel formulation based on MP that allow us to include directionality in the data and implicitly represent time. Recent works proposed more expressive architectures than MP, mainly related to higher order GNNs that allow the identification of graph substructures [24, 25]; we note that these approaches can still be viewed from a MP point of view [26]. Nevertheless, they could be of interest for the generalization to non-parcellated data, e.g. we could use mesh-like data without a one-to-one node correspondence between the mesh nodes of different subjects. Another point of interest is the generation of the adjacency matrix. It would be interesting to explore the simultaneous learning of the adjacency matrix during task optimization [27] and use the AHA connectivity pattern as prior knowledge to regularize the structural learning. Regarding the temporal aspect, most of the approaches are sequence-to-sequence methods focused on forecast multivariate time-series. These methods are usually based on recurrent neural networks [27], 1D convolutions [28], or transformer-like architectures [29]. Currently, we use the temporal aspect to add a direction in our data and exploit the relative differences between the node states in time. Nevertheless, a sequence-to-sequence approach could be implemented and use the error in the frame prediction as an unsupervised metric to identify the most meaningful meta-paths in the heterogeneous multiplex, similar to the approach present in [30] to detect anomalies in cardiac shapes from point cloud data.

#### 5. CONCLUSIONS

To the best of our knowledge this work represents the first attempt to model the cardiac dynamics from an heterogeneous spatio-temporal graph perspective, and we showed that our message-passing GNN is able to discriminate between different cardiac diseases with an accuracy comparable to the top three algorithms in the ACDC challenge which achieved an accuracy in the blind test set of at least 0.92. In future work, we want to assess the robustness of our approach to uncertainty by applying the learned model to other datasets, such as UK Biobank [31]. Moreover, we will explore end-to-end learning of the graph structure [27] and the interpretability of our results. The spatio-temporal graph-based structure opens the door to identifying which cardiac regions are more important and when for different diseases, which would be a valuable tool for clinical diagnosis.

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