ESCAPED: Efficient Secure and Private Dot Product Framework for Kernel-based Machine Learning Algorithms with Applications in Healthcare

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Abstract
To train sophisticated machine learning models one usually needs many training samples. Especially in healthcare settings these samples can be very expensive, meaning that one institution alone usually does not have enough on its own. Merging privacy-sensitive data from different sources is usually restricted by data security and data protection measures. This can lead to approaches that reduce data quality by putting noise onto the variables (e.g., in k differential privacy) or omitting certain values (e.g., for l-anonymity). Other measures based on cryptographic methods can lead to very time-consuming computations, which is especially problematic for larger multi-omics data. We address this problem by introducing ESCAPED, which stands for Efficient Secure And PrivateE Dot product framework, enabling the computation of the dot product of vectors from multiple sources on a third-party, which later trains kernel-based machine learning algorithms, while neither sacrificing privacy nor adding noise. We evaluated our framework on drug resistance prediction for HIV-infected people and multi-omics dimensionality reduction and clustering problems in precision medicine. In terms of execution time, our framework significantly outperforms their approach has a potential privacy leakage for binary encoded vectors since it utilizes private set intersection to compute the dot product of the vectors of two parties in a third-party to train an SVM model. However, the framework is not extendable to more than two data sources since this would compromise the data due to the nature of elementwise multiplication of the vectors, which they use to compute the dot product. Furthermore, due to the same reason, their approach has a potential privacy leakage for binary encoded data even for the case with two data sources. We will show that our approach outperforms their framework in such a scenario. Moreover, the randomized encoding itself (Applebaum, Ishai, and Kushilevitz 2006a) is independently applicable to our scenario. The authors claimed that any function expressed such information could otherwise be inferred. Several studies (Lunshof et al. 2008; Azencott 2018; Bonomi, Huang, and Ohno-Machado 2020) discussed various privacy issues from different aspects occurring in studies using medical data.

Throughout this paper, we refer to a source having data or an entity performing computation as “party”. One class of machine learning methods that usually require gathering the whole data, is kernel-based learning methods. To train such a model privately, one of the architectural models in the literature is the distributed model where each party in the computation has its own data and the desired kernel matrix contains the whole data that all parties have. Vaidya, Yu, and Jiang (2008) proposed an algorithm utilizing such a model to compute the gram matrix of the whole data belonging to the parties in the computation and train a support vector machine (SVM) privately afterwards. The disadvantage of the proposed algorithm is that it focuses only on binary vectors since it utilizes private set intersection to compute the dot product. In addition to the distributed model, there is also the outsourced model where the data is outsourced after encryption and then these encrypted data are used to train a kernel-based machine learning method. Liu, Ng, and Zhang (2015) proposed an approach to use an SVM on the encrypted outsourced data. Due to the nature of encryption, the proposed approach is very time consuming. Zhang et al. (2017) introduced a key-switching (Zhou and Wornell 2014) based secure dot product calculation method. The basic idea is to change the key of the dot product of the vectors, which is originally the combination of the keys utilized to encrypt these vectors, to the key of the server. Ünal, Akgün, and Pfeifer (2019) demonstrated the inefficiency of this method and proposed a randomized encoding based framework to compute the dot product of the vectors of two parties in a third-party to train an SVM model. However, the framework is not extendable to more than two data sources since this would compromise the data due to the nature of elementwise multiplication of the vectors, which they use to compute the dot product. Furthermore, due to the same reason, their approach has a potential privacy leakage for binary encoded data even for the case with two data sources. We will show that our approach outperforms their framework in such a scenario. Moreover, the randomized encoding itself (Applebaum, Ishai, and Kushilevitz 2006a) is independently applicable to our scenario. The authors claimed that any function expressed...
by a logarithmic depth arithmetic circuit can be encoded by randomized encoding. In this work, we implemented and applied the randomized encoding based approach and show that it is not as efficient as our framework in terms of the communication cost.

In this paper, we address the privacy problem of data gathering for dot product based algorithms such as kernel-based learning methods. We first implement and apply one of the fastest encoding in the literature, namely the randomized encoding, to our scenario. Due to the inefficiency of the randomized encoding based approach, we come up with a new encoding scheme enabling the secure and private computation of the dot product of vectors. On top of it, we build a new framework, called efficient secure and private dot product (ESCAped), which allows multiple data sources, which we call input-parties, to involve in the computation of the dot product. ESCAPED allows a third-party, which we call function-party, to privately obtain the dot product of input-parties’ vectors of size larger than 1 while neither gathering the data in plaintext domain nor compromising the privacy of the data. Then, the function-party trains a kernel-based machine learning method. We utilized ESCAPED to predict personalized treatment recommendation for HIV-infected patients in the supervised learning experiment and to perform privacy preserving multi-omics dimensionality reduction and clustering in the unsupervised learning experiments. To the best of our knowledge, this is the first study enabling the privacy preserving multi-omics dimensionality reduction and clustering.

