Learning Permutation Invariant Representations using Memory Networks

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Abstract

Many real world tasks such as 3D object detection and high-resolution image classification involve learning from a set of instances. In these cases, only a group of instances, a set, collectively contains meaningful information and therefore only the sets have labels, and not individual data instances. In this work, we present a permutation invariant neural network called a Memory-based Exchangeable Model (MEM) for learning set functions. The model consists of memory units which embed an input sequence to high-level features (memories) enabling the model to learn inter-dependencies among instances of the set in form of attention vectors. To demonstrate its learning ability, we evaluated our model on test datasets created using MNIST, point cloud classification, and population estimation. We also tested the model for classifying histopathology whole slide images to discriminate between two subtypes of Lung cancer—Lung Adenocarcinoma, and Lung Squamous Cell Carcinoma. We systematically extracted patches from lung cancer images from The Cancer Genome Atlas (TCGA) dataset, the largest public repository of histopathology images. The proposed method achieved a competitive classification accuracy of 84.84\%. The results on other datasets are promising and demonstrate the efficacy of our model.

1. Introduction

Deep\footnote{Authors have contributed equally.} artificial neural networks have achieved impressive performance for representation learning. The majority of these deep architectures take a single instance as an input for learning tasks. However, we often need to learn representations for unordered sequential data, or exchangeable sequences. Exchangeable data arise in many practical scenarios, and can particularly be used in Multiple Instance Learning (MIL) where a label is associated with a set, instead of a single input. An example of MIL would be classification of high resolution histopathology images, known as whole-slide images (WSIs). These images are extremely high resolution $\approx 50,000 \times 50,000$ pixels, with labels for an entire image instead of patch-level annotations. Patches could be extracted from these WSIs using various histological features. A set of patches from a WSI can be used for set classification/regression tasks; one such example of LUAD/LUSC classification is explained in Figure 1. Recurrent Neural Networks (RNNs) are popular approach to learn representation from sequential ordered instances. However, the lack of permutation invariance renders RNNs ineffective.

Figure 1: An exemplar application of learning permutation invariant representation for disease classification of Whole-Slide Images (WSIs). (a) A set of patches are extracted from each WSI of patients with lung cancer. (b) The sets of patches are fed to the proposed model for classification of the sub-type of lung cancer—LUAD versus LUSC. The model classifies on a per set basis. This form of learning is known as Multi Instance Learning (MIL).

\begin{itemize}
\item (a) Patch Extraction
\item (b) Set Classification
\end{itemize}
for exchangeable sequences.

Exchangeable models are invariant to permutations of individual instances, i.e., the output of a network remains the same for all permutations of its input set. For example, finding a maximum value in a set of numbers constitutes such a case. Zaheer et al. [28] proposed an exchangeable model, called Deep Sets, for learning set functions. They proved that a pooling operation in a latent space can approximate any arbitrary set function. This implies that our method could achieve an universal approximation of any set function.

In this paper, we propose a novel architecture for exchangeable sequences incorporating attention over the instances to learn inter-dependencies. Our main contribution is a sequence-to-sequence permutation invariant layer called the Memory Block. The proposed model uses series of connected memory block layers, to model complex dependencies within an input set using self attention mechanism. Our model achieves state-of-the-art performance for LUAD/LUSC classification of WSIs with 84.84% accuracy.

The paper is structured as follows: Section 2 discusses the related and recent works. We cover the mathematical concepts for exchangeable data in Section 3. Section 4 and Section 5 discuss the proposed model and experiments.

2. Related Work

In statistics, exchangeability has been long studied. De Finetti studied exchangeable random variables and showed that sequence of infinite exchangeable random variables can be factorised into some independent and identically distributed mixtures conditioned on some parameter $\theta$. Bayesian sets [6] introduced a method to model exchangeable sequences of binary random variables by analytically computing the integrals in de Finetti’s theorem. Orbanz et. al. [16] used de Finetti’s theorem for Bayesian modelling of graphs, matrices, and other data that can be modeled by random structures. Considerable work has also been done on partially exchangeable random variables [1].

