Differentially Private Genomic Data Release For GWAS Reproducibility

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Abstract—With the rapid development of technology in genome-related fields, researchers have proposed various approaches and algorithms in recent years. However, they rarely publish the genomic datasets they used in their works for others to reproduce and validate their methods, as sharing those data directly can lead to significant privacy risks (e.g., against inference attacks). To solve the problem and expedite cooperative scientific research, we propose a novel differentially private sharing mechanism for genomic datasets that protects the entire genomic dataset under differential privacy. To improve data utility of the GWAS statistics, we further develop a post-processing scheme that performs optimal transport (OT) on the empirical distributions of SNP values. The distributions are also achieved in a privacy-preserving manner. We evaluate our approach on several real genomic datasets and show in the experiments that it provides better protection against both genomic and machine learning-based membership inference attacks and offers higher GWAS utility than the baseline approaches.

I. INTRODUCTION

Genomic research refers to mining the genomic data using statistical or computational approaches to decode and understand the DNA information in genome. The development in genome sequencing techniques have created tremendous research opportunities in these genome-related fields in recent years. Researchers examining the published genomic data can discover potential associations between diseases/traits and genes. For instance, human’s eye color was previously considered to be determined by a single gene on the chromosomes. With the help of the recent genome-wide association studies (GWAS), researchers have found that multiple genes are involved in the decision of eye color, where a particular region on chromosome 15 plays an significant role [3]. Moreover, these studies can also help medical personnel in diagnosis and cure of diseases.

Although releasing genomic data will drastically benefits humans, it is still not recommended to share personal DNA records without any protection as genomic data carry sensitive information about individuals, e.g., characteristics and susceptibility to diseases. A malicious client can utilize a victim’s genomic records and infer the appearance or diseases the victim may have with high confidence, which harms the victim’s privacy and may even result in discrimination or safety risks. Under such threats, patients barely agree to share their personal genomic records to the medical institutions, and then researchers cannot receive enough genomic data to progress their research, thus forming a vicious circle.

Meanwhile, reproducibility is also an issue in genomic analysis. In most research areas, researchers use publicly available datasets or share their own datasets, which allows others to reproduce their approaches for validation and comparison, but it becomes much more challenging for genomic research. This is because genomic data contain too sensitive information about individuals that exposure of those data will leak their traits/diseases and harm their privacy. Several projects share genomic data (e.g., OpenSNP [4]) publicly, and they perform basic anonymization such as blurring the identifiers and sharing limited portion of the entire data. To serve research needs, some projects also label those genomic fragments with phenotypes or diseases. However, these community-driven projects have several limitations. First, the projects often rely on people donating their individual genomic records and submitting their traits. For the niche diseases/traits, it is hard to get enough samples for analysis. For instance, in the OpenSNP dataset, only a few phenotypes, e.g., handedness or eye color, reach more than 1,000 samples, while the others only have a few samples. This, combined with partial sharing of those samples, finally results in inability to perform meaningful analysis for the researchers. In addition, the data uploaded by volunteers may suffer from higher sample bias compared with those carefully filtered by experienced medical analysts, which is another disadvantage.

On the other hand, sharing their own datasets is also dangerous for the researchers. It is known that blood relatives shares many genetic variations in common. The malicious client can re-identify the blood relative(s) and run inference attacks to gain excessive knowledge about membership of the victim in a sensitive dataset (e.g., HIV patients), thus harming the victim’s privacy. Moreover, since more and more associations between genome and diseases will be found thanks to the development of GWAS, the volunteer’s genomic privacy will be more vulnerable in the long run. As a result, it is necessary to design a privacy-preserving mechanism to protect genomic privacy while sharing genomic data.

Researchers have proposed various approaches to share genomic data without invading genomic privacy of the individual involved [8], [9]. For example, homomorphic encryption is introduced for certain queries, e.g., genomic sequence alignment, when multiple parties hold their own genomic data that are sensitive and want to perform calculations on the aggregate dataset from all the parties. The design of encryption allows all the involved data maintaining encrypted throughout the operation, and thus no party is able to know the actual data from others. However, the encryption-based approaches are often inefficient concerning computational and communication
cost. As genomic data consist of millions of nucleotide e.g., the Single-nucleotide polymorphisms (SNPs) considered in this work, the real-world implementation is hardly practical. Differential privacy is the state-of-the-art definition that protects the query results from being exploited by the malicious client. Generally, it shares data perturbed by controlled noise in a specific way such that the malicious client cannot interpret whether the victim is in the dataset or not by continuously observing the data. But in reality, traditional differentially private methods publish aggregated statistics computed on the dataset (e.g., mean and variance) instead of datasets itself. Thus, the receiver cannot perform do-it-yourself calculations on the dataset. Some researchers propose synthetic methods to generate datasets from the outputs of the differentially private mechanism. Nevertheless, those mechanisms suffer from a low upper bound of data utility (e.g., statistics) as well, i.e., the published data are still noisy even if no privacy is required.

In [22], the authors propose to share binary datasets under differential privacy guarantees using the XOR mechanism and achieve high data utility in their case studies. One of the most important advantages of the XOR mechanism is that it protects and shares the entire dataset instead of the statistics. Besides, it also preserves the utility of the shared dataset by minimizing the impact of the introduced noise under privacy guarantee. Since genomic data only has limited states, in this paper, we explore the feasibility of using the XOR mechanism to share genomic data in a differentially private manner by first encoding the data as binary bits. However, although the XOR mechanism succeeds in maintaining high utility of data in binary form, it lacks usefulness for genome-related data utility, i.e., GWAS statistics. From our preliminary experiments, we find that the XOR mechanism introduces much noise to the genomic data and perturbs excessive bits in the data matrix, which breaks the statistical features (GWAS statistics). Therefore, we design a post-processing scheme that preserves high utility for genomic data and does not violate the privacy guarantee provided by the XOR mechanism.

In this work, our objective is sharing genomic datasets using privacy-enhancing technologies while preserving high genomic data utility. For that, we choose the XOR mechanism [22] to offer differential privacy guarantee to genomic datasets. Due to the differences between genomic data and binary data concerning the number of states, we use the widely accepted encoding technique for genomic data to transfer them into binary form before we execute the differentially private mechanism and then convert the binary release back to the genomic space afterwards. To solve utility loss in terms of GWAS statistics, we propose a post-processing method to improve the targeted utility. Observing that GWAS statistics are significantly correlated with the distribution of the values at each genomic position, we intend to introduce SNP value distributions to the noisy dataset released from the XOR mechanism such that the original dataset and the shared dataset contains similar SNP-wise distributions. Therefore, we design a query counting the values of the SNPs at each genomic position and apply the Laplace mechanism to protect the results and maintain the differential privacy guarantee from the XOR mechanism. Using the noisy features, we perform optimal transport (OT) [42] at each genomic position that modifies a subset of the SNP values to make the distribution of the SNP values at that position match the noisy distribution from the count query. In addition, we accelerate the approach by optimizing the noise generation process.