Background

Radial Basis Function Kernel

Among the kernel functions, the radial basis function (RBF) kernel is one of the most effective and widely used kernels (Schölkopf, Smola et al. 2002; Kauppi et al. 2015; Pfeifer and Kohlbacher 2008; Zhang et al. 2004). The computation of the RBF kernel for samples \( x, y \in \mathbb{R}^n \) can be expressed based on only the dot product of these samples. The formula is as follows:

\[
K(x, y) = \exp \left( -\frac{\|x - y\|^2}{2\sigma^2} \right)
\]

where “\( \langle \cdot, \cdot \rangle \)” represents the dot product of vectors and \( \sigma \) is the parameter that adjusts the similarity level between the samples. Equation 1 indicates that the gram matrix is enough to compute the RBF kernel. We benefit from such computation to obtain the RBF kernel matrix in ESCAPED.

Randomized Encoding

Randomized encoding (RE) is designed to hide the input value \( s \) in the computation of a function \( f(s) \) by encoding the function with a randomized function \( \hat{f}(s; r) \), where \( r \) is a uniformly chosen random value (Applebaum, Ishai, and Kushilevitz 2006a,b). Decoding of the encoding reveals only the output of the function \( f \) but nothing else.

Applebaum (2017) introduced the perfect decomposable and affine randomized encoding (DARE) of some operations in their study. For a randomized encoding to be affine and decomposable, all components of the encoding should be affine functions over the set on which the function is defined and each of these components should depend on only a single input value and a varying number of random values. Here, we give only the encodings that we used, which are addition and multiplication-addition operations.

Definition 1 (Perfect RE for Addition (Applebaum 2017)). Let there be an addition function \( t = f(s_1, s_2) = s_1 + s_2 \) defined over some finite ring \( R \). The following DARE can perfectly encode such a function:

\[
\hat{f}(s_1, s_2; r) = (s_1 + r, s_2 - r)
\]

where \( r \) is a uniformly chosen random value. The decoding can be done by summing up the components of the encoding, and the simulation of the function can be performed by sampling two random values whose sum is \( t \).

Definition 2 (Perfect RE for Multiplication-Addition (Applebaum 2017)). Let there be a function \( t = f(s_1, s_2, s_3) = s_1 \cdot s_2 + s_3 \) defined over a ring \( R \). The following DARE function \( \hat{f}(s_1, s_2, s_3; r_1, r_2, r_3, r_4) \) can perfectly encode the function \( f \):

\[
\hat{f}(s_1, s_2, s_3) = (s_1 - r_1, r_2 s_1 - r_1 r_2 + r_3, s_2 - r_2, r_1 s_2 + r_4, s_3 - r_3 - r_4)
\]

where \( r_1, r_2, r_3 \) and \( r_4 \) are uniformly chosen random values.

In order to simulate \( \hat{f} \), one can employ the simulator \( \hat{\text{Sim}}(t; c_1, c_2, c_3, c_4) := (c_1 - c_3 + c_2 + c_4 + c_5) \).

In addition to the given DAREs, the authors claim that any arithmetic circuit with logarithmic depth can be encoded by a perfect DARE (Applebaum 2017). An example of such an arithmetic circuit computing the dot product of two vectors is given in the Supplement. Taking this into account, we encode the dot product of the vectors by utilizing the aforementioned encodings. Since we only deal with the private computation of the dot product of the vectors, we optimize the generation of the encoding. Let us assume that we have vectors \( x, y \in R^D \) where \( R \) is a finite ring and \( D \in \mathbb{Z}^+ \). In the dot product computation, we have \( D \) multiplication nodes in the circuit and the results of these multiplication nodes are summed up by using the addition nodes. To generate the encoding of the dot product of vectors \( x \) and \( y \), we first find the largest 2’s power which is smaller than \( D \), which we represent here as \( P \) where \( 2^q = P \) for \( q \in \{ \mathbb{Z}^+ \cup \{0\} \} \) and \( P < D \leq 2 \cdot P \). We separate the summation of the first \( P \) of those multiplication nodes from the summation of the remaining \( D - P \) multiplication nodes by using Definition 1. We repeat the same procedure for these two parts recursively until we end up with a multiplication node. Once we reach the multiplication node \( i \) from an addition node, we utilize the DARE for multiplication-addition given in Definition 2 where \( s_1 = x_i, s_2 = y_i \) and \( s_3 \) represents the resulting value of addition/subtraction of the random values separating summations up to that node. The pseudo code of the randomized encoding generation of the dot product of two vectors of size \( D \) and the encoding of the sample arithmetic circuit are given in the Supplement.
Randomized encoding has two main applications, which are secure computing and parallel cryptography. It is commonly used in multi-party computation (MPC) to minimize the round complexity of MPC protocols (Prabhakaran and Sahai 2013). Thus, more efficient MPC protocols can be designed using randomized encoding.