Symmetry in neural networks was first proposed by Shawe et al. [20] under the name Symmetry Network. They proposed that invariance can be achieved by weight-preserving automorphisms of a neural network. Ravabaks et al. proposed a similar method for equivariance network through parameter sharing [18]. Bloem Reddy et al. [5] studied the concept of symmetry and exchangeability for neural networks in detail and established a link between functional and probabilistic symmetry, and obtained generative functional representations of joint and conditional probability distributions that are invariant or equivariant under the action of a compact group. Zhou et. al. [30] proposed treating instances in a set as non identical and independent samples for multi instance problem.

Most of the work published in recent years have focused on ordered sets. Vinyals et. al. introduced Order Matter:

Sequence to Sequence for Sets in 2016 to learn a sequence to sequence mapping. Many related models and key contributions have been proposed that uses the idea of external memories like RNNSearch [2], Memory Networks [25, 23] and Neural Turing Machines [8]. Recent interest in exchangeable models was developed due to their application in MIL. Deep Symmetry Networks [3] used kernel-based interpolation to tractably tie parameters and pool over symmetry spaces of any dimension. Deep Sets [28] by Zaheer et al. proposed a permutation invariant model. They proved that any pooling operation (mean, sum, max or similar) on individual features is a universal approximator for any set function. They also showed that any permutation invariant model follows de Finetti’s theorem. Work has also been done on learning point cloud classification which is an example of MIL problem. Deep Learning with Sets and Point Cloud [17] used parameter sharing to get a equivariant layer. Another important paper on exchangeable model is Set Transformer. Set Transformer [14] by Lee et al. used results from Zaheer et al. [28] and proposed a Transformer [23] inspired permutation invariant neural network. The Set Transformer uses attention mechanisms to attend to inputs in order to invoke activation. Instead of using averaging over instances like in Deep Sets, the Set Transformer uses a parametric aggregating function pool which can adapt to the problem at hand. Another way to handle exchangeable data is to modify RNNs to operate on exchangeable data. BRUNO [13] is a model for exchangeable data and makes use of deep features learned from observations so as to model complex data types such as images. To achieve this, they constructed a bijective mapping between random variables $x_i \in X$ in the observation space and features $z_i \in Z$, and explicitly define an exchangeable model for the sequences $z_1, z_2, z_3, \ldots, z_n$. Deep Amortized Clustering [15] proposed using Set Transformers to cluster sets of points with only few forward passes. Deep Set Prediction Networks [29] introduced an interesting approach to predict sets from a feature vector which is in contrast to predicting an output using sets.

3. Background

In this section, we explain the general concepts of exchangeability, its relation to de Finetti’s theorem, and briefly discuss Memory Networks.

**Exchangeable Sequence:** A sequence of random variables $x_1, \ldots, x_n$ is exchangeable if the joint probability of the distribution does not change on permutation of indices $1, 2, \ldots, n$. Mathematically, if $P(x_1, \ldots, x_n) = P(x_{\pi(1)}, \ldots, x_{\pi(n)})$ for a permutation function $\pi$, then the sequence $x_1, \ldots, x_n$ is exchangeable.

**Exchangeable Models:** A model is said to be exchangeable
if the output of the model is invariant to the permutation of its inputs. Exchangeability implies that the information provided by each instance \( x_i \) is independent of the order in which they are represented. Exchangeable models can be of two types depending on the application: i) permutation invariant, and ii) permutation equivariant.

A model represented by a function \( f : X \rightarrow Y \) where \( X \) is a set, is said to be permutation equivariant if permutation of input instances permutes the output labels with the same permutation \( \pi \). Mathematically, a permutation-equivariant model is represented as,

\[
f(\{x_{\pi(1)}, x_{\pi(2)}, \ldots, x_{\pi(n)}\}) = [f_{\pi(1)}, f_{\pi(2)}, \ldots, f_{\pi(n)}].
\]

Similarly, a function is permutation invariant if permutation of input instances does not change the output of the model. Mathematically,

\[
f(x_1, x_2, \ldots, x_n) = f(x_{\pi(1)}, x_{\pi(2)}, \ldots, x_{\pi(n)})
\]

Deep Sets [28] incorporate a permutation-invariant model to learn arbitrary set functions by pooling in a latent space. The authors further showed that any pooling operation such as averaging and max on individual instances of a set can be used as a universal approximator for any arbitrary set function. The authors proved that exchangeability implies the following two theorems.

**Theorem 1:** A function \( f(x) \) operating on a set \( X = \{x_1, \ldots, x_n\} \) having elements from a countable universe, is a valid set function, i.e., invariant to the permutation of instances in \( X \), if it can be decomposed to \( \rho(\sum \phi(x)) \), for any suitable transformations \( \phi \) and \( \rho \).