Furthermore, the post-processing scheme offers additional protection against membership inference attacks on top of that by the XOR mechanism which mainly mitigates attribute inference attacks [24]. Since optimal transport targets the noisy counts, the scheme will force some values to be flipped. This process slightly modifies the genomic data of each individual in the dataset, which makes it harder for the malicious client to identify one’s membership based on its genomic records. Using our entire sharing scheme, we share a genomic dataset with high data utility in a privacy-preserving way. The approach is parameterized by the privacy budget \( \varepsilon \). When \( \varepsilon \) is small, it releases a dataset with more noise introduced and thus the malicious client can hardly learn from it. Unlike synthetic approaches, our proposed perturbation-based approach has a very high upper bound of genomic data utility, i.e., the output dataset is identical to the original dataset and data utility is very high when no privacy is required, which allows tuning the tradeoff between privacy and utility in a large scale for the implementation in real world.

We implement our proposed approach on three real-world genomic datasets of different phenotypes and evaluate its performance with regard to privacy risk against membership inference attacks and genomic data utility. We construct two types of member inference attacks (MIAs), i.e., the Hamming distance-based MIA and two machine learning-based MIAs using random forest and support vector machine, respectively. For data utility, we consider three GWAS tests: the \( \chi^2 \) test, the odds ratio test, and the t-test. We build a baseline approach by using the XOR mechanism without post-processing and a dummy addition-based approach that aims at mitigating inference power. The experiments show that our approach significantly increase GWAS utility and outperforms other approaches. In terms of membership inference attacks, the proposed approach mitigates the attack power for all three attacks.

Our main contributions can be summarized as follows:

- To the best of our knowledge, our work is the first to share entire genomic datasets in a differentially private manner for GWAS reproducibility.
- We design a post-processing to significantly improve GWAS utility of genomic datasets without breaking the differential privacy guarantee.
- We accelerate the XOR mechanism used in genomic dataset sharing under differential privacy by optimizing the noise generation.
- We implement our approach on three real-world genomic datasets and show that our approach prevents the malicious client against multiple membership inference attacks and also preserves high data utility compared with the baseline and the alternative post-processing (i.e., dummy data-addition).

The rest of the paper follows the structure below. In Section III, we review some related work. We list the background of the paper in Section III and propose the system setting including the system model and the threat model in...
Section[V] In Section[V] we introduce our approach. We show our experimental results in Section [VI]. In Section [VII] we conclude the paper.

II. RELATED WORK

A. Data Reproducibility

Data reproducibility is necessary for research that benefits the development of scientific knowledge [26], [53]. To enable reproducibility, researchers typically share datasets used in the paper to the public such that everyone can reconstruct their experiments and validate their results. Some examples of the dataset are ImageNet [37] and the Iris dataset [16]. However, several papers raise concerns of sharing datasets directly without considering privacy. The above-mentioned datasets does not contain any sensitive information of individuals, and thus sharing without privacy protection has no issues. However, since some datasets, including genomic and location datasets, contain much sensitive information, basic anonymization methods (e.g., hiding (quasi-)identifiers) cannot prevent adversaries from knowing personal information [12]. To solve the problem, researchers have propose methods to share those type of datasets with privacy guarantees [21], [23]. However, no existing works have been proposed to share genomic datasets. In this paper, we propose a differentially private mechanism to share entire genomic datasets with high GWAS utility such that researchers can share their datasets without violating privacy of the individuals involved.

B. Privacy-Preserving Dataset Sharing

Researchers propose several approaches to share datasets under traditional privacy metrics [39], [29]. Dwork et al. propose a state-of-the-art definition that allows sharing datasets in a privacy-preserving way, called differential privacy [14], which prevents the attacker from inferring the sensitive information from the dataset by adding controlled noise. The authors provide two mechanisms to achieve differential privacy of the dataset, naming the Laplace mechanism and the exponential mechanism, respectively. Andrés et al. define geo-indistinguishability, a variation for geolocation sharing using the planar Laplacian mechanism [7]. Some differentially private mechanisms are designed for certain statistics and release those statistical results. Adversaries cannot gain additional information, which satisfies the guarantee of differential privacy but actually limits the usefulness of the output from those mechanism. Therefore, synthetic methods are proposed to share synthesized datasets instead of statistics. For instance, [18] releases synthetic datasets of location trajectories. The authors apply noise to four features extracted from the dataset, which satisfies differential privacy, and then propose a synthetic function to generate trajectories using those noisy features. However, one major drawback of this method is the low upper bound of data utility, which is also one of the common issues in synthetic approaches. This results from limited access to the dataset (only those features) during synthesizing, which makes it hard to reconstruct the dataset to get high data utility compared with the original one. On binary datasets, [22] design the XOR mechanism to share binary datasets under differential privacy, which generates noise on the datasets using the Exact Hamiltonian Monte Carlo-based sampling method. Nevertheless, the approach only works for binary datasets only.

To the best of our knowledge, no existing work publishes genomic data (instead of statistical data) in a differentially private manner. Yet, it is possible to adapt the binary method, i.e., the XOR mechanism, to genomic data due to the similarity between binary and genomic data, e.g., number of states and values, but data utility in a genomic manner should be prioritized. In our approach, we generate differentially private genomic datasets using the XOR mechanism by encoding the genomic states into binary form.

C. Privacy of Genomic Data

Genomic privacy has become one of the most interesting topics by researches after several papers reveal privacy concerns for genomic data. Lin et al. [27] claim that 75% independent SNPs are enough to distinguish one individual from others, while Homer et al. successfully determine the presence of an individual in a group, e.g., having a same phenotype, by analyzing aggregate statistics and the individual’s genomic data. There are several encryption-based methods. Differential privacy is also introduced to protect genomic privacy. Altman et al. evaluate privacy risks against membership inference attacks in two machine learning models and use DP-SGD to mitigate such attacks. Some papers focus on publicizing differentially private GWAS statistics including $\chi^2$ and odd ratio. Uhler et al. [41] propose methods for releasing some mainstream GWAS statistics, and Yu et al. [44] improve the work by allowing arbitrary number of case and control individuals and considering auxiliary information as the control’s data from public sources. However, our objective is differentially private data sharing for genomic datasets, and thus those approaches are not applicable. Yilmaz [43] et al. consider the correlations between SNPs and propose dependent local differential privacy for releasing individual genomic records. Nevertheless, this method works for individual genomic sequences and cannot be extended to dataset sharing. Our approach publishes entire genomic datasets under differential privacy with utility-focused post-processing to boost the performance of the GWAS statistics.