Methods
In this section, we will first explain the scenario employed in the paper. Then, we introduce the randomized encoding based approach and our proposed framework ESCAPED. Later, we will give the security definition as well as the security analysis of it based on the given definition. Finally, we will explain the data that we used.

Scenario
We consider a scenario where we have multiple input-parties and a function-party, which computes the dot product of vectors of these input-parties and then trains a kernel-based machine learning algorithm. The real life correspondence of such a scenario would be a study in which a researcher wants to employ the same type of data of different patients collected by multiple hospitals, like cancer subtype discovery. In this scenario, one would like to group cancer patients according to similarities with respect to their omics data. For a new patient the subtype could give first hints about how severe the cancer is and how well the prognosis is regarding potential treatments and life expectancy. Due to patient privacy, such data cannot be shared without any permission process, which can significantly slow down the study. However, a framework, like ESCAPED, ensuring the protection of the privacy of patients’ data enables the researcher to speed up permission processes and enables studies that would otherwise not be approved due to privacy concerns. While describing the approaches, even though both randomized encoding based approach and ESCAPED can have multiple input-parties, for simplicity, we use a scenario with three input-parties, namely Alice, Bob and Charlie with ids 1, 2 and 3, respectively, and a function-party.

Randomized Encoding Based Approach
To address the aforementioned problem, we first implemented a randomized encoding based approach and applied it to our scenario. In this scenario, each of the input-parties has their own data $X \in R^{f \times n_x}$, $Y \in R^{f \times n_y}$ and $Z \in R^{f \times n_z}$, respectively, where $f$ represents the number of features, $n_x$ represents the number of samples in the corresponding input-party and $R$ is a finite ring. Each pair of input-parties needs to communicate separately, i.e., there will be communication between Alice and Bob, Alice and Charlie, and Bob and Charlie. For simplicity, we will explain only the communication between Alice and Bob. To compute $X^TY$, they first exchange the size of their own data. Afterwards, Alice generates the scheme of the encoding of the dot product by utilizing the randomized encoding generation algorithm given in the Supplement. By using the resulting encoding scheme, she creates a new set of random values for each possible pair of samples consisting of one sample from Alice and one sample from Bob. This is quite important to protect the relative difference of the features of the input-parties’ samples from the function-party. For instance, using the component $s_1 - r_1$ in the encoding, the function-party could learn the relative differences of the input values in the case that the same random value $r_1$ is utilized for more than one pair of samples. Once Alice created all random values, she sends Bob the part of these random values that he will use to encode his own data. Afterwards, both Alice and Bob encode their data by employing the corresponding random values and send the resulting components to the function-party along with the gram matrix of their own samples. To compute the dot product of samples of Alice and Bob, the function-party combines these components according to the decoding described in Definition 1 and 2. Such communication is done between all possible pairs of the input-parties, which means if we have $M$ input-parties, there will be $\binom{M}{2}$ communication in total (more detailed communication cost analysis is given in Table 1). Once the function-party has all partial gram matrices, it constructs the gram matrix by vertically concatenating the horizontally concatenated partial gram matrices $[X^TX, X^TY, X^TZ], [Y^TX, Y^TY, Y^TZ]$ and $[Z^TX, Z^TY, Z^TZ]$. Then, it can compute the desired kernel matrix, which can be computed via the gram matrix, and train a kernel-based machine learning method. The overview of the dot product computation procedure via the randomized encoding based approach is given in the Supplement. Note that in the supervised scenario the input-parties share the labels of the samples with the function-party in plaintext domain since they do not reveal any extra and sensitive information. However, this could easily be extended if more sensitive labels are supposed to be used in the learning process.

ESCAPED
Due to the high communication cost of the randomized encoding based approach to securely compute the dot product of vectors from multiple input-parties in the function-party, we propose a new efficient and secure framework, which we call ESCAPED, based on a new encoding scheme for the dot product computation. In the computation, the input-parties do not learn anything about the data of the other input-parties or the result of any dot product computed by the function-party. Similarly, the function-party learns only the dot product of the data from the input-parties, but nothing else.

For simplicity, we will explain only the computation of the dot product of the data of Alice and Bob in ESCAPED. Figure 1 depicts the overview of ESCAPED. At first, Alice and Bob create matrices of random values $a \in R^{f \times n_x}$ and $b \in R^{f \times n_y}$, respectively, where $R$ is a finite ring. Along with these random valued matrices, Alice also creates a random value $\alpha \in R \setminus \{0\}$. Afterwards, Alice computes $X - a$ and $aa^T$, and shares them with Bob. In the meantime, Bob computes $Y - b$ and sends it to Alice. Once Alice receives the masked data of Bob, she computes $A_1 = a^T(Y - b)$. Meanwhile, Bob computes $B_1 = (X - a)^TY$ and $B_2 = \alpha a^Tb$. Then, Alice sends $A_1$ and $\alpha$, and Bob sends $B_1$ and $B_2$ to the function-party along with the gram matrix of their
Table 1 summarizes the features and the communication cost analysis of ESCAPED, the randomized encoding based approach and the approach proposed by (Ünal, Akgün, and Pfeifer 2019).