**Theorem 2:** Assume the elements are from a compact set in \( \mathbb{R}^d \), i.e., possibly uncountable, and the set size is fixed to \( M \). Then any continuous function operating on a set \( X \), i.e., \( f : \mathbb{R}^d \times M \rightarrow \mathbb{R} \) which is permutation invariant to the elements in \( X \) can be approximated arbitrarily close in the form of \( \rho(\sum \phi(x)) \).

Theorem 1 is linked to de Finetti’s theorem, which states that a random infinitely exchangeable sequence can be factorised into mixture densities conditioned on some parameter \( \theta \) which captures the underlying generative process i.e.,

\[
P(x_1, \ldots, x_n) = \int p(\theta) \prod_{i=1}^{n} p(x_i | \theta) \, d\theta \quad (1)
\]

**Memory Networks:** The idea of using an external memory for relational learning tasks was introduced by Weston et al. [25]. Later, an end-to-end trainable model was proposed by Sukhbaatar et al. [22]. Memory networks enable learning of dependencies among instances of a set. Memory network embeds the sequential data by providing an explicit memory representation for each instance in the sequence.

Taking an entire sequence and representing it as a single input offers the above-mentioned advantages with respect to memory, but of course, it has challenges. One of the main difficulties is the order in the sequence is lost, as well as the local proximity of sequence elements, which is crucial for most sequential inputs.

### 4. MEM

This section discusses the motivations, components, and offers an analysis of the proposed Memory-based Exchangeable Model (MEM)—a neural network designed to work with infinitely exchangeable sequences.

#### 4.1. Motivation

In order to learn efficient representation for a set of instances, it is important to focus on instances which are highly correlated with the rest of the set, i.e., we need to attend to specific instances more than other instances. We therefore use the memory network to learn attention mapping for each instance. Memory networks are conventionally used for NLP for mapping questions posted in natural language to an answer [25, 22]. We exploit the idea of having memories which can learn key features shared by one or more instances. Through these key features or memories, the model can learn inter-dependencies. As inter-dependencies are learnt, a set can be condensed into a compact vector such that a MLP can be used for a classification or regression learning.

#### 4.2. Components

MEM is composed of three sequentially connected units: i) a feature extraction model, ii) memory blocks, and iii) fully connected layers to predict the output. A memory block is the main component of MEM. It learns a permutation invariant representation of a given input sequence. Multiple memory blocks can be stacked together for modeling complex relationships and dependencies in exchangeable data.

A memory block is a sequence-to-sequence model, i.e., it transforms a given input sequence \( X = x_1, \ldots, x_n \) to another representative sequence \( \hat{X} = \hat{x}_1, \ldots, \hat{x}_m \). The output sequence is invariant to the element-wise permutations in the input sequence. A memory block contains \( m \) number of memory units. Each memory unit takes sequential data and produces a probability distribution over its input (known as attention vectors). The attention vectors from all memory units are transformed into the final output sequence of a given memory block. The schematic diagram of a memory block is shown in Figure 2b.
A memory unit transforms a given input sequence to an attention vector. The higher attention value represents the higher “importance” to the corresponding element of the input sequence. Essentially, it captures the relationships or “characteristics” of instances. The cross correlation or the calculated attention vector represents the instances which are highly suggestive of those “attributes” or “characteristic”.

The final output sequence $\hat{X}$ of a memory block is computed as a weighted sum of $C$ with the probability distributions $p_i$, from all the memory units. The matrix $C$ is a bijective transformation of $X$ learned using an autoencoding neural network. Each memory block has its own autoencoder model to learn this bijective mapping. The $i^{th}$ element $\hat{x}_i$ of the output sequence $\hat{X}$ is given by

$$\hat{x}_i = \sum_{c_j \in C} p_i c_j,$$

where, $C$ is a bijective transformation of $X$ learned with an auto-encoder and $p_i$ is the output of $i^{th}$ memory unit as given by (2).