III. BACKGROUND

A. Genomic Data

The human genome consists of 23 pairs of chromosomes with approximate 3 billion pairs of nucleotides in those chromosomes. There are four types of nucleotides in the genome: adenine (A), thymine (T), guanine (G), and cytosine (C). They attach to each other following a specific rule: A with T, and G with C. Among the entire population, near 99.9% of the nucleotides are identical. Only the rest 0.01% of them are different, and those part is considered as genetic variation. Genes are sections of DNA sequences that determine a trait other characteristics, while an allele is a version of the same gene. The major allele denotes the allele that occurs in the majority of the population, while the minor allele means the less frequent one. Single nucleotides polymorphisms (SNPs) is the most common genetic variation. Each SNP represents a difference of nucleotides at a certain position, and each variant should be found in at least 1 percent of the population to be classified as a SNP [6]. More than 600 million SNPs have been found by scientists in global populations. A SNP value represents the number of minor alleles at a position, and it
can be 0, 1, or 2 due to the double-helix structure of the DNA sequence.

### B. Genome-Wide Association Studies

Genome-wide association studies (GWAS) are a popular method to analyze the correlations between genetic variations and a specific trait/phenotype [13, 40, 24, 10]. In a common case-control setting of GWAS, individuals are divided into the case and control groups based on whether the individual exhibits a certain characteristic or not. A contingency table is then calculated to represent the statistical SNP information between the two groups, and it is shown in Table I. $S_i$ denotes the number of the individuals in the case group having SNP value at that position equal to $i$. $R_i$ is the count in the control group, and $n$ is the total number in both case and control groups. For instance, if our target phenotype is lactose intolerance, then $S_2 = 10$ means 10 individuals with lactose intolerance have two minor alleles at that position. Some typical indicators in GWAS come from the $χ^2$ test, the odds ratio test, and the t-test, which we go through in detail in Section VI-B.

**TABLE I: A contingency table of size $3 \times 2$.**

| Genotype | 0 | 1 | 2 | Total |
|----------|---|---|---|-------|
| Case     | $S_0$ | $S_1$ | $S_2$ | $S$ |
| Control  | $R_0$ | $R_1$ | $R_2$ | $R$ |
| Total    | $t_0$ | $t_1$ | $t_2$ | $t$ |

### C. Differential Privacy

Differential privacy is the state-of-the-art notation that mathematically quantifies the loss of privacy. It offers strong privacy guarantees for personal sensitive information in datasets, and thus the attacker cannot draw any conclusions about the unperturbed data by observing the output from the differentially private algorithm. In differential privacy, neighboring datasets $D$ and $D'$ denote two datasets that only differ in one data record by insertion, deletion, or modification. The formal definition is in [14].

**Definition 1 (differential privacy):** [14] For any neighboring datasets $D$, $D'$ that differ in one data record, we consider a randomized algorithm $M$ $\epsilon$-differentially private if for any subset of the outputs $S \subseteq \text{Range}(M)$

$$\frac{\text{Pr}(M(D) \in S)}{\text{Pr}(M(D') \in S)} \leq e^\epsilon.$$  

The parameter $\epsilon$ is the privacy budget that denotes how much privacy is leaked by the algorithm $M$. Smaller $\epsilon$ values denote less privacy loss and thus stronger protection, while $\epsilon = \infty$ means no privacy at all. Differential privacy satisfies two propositions: composability and immunity to post-processing. We introduce the two terms in Proposition 1 and 2.

**Proposition 1 (composability):** [14] If $M_1, M_1, \ldots, M_n$ are $n$ algorithms that satisfy $\epsilon_1, \epsilon_2, \cdots, \epsilon_n$-differential privacy, respectively, an algorithm $G$ releasing $\mathcal{M}(D)_1, \mathcal{M}(D)_2, \cdots, \mathcal{M}(D)_n$ is $\sum_{i=1}^n \epsilon_i$-differentially private.

**Proposition 2 (immunity to post-processing):** [14] Let $M$ be an algorithm running on a database $D$ that satisfies $\epsilon$-differential privacy. Any mapping function $\mathcal{F}$ without knowing the private database $D$ is still $\epsilon$-differentially private.

These two propositions imply a considerable potential in the application of differential privacy. According to composability, we guarantee differential privacy with an aggregate privacy budget of multiple differentially private algorithms. After that, we can post-process the outputs of these algorithms at will without violating the privacy guarantee, as long as only those outputs are considered, which is claimed by post-processing immunity. Our approach includes two differentially private mechanisms, i.e., the XOR mechanism and the Laplace mechanism, and also implements an algorithm that operates on the outputs of the methods, which also satisfies differential privacy.

1) **The Laplace Mechanism:** Numerical queries are one of the most used query types. A numerical query maps a dataset $D$ to a vector $\mathbb{R}^k$ of fixed size, i.e., $k$ real numbers. Sensitivity denotes the maximum difference of the query’s output when a record enters or leaves the dataset. For a numerical query $\eta$, $l_1$ sensitivity is used, i.e.,

$$\Delta f = \max_{D, D'} ||\eta(D) - \eta(D')||,$$

where $D$ and $D'$ are neighboring datasets and $||\cdot||$ denotes the $l_1$ norm. The most common approach to offering privacy guarantee for numerical queries is the Laplace mechanism, which simply introduces controlled noise into the query’s actual outputs. More precisely, the Laplace mechanism first pulls $k$ independent and identically distributed (i.i.d.) random variables $r_1, r_2, \cdots, r_k$ sampled from the Laplace distribution $\text{Lap}(\sigma)$ with mean equal to 0 and scale parameter $\sigma = \frac{\Delta f}{\epsilon}$. Then the mechanism $\mathcal{M}$ gives the output as

$$\tilde{\eta}(D) = \eta(D) + (r_1, r_2, \cdots, r_k).$$

2) **The XOR Mechanism:** For completeness, we revisit the definition and privacy guarantee of the XOR mechanism proposed in [22].