Security Definition

In our proof, we utilize two different adversarial models, which are the semi-honest adversary model, in other words honest-but-curious, and the malicious adversary model. A semi-honest adversary is a computationally bounded adversary which follows the protocol strictly but also tries to infer any valuable information from the messages seen during the protocol execution. On the other hand, in the malicious adversary model, a malicious adversary can arbitrarily deviate...
from the protocol specification. Although the semi-honest model has more restrictive assumptions than the malicious model, the development of highly efficient privacy preserving protocols is relatively easy under it.

Let there be \(M\) input-parties (\(I_1, \ldots, I_M\)) and a function-party \(F\) in the proposed system. We assume that an adversary \(A\) is either a semi-honest adversary corrupting a subset of input-parties or a malicious adversary corrupting the function-party. We restrict the collusion between the function-party and the input-parties not to allow the corruption of the function-party and at least one input-party at the same time. Otherwise, an adversary \(A\) who corrupts the function-party and at least one input-party obtains the inputs of all other input-parties. Even though we allow the collusion among input-parties, one might think that it is not so realistic since entities involved, such as medical institutions, lose their reputations if they misbehave in this setting.

We use the simulation paradigm (Lindell 2017) in our security proofs. In the simulation paradigm, the security is proven by showing that the simulator can simulate the input and the output of a party given the actual input and output such that the simulated input and output cannot be distinguished from the actual ones by an observer. Such an indistinguishability indicates that the parties cannot learn more than what can be learned from their inputs and outputs.

Since the function-party constructs the final output, which is the gram matrix, by using the partial outputs each of which is computed by a pair of input-parties, we can consider these computations as a separate two-party computation. The following notations are used in the security definition:

- Let \(f = (f_1, f_2)\) be a probabilistic polynomial-time functionality where \(f_p\) is the input provided by the \(p\)-th party to \(f\) and let \(\pi\) be a two-party protocol for computing \(f\).
- The view of the \(i\)-th party (\(i \in \{1,2\}\)) during an execution of \(\pi\) over \((x,y)\) is denoted by \(v_i^n(x,y)\) and equals \((w,r^i,m^i_1,\ldots,m^i_t)\) where \(w \in \{x,y\}\), \(r^i\) equals the contents of the \(i\)-th party’s internal random tape and \(m^i_j\) represents the \(j\)-th message that it received.
- The output of the \(i\)-th party during an execution of \(\pi\) over \((x,y)\) is denoted by \(o_i^n(x,y)\) and can be computed from its own view of the execution. We denote the joint output of both parties by \(o^n(x,y) = (o^n_1(x,y), o^n_2(x,y))\).

**Definition 3.** Let \(f = (f_1, f_2)\) be a functionality. We say that a protocol \(\pi\) is secure against semi-honest adversaries if there exist probabilistic polynomial time (PPT) simulators \(S_1\) and \(S_2\) such that:

\[
(S_1(x, f_1(x,y)), f(x,y)) \equiv (v_1^n(x,y), o^n_1(x,y))
\]

\[
(S_2(y, f_2(x,y)), f(x,y)) \equiv (o^n_2(x,y), o^n_2(x,y))
\]

where \(\equiv\) denotes the computational indistinguishability. More details can be found in (Goldreich 2009).

**Security Analysis**

**Theorem 1.** ESCAPED is secure against a semi-honest adversary \(A\) who corrupts any subset of input-parties.

**Proof.** The proof is provided in the Supplement. \(\square\)

**Theorem 2.** Assume that the function-party is malicious and does not collude with any input-parties. Then, ESCAPED is secure against the malicious function-party \(A\).

**Proof.** The proof is provided in the Supplement. \(\square\)

**Data**

In this section, we briefly explain the datasets that we employed in our supervised and unsupervised learning experiments, respectively.

**HIV V3 Loop Sequence Dataset:** To predict the personalized treatment of HIV-infected patients in the supervised learning experiments, we retrieved the HIV V3 loop dataset from Ünal, Akgün, and Pfeifer (2019). It consists of the protein sequence of the viruses as well as their coreceptor usage information. Due to the availability of drugs blocking the human CCR5 coreceptor, which is exclusively used by the most common variant of HIV to enter the cell, identifying the coreceptor usage is very crucial to determine whether or not to use these drugs (Lengauer et al. 2007). The dataset consists of 642 samples for the class “CCR5 only” and 124 samples for the class “OTHER”. The sequence data exists as a one-hot encoded data matrix with 766 rows and 924 columns.