The bijective transformation from $X \mapsto C$ enables equivariant correspondence between the elements of the two sequences $X$ and $\hat{X}$. It enables maintaining the same level of expressiveness or information in $C$ as that of $X$. We used a deep auto-encoder as a bijective transformation function:

$$x \mapsto [E] \mapsto [D] \mapsto x,$$

where, $E$ and $D$ are encoder and decoder networks, respectively.
The overall architecture of the proposed Memory-based Exchangeable Model (MEM). The input to the model is a sequence. For e.g., a sequence of images or vectors. Each element of the input sequence $X$ is passed through (a) feature extractor (CNN or MLP) to extract a sequence of feature vectors $F$, which is passed to (c) sequentially connected memory blocks. A memory block outputs another sequence which is a permutation-invariant representation of the input sequence. The output from the last memory block is vectorized and given to (c) MLP layers for classification/regression.

4.3. Analysis

This section discusses the mathematical properties of our model. We use theorems from Deep Sets [28] to prove that our model is permutation invariant and universal approximator for arbitrary set functions.

**Property 1:** Memory units are permutation equivariant. Consider an input set $x = x_1 \ldots x_n$ and each memory unit is represented by a transformation $\theta(x)$ where $\theta(x)$ is obtained by averaging over column of cross-correlation matrix. Since cross-correlation is a permutation equivariant operation, $\theta(x)$ is a permutation equivariant transformation.

**Property 2:** Memory Blocks are permutation invariant. Each memory block layers consists of multiple memory units represented by transformation function $\theta(x)$. The output of the kth memory block layer consisting of m block units is a sequence $\hat{x}$ consisting of m instances. Mathematically, it can be written as $\hat{x}_i = \sum_{j=1}^{m} \theta_i(x).C_k(x)$ where, $C_k(.)$ is a bijective transformation. Since both $\theta_i$ and $C_k$ transformations are permutation equivariant, their summation will be permutation invariant.

**Property 3:** MEM is a universal approximator of any arbitrary function. The output of our model can be written as $\rho \sum C(x).\theta(x)$ where $\rho$ represents the transformation of the subsequent memory block layer. Following Theorem 2. in Section 3, MEM can be used as universal approximator for a set function.

4.4. Proposed Model

1. Each element of a given input sequence $X = x_1, \ldots, x_n$ is passed through a feature extraction model to produce a sequence of feature vectors $F = f_1, \ldots, f_n$. The feature extraction model can be a Convolutional Neural Network (CNN), or a Multi-Layer Perceptron (MLP), or any other type of differentiable feature extractor.

2. The feature sequence $F$ is then passed through a memory block to obtain another sequence $F'$ which is a permutation-invariant representation of the input sequence.

3. The number of elements in $F'$, i.e., $|F'|$ and dimensionality of each element of $F'$, i.e., $|f_i'|$ are defined by the hyper-parameters of memory blocks.

4. The multiply memory blocks can be stacked in series. The output from the last memory block is either vectorized or pooled, which is subsequently passed to a MLP layer for classification or regression. There are different configurations that arise due to vectorization and pooling operations at the final memory block. These different configurations are discussed in the next section.

5. Model Evaluation

We performed two series of experiments comparing MEM against the simple pooling operations. In the first series of experiments, we established the learning ability of the proposed model using toy datasets. For the second experiment series, we used our model for classification of subtypes of lung cancer against the largest public dataset of histopathology whole slide images (WSIs) [24].

We experimented with different choices of pooling operations—max, mean, dot product, and sum. Our model also has a special pooling $mb1$, i.e., a memory block with a single memory unit. Therefore, we tested 9 different models for each experiment—five configurations of our model, and four configurations with just pooling operations.

5.1. Experiment Series 1: Toy Datasets

To demonstrate the advantage of MEM over simple pooling operations, we consider four toy problems, involving regression or classification over sets. We assembled these toy problems using simple computer vision datasets.
Accuracy cross entropy loss with Adam optimizer [12] and trained 5,000 sets from the testing data of MNIST. We used binary training data with 20,000 sets randomly sampled from the constructed dataset by randomly sampling five images any two digits such that their sum is a prime number. We is a classification problem over a set of \textit{Sum of Prime} images.

The Figure 4 shows the performance within a set of MNIST images.

\textbf{Sum of Even Digits} is a regression problem over the set of images containing handwritten digits from MNIST. For a given set of images $X = \{x_1, \ldots, x_n\}$, the goal is to find the sum of all even digits. We used the mean absolute error $|p - s|$ as the loss function, where $s$ is the required sum and $p$ is the model’s prediction. We split the MNIST dataset into 70-30\% training, and testing data-sets, respectively. We sampled 100,000 sets of 2 to 10 images from the training data. We trained each model for 100 epochs using the SGD optimizer. For testing, we sampled 10,000 sets of images containing $m$ number of images per set where $m \in [2, 10]$. The Figure 4 shows the performance of MEM against simple pooling operations with respect to the number of images in the set.