**Definition 2: (XOR Mechanism).** Given a binary- and matrix-valued query $\eta(D) \in \{0, 1\}^{N \times P}$, the XOR mechanism is defined as

$$\mathcal{X}\mathcal{O}\mathcal{R}(\eta(D), B) = \eta(D) \oplus B,$$

where $\oplus$ is the XOR operator, and $B \in \{0, 1\}^{N \times P}$ is a binary matrix noise attributed to the matrix-valued Bernoulli distribution with quadratic exponential dependence structure, i.e., $B \sim \text{Ber}_{N \times P}(\Theta, \Lambda_1,2, \cdots, \Lambda_{N-1, N})$. The probability density function (PDF) of this distribution is parameterized by matrices $\Theta, \Lambda_1,2, \cdots, \Lambda_{N-1, N} \in \mathbb{R}^{P \times P}$ and is expressed as

$$f_B(B) = C(\Theta, \Lambda_1,2, \cdots, \Lambda_{N-1, N}) \times \exp \left\{ \text{Tr}[B \Theta B^T] + \sum_{i=1}^{N} \sum_{j \neq i}^{N} \text{Tr}[B_{i,j} B A_{i,j} B^T] \right\},$$

where $C(\Theta, \Lambda_1,2, \cdots, \Lambda_{N-1, N})$...
where
\[
C(\Theta, \Lambda_{1,2}, \cdots, \Lambda_{N-1,N}) = \left[ \sum_{B_k} \exp \left\{ \text{Tr}[B_k \Theta B_k^T] + \sum_{i=1}^{N} \sum_{j \neq i}^{N} \text{Tr}[J_{ij} B_k \Lambda_{i,j} B_k^T] \right\} \right]^{-1},
\]
is the normalization constant, \(B_k \in \{0, 1\}^{N \times P}\), and \(J_{ij}\) is the matrix of order \(N \times N\) with 1 at the \((i,j)\)-th position and 0 elsewhere.

**Theorem 1:** The XOR mechanism achieves \(\epsilon\)-differential privacy of a matrix-valued binary query if \(\Theta\) and \(\Lambda_{i,j}\) satisfy
\[
s_f \left( \|\lambda(\Theta)\|_2 + \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} \|\lambda(\Lambda_{i,j})\|_2 \right) \leq \epsilon, \tag{1}
\]
where \(s_f\) is the sensitivity of the binary- and matrix-valued query, and \(\|\lambda(\Theta)\|_2\) and \(\|\lambda(\Lambda_{i,j})\|_2\) are the \(l_2\) norm of the vectors composed of eigenvalues of \(\Theta\) and \(\Lambda_{i,j}\), respectively.

In Section V-A, we will discuss how to obtain \(s_f\) when considering binarized genomic dataset. In practice, it is computationally prohibitive to evaluate the normalization constant in the PDF of the matrix-valued Bernoulli distribution, thus, to sample from it, an Exact Hamiltonian Monte Carlo (EHMC) [32]. More details about the parameter setting is deferred to Section VI-C.

**IV. System Setting**

In this section, we introduce our system and threat models.

**A. System Model**

The system workflow is shown in Figure 1. We consider two parties involved in our system: a researcher and several clients. The researcher receives genomic dataset(s) from hospitals or other medical institutions, where doctors and scientists acquire the genomic records by performing DNA sequencing on patients’ samples during treatments and store them upon the patients’ approval. The researcher studies the unpublished genomic data by performing GWAS locally and proposes some innovative findings. Reproducibility is critical to increase the reliability of the discoveries. Therefore, it wants to share the data such that others can verify their findings. However, genomic data are so sensitive that any exposure without proper protection (in terms of genomic privacy) may lead to severe consequence if used by the malicious client, e.g., inferring whether an individual has a disease with high confidence. To avoid this, the researcher cannot share those data in raw format by all means. Instead, the researcher wants to implement a data sharing approach that protects the data in a privacy-preserving manner such that the data can be used for reproducibility while no individuals’ genomic privacy is threatened.

To be more specific, after receiving a genomic dataset from some institutions and performing optional pre-processing to formalize the dataset, the researcher will conduct GWAS on the formalized dataset and claims some observations and findings. To enable reproducibility while not violating individuals’ genomic privacy, the researcher implements our privacy-preserving sharing approach for genomic datasets and publishes a noisy dataset to the client(s). In particular,

\[
\begin{align*}
(\Theta, \Lambda_{1,2}, \cdots, \Lambda_{N-1,N}) & = \left[ \sum_{B_k} \exp \left\{ \text{Tr}[B_k \Theta B_k^T] + \sum_{i=1}^{N} \sum_{j \neq i}^{N} \text{Tr}[J_{ij} B_k \Lambda_{i,j} B_k^T] \right\} \right]^{-1},
\end{align*}
\]

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We consider two types of MIAs, one Hamming distance test (HDT)-based, and two machine learning (ML)-based methods. All MIAs rely on a case-control setting, i.e., a case group with patients having the disease and a control group of individuals without such disease. As is introduced above, the malicious client can build a reference dataset containing individuals among the population from public sources, which can be considered as the control group in MIA, while the dataset to be shared is considered as the case group. In what follows, we introduce the attacks in detail.

1) Hamming Distance Test (HDT)-based MIA: This attack is first introduced in [19]. It leverages the pairwise Hamming distance between genomic sequences in the case group (received from the researcher and is subject to perturbation to achieve privacy guarantee) and control group (constructed from publicly available dataset). In particular, for each individual \( i \) in the released dataset (i.e., the case group), the malicious client first calculates individual \( i \)’s Hamming distances with all individuals in the control group, and then records the minimum Hamming distance (MHD) for individual \( i \). The malicious client then collects all MHDs for individuals in the case group and selects a threshold \( \gamma_h \) following 5\% false positive rate. When identifying a victim, the malicious client calculates the minimum Hamming distance between the victim’s sequences and all individuals in the control group. If the minimum Hamming distance is lower than the threshold \( \gamma_h \), the target victim is considered as a member in the case group, and vice versa.

2) Machine Learning (ML)-based MIAs: Machine learning based methods have been one of the most popular approaches in recent years, and they have also been widely used in genomic areas [15], [25], [30]. We assume the malicious client uses two types of machine learning-based MIAs: random forest (RF) [33] and support-vector machine (SVM) [51]. Random forest is an ensemble classification method that consists of a set of decision trees. It outperforms the traditional decision tree method generally since it avoids over-fitting [5], which is a significant drawback of decision tree. On the other hand, support vector machine is another state-of-the-art supervised learning model that solves the classification/regression tasks in a hyperplane. To perform the two ML-based MIAs, the malicious client needs a dataset that contains both positive (with the disease) and negative samples (without the disease) to train the machine learning model. Therefore, the malicious client uses the shared dataset as the positive samples and the genomic records from public datasets as the negative samples during the training process. The malicious client uses the model to predict whether the targeted victim is in the shared dataset or not by input the victim’s genomic sequence to the trained model.