**Head and Neck Squamous Cell Carcinoma Dataset:** We aim to perform the privacy preserving multi-omics dimensionality reduction and clustering on the TCGA data for head and neck squamous cell carcinoma (HNSC) (Network et al. 2015) to stratify patients into clinically meaningful subgroups. Therefore, we replicate a recent state-of-the-art study (Röder et al. 2019) in a privacy-preserving setting, obtaining the data from the authors. The data consists of 465 patients with their gene expression (IlluminaHiSeq), DNA methylation (Methylation450k), copy number variation (gistic2), and miRNA expression (IlluminaHiSeq) data. They have 19433, 57159, 23817 and 581 features, respectively. We also obtained the survival times of the patients.

**Results**

In order to simulate multiple input-parties, we created a process for each input-party and shared the data among them equally. We also created an additional process to simulate the function-party. All processes communicate with each other over TCP sockets and we assume that the communication is secure. We conducted the experiments on a server which has 512 GB memory, an Intel Xeon E5-2650 processor and a 64-bit operating system. We utilized Python to implement ESCAPED and the randomized encoding based approach.

**Classification of HIV coreceptor usage**

In these supervised learning experiments, we utilized an SVM with an RBF kernel matrix. We optimized the parameters of the SVM, which are the misclassification penalty \(C \in \{2^{-5}, 2^{-4}, \ldots, 2^{10}\}\) and the weight \(w_1 \in \{2^0, 2^1, \ldots, 2^5\}\) of the minority class, and the similarity adjustment parameter \(\sigma \in \{2^{-5}, 2^{-4}, \ldots, 2^{10}\}\) of the RBF kernel via 5-fold cross-validation and F1-score. Note that we tuned the parameters outside of the approaches and utilized them in the experiments directly. However, one can employ both ESCAPED and the randomized encoding based approach for tuning. To
We utilized our proposed framework, ESCAPED, to compute the dot product of samples of three different input-parties on a function-party. Once the function-party has the gram matrix, it computes the RBF kernel matrix based on the optimal \( \sigma \) using Equation 1. We separated 20% of the data of each input-party for testing. The function-party trains an SVM model on the rest of the data by employing the optimal parameters \( w_f \) and \( C \). Then, we tested the model on the test data. At the end, we evaluated the prediction of our model via \( F1 \)-score and area under receiver operating characteristic curve (AUROC).

We repeated the whole experiment for each optimal parameter set and we obtained 0.843 (±0.013) AUROC and 0.615 (±0.016) \( F1 \)-score on the average. To demonstrate the scalability of ESCAPED in terms of the total dataset size, we conducted experiments in which we used a quarter, a half and the full dataset. The execution time of ESCAPED increases almost quadratically with respect to the size of the dataset. Figure 2a shows the trend of the increase in the execution time in parallel to the increment in the dataset size. Furthermore, we analyzed the performance of the framework for varying number of input-parties each of which has the same number of samples. Figure 2b displays the effect of the number of input-parties involved in the computation on the execution time of various parts. The total execution time and the total communication time between input-parties and the function-party (black and red, respectively) are almost linear. The total communication among input-parties (orange), however, displays a slightly different pattern. Since there is an idle party in each turn of the communication among input-parties when there is an odd number of input-parties, the execution time for the cases having even number of input-parties is almost the same with the case where we have one less input-party.

We repeated the optimization step 10 times with different random folds and conducted separate experiments by utilizing each optimal parameter set. We evaluated the experiments via \( F1 \)-score and area under receiver operating characteristic curve (AUROC). To demonstrate the applicability of ESCAPED on un-supervised learning problems on multi-view data, we employed it to determine biologically meaningful patient subgroups of

Table 1: The summary of the comparison of the methods utilized in this study from different aspects is given. The ability of handling varying number of input-parties (IP) in the framework proposed by Ünal, Akgün, and Pfeifer (2019) (UAP), the randomized encoding based approach (RE) and ESCAPED are given in the first part of the table. Moreover, \( n \) being the number of samples in each IPs, \( M \) being the number of IPs and \( f \) being the number of features of samples, where \( n, M, f \in \mathbb{Z}^+ \) and \( M \geq 2 \), the communication cost analysis of RE and ESCAPED in terms of the communication cost among IPs, between IP and the function-party (FP) and the total communication cost are given in the second part of the table.

| Approach   | Number of IPs | Communication cost |
|------------|---------------|--------------------|
|            | Two IPs       | Among IPS          |
|            | Three or more IPs | Between IPs and FP |
|            | Total         |                    |
| UAP        | Yes           | 3Rf \times n^2 *   |
| RE         | Yes           | 4Rf \times n^2 *   |
| ESCAPED    | Yes           | 3(M/2)Rf \times n   |
|            | Yes           | 3(M/2)Rf \times n^2 |
|            | 3(M/2)(Rf \times n + Rn^2) |

The communication cost analysis is given after an update on UAP to protect the privacy of relative differences between features of samples. Without any update, the communication costs would become \( 3Rf \times n \), \( 4Rf \times n^2 \) and \( 3Rf \times n + 4Rf \times n^2 \), respectively.