\textbf{Sum of Prime} is a classification problem over a set of MNIST images. A set is labeled positive if it contains any two digits such that their sum is a prime number. We constructed the dataset by randomly sampling five images from the MNIST dataset. This example requires model to predict the label in presence of two digits only, therefore attention plays an important role. We constructed the training data with 20,000 sets randomly sampled from the training data of MNIST. For testing, we randomly sampled 5,000 sets from the testing data of MNIST. We used binary cross entropy loss with Adam optimizer [12] and trained the network for 100 epochs. The results are reported in the second column of Table 1 that shows the robustness of memory block.

\textbf{Maxima of a Set} is a regression problem to predict the highest digit present in the set of images from MNIST. We constructed a set of five images by randomly selecting samples from MNIST dataset. The label for each set is the largest number present in the set. For example, images of $\{2, 5, 3, 6\}$ is labeled as 6. Then we constructed 20,000 training sets and for testing we randomly sampled 5,000 sets each time. We used MSE loss with Adam optimizer and trained the model for 200 epochs. We used the linear activation as the last layer of our model. We obtained the predicted maxima by rounding the model’s prediction. The detailed comparison of accuracy and MAE between different models is given in the second last column of Table 1. We found that FF+Max learns the identity mapping and thus results in a very high accuracy. In all the training sessions, we consistently got the training accuracy of 100\% for the FF+Max configuration, whereas MEM has much less discrepancy between train and test accuracy values.

\textbf{Counting of Unique Images} is another regression problem over a set. It involves counting the unique objects in set of images from fashion MNIST dataset [27]. We constructed the training data by selecting a set, as follows:

1. Randomly select an integer $n$ between 2 and 10.
2. Randomly select another integer $u$ between 1 and $n$.
3. Select $u$ number of unique objects from fashion-MNIST training data.
4. Then add $n-u$ number of randomly selected objects selected in the previous step.

The task is to count unique objects $u$ in a given set. We used \textit{softplus} activation for the last layer, defined as $f(x) = \log(1 + e^x)$. We maximized the Poisson likelihood to train the model. The model was run for 200 epochs using SGD optimizer. The results achieved for MEM and feature

| Methods                  | Sum of Even Digits | Sum is Prime Images | Counting Unique Images | Maxima of Set | Gaussian Clustering |
|--------------------------|--------------------|---------------------|------------------------|---------------|---------------------|
|                          | Accuracy           | MAE                 | Accuracy               | MAE           | Accuracy            |
| FF + MEM + MB1 (ours)    | 0.9367 ± 0.0016    | 0.2516 ± 0.0015     | 0.9438 ± 0.0043        | 0.7108 ± 0.0084 | 0.9326 ± 0.0056     | 0.1449 ± 0.0068 | 1.348 |
| FF + MEM + Mean (ours)   | 0.9355 ± 0.0015    | 0.2437 ± 0.0067     | 0.7208 ± 0.0217        | 0.4264 ± 0.0062 | 0.9523 ± 0.0109     | 0.9445 ± 0.0035 | 0.1073 ± 0.0067 | 1.523 |
| FF + MEM + Max (ours)    | 0.9431 ± 0.0020    | 0.2295 ± 0.0098     | 0.961 ± 0.0060         | 0.6888 ± 0.0066 | 0.4140 ± 0.0079     | 0.949 ± 0.0022  | 0.1086 ± 0.0060 | 1.388 |
| FF + MEM + Dotprod (ours) | 0.841 ± 0.0045     | 0.3932 ± 0.0065     | 0.9450 ± 0.0086        | 0.7284 ± 0.0055 | 0.3664 ± 0.0037     | 0.9517 ± 0.0041 | 0.0999 ± 0.0097 | 1.363 |
| FF + MEM + Sum (ours)    | 0.9353 ± 0.0022    | 0.2739 ± 0.0081     | 0.6652 ± 0.0309        | 0.3138 ± 0.0094 | 1.2696 ± 0.0151     | 0.943 ± 0.0031  | 0.1118 ± 0.0058 | 1.611 |
| FF + Mean               | 0.9559 ± 0.0019    | 0.2958 ± 0.0040     | 0.5280 ± 0.0007        | 0.3140 ± 0.0071 | 1.219 ± 0.0136      | 0.9323 ± 0.0075 | 1.0029 ± 0.0155 | 2.182 |
| FF + Max                | 0.6291 ± 0.0047    | 1.3292 ± 0.0211     | 0.9257 ± 0.0033        | 0.7088 ± 0.0060 | 0.3933 ± 0.0059     | 0.958 ± 0.0012  | 0.0742 ± 0.0032 | 1.608 |
| FF + Dotprod            | 0.1503 ± 0.0015    | 1.8015 ± 0.0016     | 0.9224 ± 0.0028        | 0.7254 ± 0.0063 | 0.3726 ± 0.0054     | 0.9548 ± 0.0017 | 0.1355 ± 0.0027 | 8.538 |
| FF + Sum               | 0.6333 ± 0.0043    | 0.5763 ± 0.0069     | 0.5264 ± 0.0050        | 0.2982 ± 0.0042 | 1.3415 ± 0.0169     | 0.3344 ± 0.0038 | 0.9645 ± 0.0111 | 12.05 |