Another commonly adopted MIA is based on the likelihood ratio test (LRT) [38]. However, we do not consider it in this paper, because it only uses GWAS statistics, e.g., minor allele frequencies. In contrast, HDT-based MIA directly utilizes the pairwise Hamming distance between individuals in the case and control group. Thus HDT-based MIA is much more powerful than LRT-based MIA. This has been empirically verified in [19].
Fig. 2: The system workflow. 1) Encode the genomic dataset \( D \) to binary form \( D^b \). 2) Divide the binary matrix into sub-matrices and record the shapes with their counts. 3) Generate noise matrices of the shapes using EHMC-based sampling. 4) Construct the whole noise matrix by randomly assigning the sub-noise matrices. 5) Produce the private matrix \( \hat{D}^b \) using the XOR mechanism. 6) Decode \( \hat{D}^b \) to \( \hat{D} \). 6) Calculate the query results \( C \) of \( \eta_c \) and apply Laplacian noise to each result as \( \tilde{C} \). 7) Perform optimal transport on \( \hat{D} \) based on \( \tilde{C} \) and generate \( D' \) as the shared dataset.

V. METHODOLOGY

We introduce our differentially private sharing approach of genomic data in this section. The workflow is shown in Figure 2. First, we encode the genomic dataset to be shared by the researcher as a binary matrix, where each SNP value is represented using two bits. Second, we implement a differentially private mechanism on the encoded dataset that perturbs the binary matrix using the XOR mechanism and then regenerate the genomic data by decoding the noisy matrix. Observing that the perturbed data lose data utility with regard to GWAS statistics, especially when the privacy budget (\( \epsilon \)) decided by the researcher is small, we further propose a post-processing method that aims at improving GWAS statistics of the shared dataset using optimal transport [2]. Furthermore, we accelerate the XOR mechanism by reusing the sub-noise matrices. In the rest of the section, we go through all the steps in detail.

A. Differentially Private Generation of Genomic Data

In binary data, each position has two options (0 and 1), while genomic data have three (0, 1, and 2) (c.f. III-B). We encode a SNP value to 2 bits following Table III (which is a common practice in genetic research [1]) and generate a new binary matrix \( D^b \in \{0, 1\}^{n \times 2p} \). Thus, we convert our problem to sharing a differentially private binary dataset.

We consider using the XOR mechanism [22] to perturb the binarized SNP data, because it can directly generate binary noise matrix attributed to the matrix-valued Bernoulli distribution with quadratic exponential dependence structure [28] and preserve the potential correlations among the data entries. Besides, when determining the parameters of the distribution given the privacy budget \( \epsilon_x \), the XOR mechanism adopts a heuristic approach to boost the expected utility of the perturbed results while still satisfying \( \epsilon_x \)-differential privacy guarantee. The output of the XOR mechanism has larger scale from almost no noise to heavy noise than other synthetic methods, which is beneficial for the researcher to choose an appropriate privacy budget.

To be more specific, the XOR mechanism perturbs the binary SNP data via \( \hat{D}^b = D^b \oplus B \), where \( D^b \) is the original binary SNP dataset, \( \hat{D}^b \) is the result after perturbation, \( \oplus \) is the XOR operation, and \( B \in \{0, 1\}^{n \times 2m} \) is the binary noise sampled from the matrix-valued Bernoulli distribution. The parameters in the distribution is calibrated using \( \epsilon \) and the sensitivity \( s_f \) of the binary encoding of \( D \) and \( D' \) (\( D \sim D' \)). Here, \( D \sim D' \) denotes that \( D \) and \( D' \) are neighboring genomic datasets that differ only by the genomic sequence of a single individual. Mathematically, we have

\[
\begin{align*}
\mathcal{S} & = \sup_{D, D'} \|D^b \oplus D'^b\|_F^2. \\
\|\cdot\|_F & \text{ denotes the Frobenius norm, and } s_f \text{ essentially counts the number of maximum different entries of the binary encoded } D \text{ and } D'. \text{ After we generate a noisy binary matrix } \hat{D}^b, \text{ we decode it back into a noisy genomic dataset } \hat{D} \text{ following Table III.}
\end{align*}
\]

| Genomic | Binary |
|---------|--------|
| 0       | 00     |
| 1       | 01     |
| 2       | 11     |
B. Post-processing Aiming at the GWAS Statistics

The XOR mechanism achieves differential privacy and preserves high data utility on binary datasets such as social networks and gray-scale images. However, since genomic data are not in a binary form themselves, data utility of the decoded data is not promised by the mechanism. Additionally, genomic data have a different definition concerning data utility. As is introduced in [11], the GWAS statistics of genomic data become the most interesting features by the researchers recently, and thus, in this paper, we define data utility to be usefulness of GWAS output. To analyze robustness of data utility using the XOR mechanism, we perform some preliminary experiments and observe significant utility loss in the datasets shared by the XOR mechanism. For example, as is shown in Figure 3, the \( \chi^2 \) utility of the shared lactose intolerance dataset is merely 0.37 even when a high \( \epsilon_c = 8.0 \) is chosen (with only about 2% of the SNP values changed), while other shared datasets suffer from worse utility. Therefore, clients cannot validate the researcher’s discoveries based on those GWAS results with excessive noise.

To solve this issue, we propose a utility-focused post-processing method. The method consists of two steps. First, we count the SNP values at each position and protect them under differential privacy. Second, using optimal transport (OT) [2], we adjust some SNP values to make the value distribution in the noisy dataset \( \hat{D} \) released by the XOR mechanism identical to the distributions in the first step. In the following paragraphs, we illustrate the details of the post-processing method.

We observe that most of the GWAS statistics are correlated with the SNP-wise value distribution. If we make the distribution close to the one in the original dataset, GWAS-based utility should increase. Thus, we first extract this distribution from the unperturbed genomic data as an additional feature of the dataset. In particular, we define a count query \( \eta_c(\cdot, \cdot) \) as:

\[
\eta_c(D, j, k) = \sum_{i=1}^{m} 1_{D_{ij}=k}
\]

that counts the SNP value \( k \) at position \( j \) in the dataset \( D \), where \( j \in [1, p] \) denotes the SNP position and \( k \in K \) and \( K = \{0, 1, 2\} \) is the alphabet of SNP values. We issue the query at each position \( j \) for each SNP value \( k \in K \) and store the query results as \( C^{K\times p} \), where \( C_{kj} \) is the occurrence of value \( k \) at position \( j \). Since the count query results are also considered as a sensitive feature, we also need to protect its privacy from the malicious client. As a result, we apply Laplacian mechanism to each query result \( C_{kj} \) and output a noisy result \( \hat{C}_{kj} = C_{kj} + \text{Lap}(2/\epsilon_c) \), where \( \text{Lap}(\cdot) \) denotes a noise sampled from the Laplacian distribution. The sensitivity of the count query is 2, which is the maximum difference of the query when an individual is changed. Since the Laplacian distribution has a long-tailed structure, some count results will make no sense, e.g., the count is negative. To preserve utility, we set those negative values to 0, which does not violate differential privacy due to Proposition 2. The privacy budget \( \epsilon_c \) is chosen by the researcher. As a result, the researcher should select an appropriate \( \epsilon_c \) to balance privacy and utility of the shared data that the clients can validate the researcher’s contribution while the malicious client cannot infer much information from the released dataset.