Clustering of HNSC cancer patients

To demonstrate the applicability of ESCAPED on un-supervised learning problems on multi-view data, we employed it to determine biologically meaningful patient subgroups of HNSC cancer patients...
We employed ESCAPED to compute the kernel matrix for whose survival is longer than 5 years. Then, they evaluated (IP) and the function-party (FP), and the communication time among IPs is shown. The execution time increases quadratically in parallel to the increment in the dataset size. The execution time comparison of ESCAPED and the UAP (Ünal, Akgün, and Pfeifer 2019) for two input-parties case is given.

Figure 2: (a) The execution time of ESCAPED is shown for varying sizes of the dataset. (b) The analysis of ESCAPED for varying number of input-parties in terms of the total execution time, the communication time between the input-parties (IP) and the function-party (FP), and the communication time among IPs is shown. (c) The execution time of the randomized encoding based approach is depicted for different sizes of the dataset. The execution time increases quadratically in parallel to the increment in the dataset size. (d) The execution time comparison of ESCAPED and the UAP (Ünal, Akgün, and Pfeifer 2019) for two input-parties case is given.

cancers patients. Speicher and Pfeifer (2015) studied such a problem and suggested a regularized multiple kernel learning algorithm with dimensionality reduction (rMKL-DR). The method was recently evaluated as the best method on a large benchmark study comparing many different methods (Rapponport and Shamir 2018). Later, Röder et al. (2019) published the online version of the method called web-rMKL. In that study, one of their use cases is the identification of subgroups of HNSC. To stratify patients into biologically meaningful subgroups, they employed four different data types, which are gene expression, DNA methylation, miRNA expression and copy number variation. They computed one RBF kernel matrix, whose $\gamma$ is chosen based on the rule of thumbs, for each data type and input these kernel matrices to the web-rMKL to obtain the subgroups of patients. They pruned patients whose survival is longer than 5 years. Then, they evaluated the results by survival analysis and obtained a $p = 0.0006$ in log-rank test. To show the applicability of ESCAPED, we replicated their study in a privacy preserving way. We utilized the same dataset and split it into three input-parties equally. We employed ESCAPED to compute the kernel matrix for each data type based on the data belonging to different input-parties. It took 129.17 ($\pm 3.81$) sec to compute the required kernel matrices. We, then, input the resulting kernel matrices to web-rMKL with the same parameter choices to cluster patients. We applied the same filters and evaluated the results by survival analysis as they did. At the end, we obtained the same $p$-value indicating that ESCAPED is capable of performing privacy preserving multi-omics dimensionality reduction and clustering. We were unable to conduct these experiments via the randomized encoding based approach due to the excessive memory usage stemming from the inefficiency of the randomized encoding on high dimensional data.

Conclusion

The tension between the unavoidable demand of machine learning algorithms for data and the importance of the privacy of the sensitive information in data urges the researchers to come up with efficient and privacy preserving machine learning algorithms. To address this necessity, we introduced ESCAPED to enable the secure and private computation of the dot product of the vectors from multiple sources on a third-party, showing the promise to efficiently make also other learning algorithms privacy preserving. As a future work, other commonly used operations in machine learning algorithms could be included in the framework to extend the scope of it. Furthermore, the interpretability of the resulting model could be improved to allow more sophisticated analyses to be done via the model.

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**Ethics Statement**

Thanks to the promising results of ESCAPED, our study could open up new collaboration opportunities among hospitals, universities, institutes, data centers and many other entities with faster permission processes by providing secure and private computation of dot product enabling not only the kernel-based learning algorithms but also other methods requiring the dot product. This would help to speed up healthcare research helping humanity and the world in general. We could not think of a negative ethical impact of our work.

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1 Randomized Encoding Generation Algorithm

The pseudo code of the randomized encoding generation of the dot product of two vectors of size $D$ is given in Algorithm 1.

Algorithm 1 Randomized Encoding Generation for Dot Product

**Input**
- $eX$: the list of the indices of the random values for $X$
- $eY$: the list of the indices of the random values for $Y$
- $eO$: the list of the indices of the random values for the offline part
- $eOS$: the list of the sign of the random values of the offline part
- $R$: the starting value of the random values that will be generated