Table 1: Results on the toy datasets for different configurations of MEM and feature pooling.
pooling is similar to feature pooling, see the third column of Table 1.

Amortized Gaussian Clustering is a regression problem that involves estimating the parameters of a population of Mixture of Gaussian (MoG). Similar to Set Transformer [14], we test our model for learning parameters of Gaussian Mixture with \( k \) components such that the likelihood of the observed samples is maximum. This is in contrast to EM algorithm which updates parameters of the mixture recursively until the stopping criterion is satisfied. Instead, we use MEM to directly predict parameters of MoG i.e. \( f(x; \theta) = \{ \pi(x), (\mu(x), \sigma(x))_{j=1}^{k} \} \).

For simplicity we sample from MoG with only four components. The Generative process for each training dataset is as follows

1. Mean of each gaussian is selected from a uniform distribution i.e. \( \mu_j \sim \text{Unif}(0, 8) \).
2. Select a cluster for each instance in the set, i.e., \( \pi \sim \text{Dir}([1, 1]^T); z_i \sim \text{Categorical}(\pi) \).
3. Generate data from an univariate Gaussian \( \mathcal{N}(\mu_{z_i}, 0.3) \).

We created a dataset of 20,000 sets each consisting of 500 points sampled from different MoGs. We use Negative Log Likelihood (NLL) as the loss function and use Adam optimizer to minimize the NLL loss. Results in Table 1 shows that MEM is significantly better than feature pooling.

### 5.2. Experiment Series 2: Real-world Datasets

To show the robustness and scalability of the model for the real-world problems, we have validated MEM on two larger datasets. Firstly, we tested our model on a point cloud dataset for predicting the object type from the set of 3D coordinates. Secondly, we used the largest public repository of histopathology images (TCGA) [24] to differentiate between two main sub-types of lung cancer. Without any significant effort in extracting histologically relevant features and fine-tuning, we achieved remarkable accuracy value 84.84% on the 5-fold validation.

### 5.3. Point Cloud Classification

We evaluated MEM on a more complex classification task using ModelNet40 [26] point cloud dataset. The dataset consists of 40 different objects or classes embedded in a three dimensional space as points. We produce point-clouds with 100 and 1000 points each (x, y, z-coordinates) from the mesh representation of objects using the point-cloud library's sampling routine [19]. We trained our model with categorical cross-entropy loss with Adam optimizer along with batch normalization [10] and dropout [21]. We compare the performance against Deep Sets [28] and Set Transformer [14]. We experimented with different configurations of our model and found that FF+MB1 works best for 100 points cloud classification.

We achieve classification accuracy of 85.21% using 100 points. Our model performs better than Deep Sets and Set Transformer for 100 points which shows the effectiveness of having attention from memories. For 1000 points we achieved the accuracy value of 87.3% which is comparable to Deep Sets. The major focus of our approach is to rely on inter-dependencies and “attention” among instances to form a representation of a set. For 100 points, our model performs better as inter-dependencies play a major role than for 1000 points. When there are lot of points, the information might be contained already as whole and relational representations do not contribute much. The comparison of our model with Deep Sets and Set Transformer is shown in Table 2.