Now we have the noisy count results \( \hat{C} \) protected under differential privacy. In order to improve data utility concerning GWAS statistics in the noisy matrix \( \hat{D} \), our plan is to make the count results of the noisy dataset \( \hat{D} \), denoted as \( \hat{C} \), look like \( C \). To achieve this, we need to modify a subset of the SNP values in \( \hat{D} \) such that the count results \( \hat{C} \) on the updated genomic matrix \( \hat{D}' \) are similar to \( C \). Meanwhile, the modification brings additional noise that may influence GWAS utility, so we want to minimize the noise introduced to \( \hat{D} \). Recall in genomic data, the SNP value represents the number of the minor alleles and has three possible outputs: 0 (AA), 1 (Aa), and 2 (aa), and the change in SNP value represents the number of nucleotides that are changed. Therefore, we define the cost \( C_{pq} = |p - q| \) for the change from \( p \) to \( q \), where \( p, q \in K \).

We construct an optimization problem at each genomic position \( j \). We consider \( \hat{C}_{kj} \) for \( k \in K \) and \( \hat{C}_{kj} \) for \( k \in K \) as two mass distributions at position \( j \) and want to find a transport plan \( T^{K\times K} \) which moves the mass of \( \hat{C}_{kj} \) to make it resemble \( C_{kj} \). The total cost is defined as

\[
<T, C> = \sum_{p=1}^{K} \sum_{q=1}^{K} T_{pq} C_{pq}
\]

where \( C_{pq} = |p - q| \). Thus, the optimal transport optimization is formulated as

\[
\min_T <T, C>
\]

s.t.

\[
\sum_{q=1}^{K} T_{pq} = \hat{C}_{pj} \quad \forall p \in \{0, 1, 2\}
\]

\[
\sum_{p=1}^{K} T_{pq} = \hat{C}_{qj} \quad \forall q \in \{0, 1, 2\}
\]

\[
T_{pq} \geq 0 \quad \forall (p, q) \in \{0, 1, 2\} \times \{0, 1, 2\}
\]

where the mass distributions \( \hat{C}_{norm} \) and \( \hat{C}_{norm} \) are computed as

\[
\hat{C}_{norm} = \frac{\hat{C}_{kj}}{\sum_k \hat{C}_{kj}}, \quad \hat{C}_{norm} = \frac{\hat{C}_{kj}}{\sum_k \hat{C}_{kj}}
\]

for each \( k \in K \), respectively. \( T \) is essentially a joint mass distribution at each position \( j \) (i.e., \( \sum_{p,q} T_{pq} = 1, \forall j \)) whose row- (or column-) wise marginalization is the marginal distribution of SNP taking value \( p \) (or \( q \)) at position \( j \).

This one-dimensional optimization problem can be solved using optimal transport (OT) [42]. In transportation theory, optimal transport aims to minimize the cost while performing a mass moving task to transfer the distribution from one to the other, which exactly fits our need. The procedure of the transportation in our approach at position \( j \) can be described as follows. First, we get the noisy count \( \hat{C}_{kj} \) and the count \( C_{kj} \) on \( \hat{D} \) for \( k \in K \). After noise addition, the total count \( \sum_k \hat{C}_{kj} \) is not necessarily equal to \( \sum_k C_{kj} \). Thus, in the second step, we normalize the count results following Equation 3. Third, we calculate the transportation plan \( T^{K\times K} \) using the normalized counts by optimal transport, where \( T_{pq} \) denotes the number of SNP value \( p \) (normalized) that should be changed to \( q \). Then we change the SNP values based on \( T_{pq} \), i.e., we transfer
and thus also satisfying differential privacy due to immunity to differentially private data without accessing the original values, even when the required number of sub-matrices of size $n_s \times p_s$, i.e., $c_s \geq \lceil \frac{np}{n_s p_s} \rceil$ and put them into a candidate pool. For each sub-matrix, we randomly sample (without replacement) one from the candidate pool. By doing so, we significantly accelerate the most time-consuming part of our approach, i.e., EHMC-based sampling, and make generation of large datasets possible not just theoretically.

Now, we can arrive at the end-to-end privacy guarantee of our proposed scheme.

Claim 1: The proposed genomic database sharing scheme is $(\epsilon_x + \epsilon_c)$-differentially private.

Proof: Generation of genomic datasets using the XOR mechanism follows $\epsilon_x$-differential privacy, and extracting count results satisfies $\epsilon_c$-differential privacy. Other intermediate steps, e.g., decoding and optimal transport, are executed on differentially private data without accessing the original values, thus also satisfying differential privacy due to immunity to post-processing (Proposition 2). Based on sequential composition of the two differentially private methods (Proposition 1), we can achieve the conclusion in the above claim.

\section{VI. Evaluation}

We implement our approach on real genomic data. Through the experiments, we evaluate privacy risks against three membership inference attacks introduced in Section IV-B and analyze data utility of published genomic datasets. We show that our proposed sharing mechanism outperforms the baseline approach with regard to privacy, GWAS utility, and time cost.

\subsection{A. Dataset}

We use the OpenSNP dataset \cite{4} in the experiments. To show general performance of the proposed approach, we select three phenotypes, i.e., lactose intolerance, hair color, and eye color, from the OpenSNP dataset and build a dataset for each phenotype, including one large dataset and two normal ones. To evaluate the membership inference attacks that require a case-control setup, i.e., the Hamming distance and the machine learning tests, we build a control group with the same number of individuals that do not have the phenotype for each dataset.
1) Lactose Intolerance: The dataset includes 9091 SNPs of 60 individuals that are lactose intolerable.

2) Hair Color: The dataset records the genomic data with 9386 SNPs of 60 individuals who have dark hair. For the control group we choose 60 individuals with blonde or similar hair.

3) Eye Color: The eye color dataset is a large one with 28396 SNPs among 401 individuals. Those individuals have brown eyes, and the control ones have blue eyes.