**Output**
- $R$: the latest value of the generated random values

1: **procedure** REGen($eX$, $eY$, $eO$, $eOS$, $R$)
2: \[ D \leftarrow \text{length of } eX \]
3: \[ \text{if } D = 1 \text{ then} \]
4:  \[ eX[0] \leftarrow [0, R+1, R, R+1, R+2] \quad \triangleright \text{In the generated random values afterwards, the first one, indicated by 0 here, is always 1} \]
5:  \[ eY[0] \leftarrow [0, R, R+1, R+3] \]
6:  \[ eO[0] \leftarrow [eO[0], R+2, R+3] \]
7:  \[ eOS[0] \leftarrow [eOS[0], -1, -1] \]
8: \[ R \leftarrow R + 4 \]
9: \[ \text{return } R \]
10: **end if**
11: \[ q \leftarrow \text{argmax}_q (2^q < D) \quad \triangleright q \in \{\mathbb{Z}^+ \cup \{0\}\} \]
12: \[ P \leftarrow 2^q \]
13: \[ eO[0] \leftarrow [eO[0], R] \]
14: \[ eOS[0] \leftarrow [eOS[0], +1] \quad \triangleright +1 \text{ represents positive sign} \]
15: \[ eO[P] \leftarrow [eO[P], R] \]
16: \[ eOS[P] \leftarrow [eOS[P], -1] \quad \triangleright -1 \text{ represents negative sign} \]
17: \[ R \leftarrow R + 1 \]
18: \[ R \leftarrow \text{REGen}(eX[0 : P], eY[0 : P], eO[0 : P], eOS[0 : P], R) \]
19: \[ R \leftarrow \text{REGen}(eX[P : D], eY[P : D], eO[P : D], eOS[P : D], R) \]
20: \[ \text{return } R \]
21: **end procedure**
2 Sample Encoding

A sample arithmetic circuit computing the dot product of two vectors is given in Figure 1, where we use two vectors of size 7. The encoding of the corresponding circuit is given in Equation 1.

Figure 1: An arithmetic circuit to compute the dot product of the vectors $x$ and $y$ where $x, y \in \mathbb{R}^7$.

\[
\begin{align*}
\hat{f}(x, y, R) &= \left( x^T \begin{bmatrix} x_1 \\ r_7 \\ -r_6 \\ -r_6r_7 + r_8 \\ r_6 \\ -r_7 \\ r_9 \\ r_0 + r_1 + r_3 - r_8 - r_9, \\ y_1 \\ -r_{10} \\ -r_10 + r_{12} \\ r_10 \\ -r_9 \\ -r_3 - r_{12} + r_{13}, \\ r_11 \\ -r_{14} \\ -r_{14}r_{15} + r_{16} \\ r_{14} \\ -r_{15} \\ -r_1 + r_4 - r_{16} + r_{17}, \\ r_{15} \\ -r_{18} \\ -r_{18}r_{19} + r_{20} \\ r_{18} \\ -r_{19} \\ -r_4 - r_{20} - r_{21}, \\ r_{19} \\ -r_{22} \\ -r_{22}r_{23} + r_{24} \\ r_{22} \\ -r_{23} \\ -r_0 + r_2 + r_5 - r_{24} - r_{25}, \\ r_{23} \\ -r_{26} \\ -r_{26}r_{27} + r_{28} \\ r_{26} \\ -r_{27} \\ -r_5 - r_{28} - r_{29}, \\ r_{27} \\ -r_{30} \\ -r_{30}r_{31} + r_{32} \\ r_{30} \\ -r_{31} \\ -r_2 - r_{32} - r_{33} \end{bmatrix} \right) \end{align*}
\]

Figure 1: An arithmetic circuit to compute the dot product of the vectors $x$ and $y$ where $x, y \in \mathbb{R}^7$.

Let $\hat{f}(x, y, R)$ be $\left( \begin{bmatrix} c_1 \\ c_2 \\ c_3, \ldots, c_{31} \\ c_{32} \\ c_{33} \end{bmatrix}, c_{34}, c_{35} \right)$, decoding of $\hat{f}$ is done by computing the following:

\[
f(x, y) = x^T y = \sum_{i \in S} c_i + c_{i+2} + c_{i+1} + c_{i+3} + c_{i+4}
\]

where $S = \{1, 6, 11, 16, 21, 26, 31\}$ is the set of indices indicating the beginning of each encoded multiplication $x_i \cdot y_i$ for $i \in \{1, 2, \ldots, 7\}$.
3 The Scheme of Randomized Encoding Based Approach

The scheme of the randomized encoding based approach to compute the gram matrix is depicted in Figure 2.

Figure 2: The overview of the randomized encoding based approach to compute the dot product of samples from multiple input-parties is depicted. Each dash type corresponds to a specific part of the gram matrix computed by a pair of input-parties. (a) At first, the input-parties exchange their number of samples. (b) Then, they generate all the random values and send the required ones to the corresponding input-party. (c) Afterwards, they compute their components in the encoding and share them with the function-party. (d) Finally, the function-party computes the dot product of the samples. (e) The dimension of the matrices are shown separately for better readability.
4 Security Proof

Theorem 1. Efficient secure and private dot product framework (ESCAPED) is secure against a semi-honest adversary $A$ who corrupts any subset of input-parties.