### 5.4. Lung Cancer Subtype Classification

Lung Adenocarcinoma (LUAD) and Lung Squamous Cell Carcinoma (LUSC) are two main types of non-small cell lung cancer (NSCLC) that account for 65-70% of all lung cancers [7]. Classifying patients accurately is important for prognosis and therapy decisions. Automated classification of these two main subtypes of NSCLC is a crucial step to build computerized decision support and triaging systems. We present a two-staged method to differentiate LUAD and LUSC for whole slide images, short WSIs, that are very large images. Firstly, we implement a method to systematically sample patches/tiles from WSIs. Next, we extract image features from patches using Densenet [9]. We arrange image features in sets (per WSI basis) and train MEM to classify the two subtypes. The highest 5-fold classification accuracy score achieved is 84.84%.

To the best of our knowledge, this is the first ever study conducted on all the lung cancer slides in TCGA dataset (comprising of 2 TB of data consisting of 2.5 million patches of size 1000×1000 pixels). All research works in literature use a subset of the slides with their own test train split instead of cross validation, making it difficult to compare against them. However, we have achieved greater than or similar to all existing research works without utilizing any expert’s opinions (pathologists) or domain-specific

| Configuration | 100 pts | 1000 pts |
|---------------|---------|----------|
| Deep set      | 0.8200  | 0.8700   |
| Set Transformer| 0.8454  | 0.8915   |
| Ours (FF + MEM + MB1) | **0.8521** | 0.8730   |

Table 2: Test accuracy for the point cloud classification task using 100,1000 points.
techniques.

We downloaded 2,580 WSIs from TCGA public repository \[24\] with 1,249, and 1,331 slides for LUAD and LUSC, respectively. To train our model, each WSI is converted to a set of features. These features correspond to deep features extracted from a set of representative patches from a given WSI. We process each WSI as follows:

- **Tissue Extraction** – Every WSI contains a bright background that generally contains irrelevant (non-tissue) pixel information. We removed non-tissue regions using color thresholds.

- **Selecting Representative Patches** – Segmented tissue is now divided into patches. All the patches are then grouped into a pre-set number of categories (classes) via a clustering method. A 10% of all clustered patches are selected uniformly distributed within each class to assemble representative patches. Six of these representative patches for each class (LUAD and LUSC) is shown in Figure 5.

- **Feature Set** – A set of features for each WSI is created by converting its representative patches into image features. We use DenseNet \[9\] as the feature extraction model. There are different number of features for each WSI.

The results are shown in Table 3. We achieved the maximum accuracy of 84.84% with FF + MEM + Sum configuration. It is difficult to compare our approach against other approaches in literature due to non-standardization of the dataset. Coudray et al. \[4\] used cell density maps, achieving an accuracy value of 83.33% and AUC of 0.9068. However, they used much smaller portion of TCGA, i.e., 338 TCGA diagnostic WSIs (164 LUAD and 174 LUSC) were used to train, and 150 (71 LUAD and 79 LUSC).

### Table 3: 5-fold cross validation accuracy for LUAD vs LUSC classification.

| Configuration                     | Accuracy       |
|-----------------------------------|----------------|
| FF + MEM + Sum (ours)             | 0.8484 ± 0.0210|
| FF + MEM + Mean (ours)            | 0.8465 ± 0.0225|
| FF + MEM + MB1 (ours)             | 0.8457 ± 0.0219|
| FF + MEM + Dotprod (ours)         | 0.6345 ± 0.0739|
| FF + sum                          | 0.5159 ± 0.0120|
| FF + mean                         | 0.7777 ± 0.0273|
| FF + dotprod                      | 0.4112 ± 0.0121|

6. **Conclusion**

In this paper, we introduced Memory-based Exchangeable Model (MEM) for learning permutation invariant representations. The proposed method uses attention mechanisms over “memories” (higher order features) for modelling complicated interactions among elements of a set. Typically for MIL, instances are treated as independently and identically distributed. However, instances are rarely independent in real tasks, and we overcome this limitation using “attention” mechanism in memory units, that exploits relations among instances. We also provided some theoretical properties of our model, including the fact that it
is a universal approximator for permutation invariant functions. We achieved good performance on all problems that requires exploiting instance relationships. Our model scales well on real world problems as well, achieving accuracy score of 84.84% on classifying lung cancer subtypes on the largest public repository of histopathology images.

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