B. Evaluation Metrics

We analyze the performance of our approach from three perspectives: privacy risks, data utility, and time complexity. For privacy risk, we follow the threat model in Section IV-B and analyze the attack power of three membership inference attacks. We use recall as accuracy metric for the two machine learning attacks since we only focus on protecting the individuals in the published dataset with a common trait/disease. For membership inference attacks, we input each individual’s genomic data in the original dataset into the attack model and evaluate the detection accuracy, i.e., the percentage of the individuals being in the dataset predicted by the model.

In terms of data utility, we select three GWAS utility metrics: \(\chi^2\) test, odds ratio test, and t-test. A \(\chi^2\) test examines whether the two sample groups have the same frequencies, i.e., whether there is a significant difference between the two frequencies in a statistical manner. We calculate the \(p\)-value of the two tests and evaluate the performance along with the MAF and the \(p\)-value from the odds ratio test. The odds ratio test is used to quantify the associations between a phenotype or a disease and a SNP. Following [19], we first calculate the odds ratio as Equation 4.

\[
OR = \frac{(S_1 + S_2)/(R_1 + R_2)}{S_0/R_0} = \frac{R_0(S_1 + S_2)}{S_0(R_1 + R_2)}
\]

Then we get the 95% confidence interval as \(\exp\{\ln(OR)\} \pm 1.96 \times SE\{\ln(OR)\}\), where \(SE\{\ln(OR)\} = \sqrt{\frac{1}{S_1 + S_2} + \frac{1}{S_0} + \frac{1}{R_1 + R_2} + \frac{1}{R_0}}\) and \(\exp(\cdot)\) is the exponential function and \(SE(\cdot)\) is the standard error of the log odds ratio. After that, we compute the standard normal deviation (z-value) as \(\frac{\ln(OR)}{SE\{\ln(OR)\}}\), and the \(p\)-value is the area of the normal distribution that is outside \(\pm z\). A t-test is a method of hypothesis testing and analyzes the means between two groups of samples. It assumes a null hypothesis that the two groups are drawn from the same population, while the alternative hypothesis is that they are from two different populations. For all three utility experiments, we consider the \(w\) most significant SNPs concerning \(p\)-value as the researcher’s discoveries. As is mentioned in Section IV-A we set a relaxed metric for the client. For all three utility tests, we check the percentage of the \(w\) SNPs are among the \(w/0.05\) most significant SNPs in the published dataset. The client trusts the researcher and thinks the discoveries are reproducible if the percentage is high. Otherwise, the client is not convinced.

C. Experiment Setup

Unless specified, we use the following parameters throughout the experiments. Privacy budgets are chosen depending on the size of the dataset. For the lactose intolerance dataset and the hair color dataset, we use \(\epsilon_s \in [0.1, 8.0]\). For the eye color dataset, we set \(\epsilon_c \in [0.1, 15.0]\) as a larger dataset is more noisy with the same privacy budget. Besides, concerning privacy budgets of the count query \(\eta_c\), we use \(\epsilon_c \in [0.01, 5.0]\) for the lactose intolerance and hair color datasets, while we use \(\epsilon_c \in [0.1, 11.0]\) for the eye color dataset. We use \(n_s = 39\) and \(p_s = 99\) during the sub-noise matrix generation. The two parameters influence the running time of sub-noise matrix generation and also determine the size of \(A_{ij}\) and \(\Theta\) and the value of \(s_f\) in Theorem 1. In fact, \(n_s\) and \(p_s\) can be arbitrarily selected, as long as \(s_f > 1\) holds, \(c\)-differentially private sharing of the genomic database is attained. We set \(w = 300\) for utility evaluation.

As discussed in Section III-C2 directly sampling the required sub-noise matrices (using various combination of \(n_s\) and \(p_s\)) from the matrix-valued Bernoulli distribution is difficult, thus, we adopt the Exact Hamiltonian Monte Carlo (EHMC) based sampling scheme, which generates the desired binary noise samples converging to the target distribution by modeling the sampling procedure using Hamiltonian dynamics.

It is noteworthy that in all our considered dataset, the number of data instance is far less than the number of attributes (SNP), e.g., 401 \(\ll\) 28396 in the Eye color dataset. Thus, learning models directly trained on these datasets will not generalize well. Thus, when implementing machine learning-based MIAs, we first obtain the first 5 principal components of the datasets by performing principal component analysis (PCA) [34], then train the models based on the principal components. All the evaluation experiments are repeated multiple times and take the averaged results are reported.

Notice there is no existing work that publishes genomic data in a privacy-preserving way, especially in a differentially private manner. Alternatively, we define the baseline approach as generating differentially private genomic data using the XOR mechanism with the encoding/decoding techniques without any post-processing method. We compare our approach with the baseline differentially private approach, i.e., the XOR mechanism. Furthermore, we design an alternative post-processing to compare. The intention of designing this approach is to lower membership inference attack power. Since membership inference attacks rely on distinguishable features, either explicit or implicit, between the case and control groups, we mitigate such attacks by adding \(d\) noisy samples converging to the target distribution by modeling the sampling procedure using Hamiltonian dynamics.

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D. GWAS-based Utility

We show the comparison of GWAS-based utility in Figure 4.

1) $\chi^2$ Utility: Figure 4(a), (b), and (c) show $\chi^2$ utility of different approaches on different genomic datasets. The results show that our proposed approach provides robust improvement with regard to $\chi^2$ utility. We first observe that the released datasets directly from the XOR mechanism plus with encoding and decoding suffer from significant $\chi^2$ utility loss for all three datasets. In the lactose intolerance and hair color datasets, the utility increases with the increase of the privacy budget of the XOR mechanism, but it does not exceed 0.4 even when $\varepsilon_x = 8.0$. For the eye color dataset, the $\chi^2$ utility is only slightly above 0, which means the utility is totally lost. By using our proposed post-processing scheme, the $\chi^2$ utility is 0.81 when $\varepsilon_x = 2.0$ and reaches 0.96 if $\varepsilon_x \geq 5.0$ for the lactose intolerance dataset. The hair color dataset and eye color datasets have a lower $\varepsilon_x$ requirement for the same utility performance. In comparison, the dummy-based approach has similar but slightly higher utility than the XOR release.

2) Odds Ratio Utility: Figure 4(d), (e), and (f) show the comparisons of odds ratio utility. Similar to $\chi^2$ utility, odds ratio utility is higher for larger $\varepsilon_x$ and does not reach 0.45 in the lactose intolerance dataset, while the maximum is only below 0.1 in the hair color dataset. After applying our proposed approach, the utility significantly increases to 0.70, 0.73, and 0.95 for the lactose intolerance, hair color, and eye color datasets, respectively, when $\varepsilon_x = 1.0$. The dummy-based method decreases the utility, especially in the lactose intolerance dataset, and gets around 0.05 utility for the two normal-size datasets and almost 0 for the larger one, i.e., the eye color dataset.