Proof. According to the definition of the semi-honest adversary, $A$ cannot deviate from the protocol description. Thus, $A$ has to use the real inputs of the corrupted input-parties. Based on this information, it is easy to prove the correctness of ESCAPED. For simplicity, we present our proof using a scenario with three input-parties ($I_1, I_2, I_3$). The private data of $I_1, I_2,$ and $I_3$ are $X, Y,$ and $Z,$ respectively, and the function-party $F$ wants to learn $X^TY, X^TZ,$ and $Y^TZ.$ Equation 2 shows the correctness of ESCAPED.

\[
\begin{align*}
X^TY &= a^T(Y - b) + (X - a)^T Y + \frac{1}{\alpha}\alpha a^T b \\
&= a^T Y - a^T b + X^T Y - a^T Y + a^T b \\
&= X^T Y \\
X^TZ &= a^T(Z - c) + (X - a)^T Z + \frac{1}{\alpha}\alpha a^T c \\
&= a^T Z - a^T c + X^T Z - a^T Z + a^T c \\
&= X^T Z \\
Y^TZ &= b^T(Z - c) + (Y - b)^T Z + \frac{1}{\beta}\beta b^T c \\
&= b^T Z - b^T c + Y^T Z - b^T Z + b^T c \\
&= Y^T Z
\end{align*}
\]

After showing the correctness, we now prove the security of ESCAPED. $I_1, I_2,$ and $I_3$ learn $(Y - b, Z - c), (X - a, \alpha a, Z - c),$ and $(X - a, \alpha a, Y - b, \beta b),$ respectively. These values are generated by using random values $\alpha$ and $\beta,$ and matrices of uniformly chosen random values, $a, b$ and $c.$ Thus, they can be perfectly simulated by matrices of uniformly random values, which indicates the security of ESCAPED. More clearly, an input-party gets the randomly masked input data of other input-parties as well as their randomly masked masks. For instance, $I_2$ receives $(X - a), (Z - c)$ and $\alpha a.$ Since both the mask of the data, $a,$ and the mask of the data, $a$ and $b,$ are uniformly random, it is impossible for $I_2$ to learn the input data of other input-parties, which are $X$ and $Z$ in this case.

\(\square\)

Theorem 2. Assume that the function-party is malicious and does not collude with any input-parties. Then, ESCAPED is secure against the malicious function-party $A.$

Proof. Since the function-party does not have any input, it cannot change the output of any input-parties. This guarantees and proves the correctness of ESCAPED against the malicious function-party.

The security of the framework from the perspective of the function-party leans on two facts. The first one is that the number of features of the input data is unknown for the function-party. $A$ cannot be sure which vector space the samples are coming from. This makes unique prediction impossible. The second one is that $A$ gets the gram matrix of input data among input-parties, that is $X^TY, X^TZ$ and $Y^TZ,$ the gram matrix of their own samples, that is $X^TX, Y^TY$ and $Z^TZ,$ the gram matrix of the input data and the random mask, which are $a^TY, a^TZ$ and $b^TY,$ and the gram matrix of some of the random masks, more precisely $a^Tb, a^Tc$ and $b^Tc.$ They form an incomplete gram matrix $K = D^TD,$ where $D = \begin{bmatrix} X & Y & Z & a & b & c \end{bmatrix}$ (see Figure 3). Even if the number of features is known by $A$ and the complete version $K = D^TD$ is available, one can come up with multiple matrices satisfying the gram matrix $K.$ Assume that there is a rotation matrix $R \in \mathbb{R}^{N \times N}$ where $N = 2(n_a + n_b + n_c).$ Then, we can compute a matrix $E$ such that $E = R^{-1}D.$ Hence, we can express $D$ as $D = RE.$ Then, the computation of $K = D^TD$ becomes as follows:

\[
\begin{align*}
K &= D^TD \\
&= (RE)^T (RE) \\
&= E^T R^T RE \\
&= E^T R^{-1} RE \\
&= E^T E
\end{align*}
\]
due to the property of the rotation matrices, which is $R^{-1} = R^T$. Based on this observation, we can say that for every new rotation matrix $\Theta \in \mathbb{R}^{N \times N}$ there exists a new matrix $\beta = \Theta^{-1}D$ satisfying $K = \beta^T \beta$. Since Aguilera and Pérez-Aguila [1] demonstrated a way to generate rotation matrices for any dimension, one cannot obtain a unique matrix satisfying $K$. To be exact, one cannot recover $D$ from $K = D^T D$, which implies that it is not possible to recover $D$ from $\tilde{K} = D^T D$ either.

\[\begin{array}{cccc}
X & Y & Z & a \\
Y & X & Z & b \\
Z & X & Y & c \\
a & b & c & X \\
b & c & a & Y \\
c & a & b & Z \\
\end{array}\]

Figure 3: The computed incomplete gram matrix in which only the shaded parts are available.

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[1] A. Aguilera and R. Pérez-Aguila. General n-dimensional rotations. 2004.