3) T-Test Utility: As is shown in Figure 4(g), (h), and (i), t-test utility shows consistent improvement when the researcher uses the proposed approach to share genomic datasets and chooses $\varepsilon_x$ greater than 1.0. However, in the eye color dataset, the improved utility when $\varepsilon_x = 3.0$ is still not close to that in the original dataset. The reason is related to large size of dataset. T-test utility checks the population means of two sample sets, which is parameterized by sample count $n$ and mean value $\mu$ and standard deviation $\sigma$. Since there are only three states (0, 1, and 2) in genomic datasets, $\mu$ and $\sigma$ have smaller difference between the two sets when it comes to datasets of large size, which makes the noise introduced by the count query $\eta_x$ has more impact while calculating the corresponding p-values. As a result, the noise introduced to the data has more impact to t-test utility and makes the “top-300” SNPs much harder to stay in the relaxed region, resulting in lower t-test utility. Meanwhile, it also contributes to the line fluctuation in Figure 4. Since the eye color dataset contains far more SNPs than in the other two datasets (28396 vs. around 9000 SNPs), it requires a much larger $\varepsilon_x$ to maintain high t-test reproducibility. In Figure 4(i) when $\varepsilon_x = 5.0$, t-test utility is around 0.44 when $\varepsilon_x = 3.0$ and increases if $\varepsilon_x \geq 11.0$ is chosen. Alternatively, the researcher can increase the number of the most significant SNPs or set a more relaxed metric, e.g., checking among the top $\frac{390}{0.4}$ SNPs, instead of the preset $\frac{390}{0.6}$ SNPs, in the released dataset for those larger datasets. The utility of the lactose intolerance dataset from the dummy-based method does not increase regardless of the $\varepsilon_x$ value.

4) Discussion: Notice that all three utility metrics are not significantly influenced by the privacy budget $\varepsilon_x$ used by the XOR mechanism, which is intuitive as GWAS statistics are often highly correlated with the SNP-wise value distribution, as discussed in Section V-B. This means that the researcher only needs to consider GWAS utility while selecting an appropriate $\varepsilon_x$ during the generation process.

E. Robustness Against Membership Inference Attacks

In Figure 5, we show the comparisons of the robustness against membership inference attacks achieved by us, the dummy-based approach, and the baseline without post-processing.

1) Hamming Distance: The evaluation results against Hamming distance attacks are shown in Figure 5(a), (b), and (c). Our propose scheme offers robust mitigation against Hamming distance attacks compared with the non-private approach. It outperforms the XOR release if $\varepsilon_x > 4.0$ in the lactose intolerance dataset, while the attack power is slightly more vulnerable in the hair color dataset when $\varepsilon_x > 5.0$ and in the lactose intolerance dataset when $\varepsilon_x < 4.0$. As is shown in Figure 5(a), (b), the released dataset becomes more vulnerable if the researcher uses a higher $\varepsilon_x$. It is intuitive since Hamming distance attacks target the distance of genomic records between case and control individuals. Lower privacy, i.e., higher $\varepsilon_x$, causes the genomic data more similar to the original ones, making the malicious client easier to infer membership using the distance metric. For the eye color dataset, the inference power significantly decreases to 0.05 after applying our proposed approach, and it outperforms the XOR release for all $\varepsilon_x$ values.

2) Random Forest: We evaluate our approach against random forest attacks in Figure 5(d), (e), and (f). We observe consistent mitigation compared with all the rest approaches except two points when $\varepsilon_x = 0.01$ in the lactose intolerance dataset. For the other two datasets, our approach outperforms others for all privacy parameter combinations. Even in the worst case, i.e., when $\varepsilon_x = 6.0$ and $\varepsilon_c = 0.01$ in the hair color dataset, the random forest attack is merely as powerful as random guesses.

3) Support Vector Machine: Figure 5(g), (h), and (i) show the performance against attacks using support vector machine. Our approach mitigates SVM-based MIAs compared with the non-private approach. The performance of our approach is close to the XOR release and outperforms it in the hair color datasets when $\varepsilon_x > 2.0$. The dummy-based approach behaves similar to the XOR release and does not show significant mitigation against the MIAs.

F. Analysis of Time Cost

We compare running time of the generation approach between ours (with acceleration in Section V-C) and the original one [22], shown in Figure 6. Our method shows significant improvement if $n$ or $p$ is large, i.e., when the number of noise matrices are pruned, and no decrease in time if $(n, p) = (50, 1000)$ since no acceleration is performed. With the increase of $n$ and $p$, the time cost of our approach slightly grows, while it expands linearly but sharply if no acceleration is executed. We can conclude that our mechanism outperforms the original approach in [22].
Fig. 4: Comparisons of different approaches with regard to three GWAS utility metrics. All lines with $\epsilon$ values indicate our proposed scheme under various privacy budgets. Utility is evaluated by the percentage of the top $\omega$ SNPs in the original dataset $D$ remaining among the top $\omega$ in the shared dataset $D'$, where $\omega = 300$.

VII. CONCLUSION

In this paper, we propose a sharing mechanism for genomic datasets under differential privacy to provide reproducibility for genomic-wide association studies. We implement the XOR mechanism with encoding and decoding techniques to generate differentially private datasets. We also improve GWAS utility by performing optimal transport using noisy count results from the genomic dataset as the target distribution. Furthermore, we accelerate the generation method. Our approach shows significant improvements concerning GWAS utility and consistent mitigation against membership inference attacks.

In future work, we are working on increasing reproducibility for specific genomic studies apart from GWAS, such as transcriptome-wide association study, genetic epidemiology, and gene–environment interaction. We will also explore the feasibility of applying the shuffling scheme [11] to generate differentially private genomic databases. Additionally, we will also consider the problem of achieving both liability and privacy guarantees during genomic database sharing by incorporating database fingerprinting techniques [21, 20] into our framework.

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Fig. 5: Comparisons of different approaches against three membership inference attacks. All lines with $\epsilon$ values indicate our proposed scheme under various privacy budgets. “Power” in y-axis of all figures denotes the detection accuracy of whether an individual is a member in the original genomic database $D$ inferred by considered MIAs (discussed in Section VI-B), and the lower the value of “Power”, the higher the privacy against MIAs.

Fig. 6: Time complexity comparisons between ours and [22].

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