Secure multi-party linear regression
at plaintext speed

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1 Preface

I originally conceived, wrote, and shared the following note the weekend of May 5-7, 2017. While the core ideas are simple, their broad utility in combination for privacy-preserving multi-party linear regression appears to still be novel.

I was personally motivated by the application to genome-wide association studies (GWAS) in which several centers have sets of genomes and corresponding phenotypes that cannot be shared. At the time, there was still no way to run principal components analysis securely at scale in order to control for confounding by ancestry. So I was very excited to discover that recently Hyunghoon Cho and colleagues dramatically improved the scalability of secure-multiparty PCA, with application to secure GWAS in the model in which each individual secret-shares their genome\textsuperscript{1}. With secure PCA in hand, the ideas below enable secure multi-party GWAS at the other extreme of collaboration between, say, a dozen large biobanks, \textit{with the regression step itself done scalably and with essentially the same efficiency as plaintext computation}.

One can imagine a future in which secure multi-party GWAS is done on a public cloud in online fashion as new batches of samples come online. Those regressions that suggest promising hits might motivate more intensive open collaboration on select data in order to bring to bear more sophisticated quality control and statistical models en route to a joint search for biological mechanism and therapeutic target.

\textsuperscript{1}Hyunghoon Cho, David J Wu, Bonnie Berger. \textit{Secure genome-wide association analysis using multiparty computation}. Nature Biotechnology volume 36, p. 547-551 (May 2018)
2 Association scan

We will call the following variation on linear regression an association scan. Suppose we have positive integers $N$, $M$, and $K$ with $N > K + 1$ and data for $N$ samples:

- $y$, an $N$-dimensional response vector.
- $X$, an $N \times M$ matrix of $M$ transient covariate vectors.
- $C$, an $N \times K$ matrix of $K$ linearly independent permanent covariate vectors.

Let $X_m$ denote the $m$th column of $X$, e.g., the $m$th transient covariate vector. We now think of $y$ as a single draw from an $N$-dimensional normal distribution mean parameters a real number $\beta_m$ and a $K$-vector $\gamma_m$, and variance parameter $\tau_m^2$:

$$y \sim \text{Normal}(X_m \beta_m + C \gamma_m, \tau_m^2 I_{N \times N}) \quad (1)$$

Let $\hat{\beta}_m$ be the maximum likelihood estimate for the transient coefficient and let $\hat{\sigma}_m$ be the standard error of this estimate. Then under the null hypothesis $\beta_m = 0$, the statistic $\frac{\hat{\beta}_m}{\hat{\sigma}_m}$ is drawn from a $t$-distribution with $N - K - 1$ degrees of freedom.

**Association scan problem:** determine the vectors $\hat{\beta} = (\hat{\beta}_1, \ldots, \hat{\beta}_M)$ and $\hat{\sigma} = (\hat{\sigma}_1, \ldots, \hat{\sigma}_M)$ efficiently and scalably; the vectors of t-statistics and p-values then follow.

**Example:** In genome wide association studies, which scan the genome for correlation of genetic and phenotypic variation, we have $N$ samples (individuals), $M$ common variants to test one by one, and $C$ sample-level covariates like intercept, age, sex, batch, and principal component coordinates. Typically $N$ is $10^2$ to $10^6$, $M$ is $10^5$ to $10^8$, and $K$ is 1 to 20. In gene burden tests, $M$ is about $2 \times 10^4$.

Let $Q$ be an $N \times K$ matrix whose columns form an orthonormal basis for the column space of $C$. Let $X \cdot y$ denote the vector with values $X_m \cdot y$. Let $X \cdot X$ denote the vector with values $X_m \cdot X_m$. Let $\hat{\beta}^2$ denotes coordinate-wise squaring of $\hat{\beta}$. 
Lemma 2.1. A closed form solution to the association scan problem:

\[ \hat{\beta} = \frac{X \cdot y - Q^T X \cdot Q^T y}{X \cdot X - Q^T X \cdot Q^T X} \] (2)

\[ \hat{\sigma}^2 = \frac{1}{N - K - 1} \left( \frac{y \cdot y - Q^T y \cdot Q^T y}{X \cdot X - Q^T X \cdot Q^T X} - \hat{\beta}^2 \right) \] (3)

Proof. Plimpton 332 tablet.

Algorithm: We assume the columns of \( X \) are distributed across machines with \( C \) total cores.

1. Compute and broadcast \( Q \) using QR decomposition.
2. Compute and broadcast \( y \cdot y, Q^T y, \) and \( Q^T y \cdot Q^T y \).
3. In parallel, compute \( X \cdot X, Q^T X, Q^T X \cdot Q^T y \) and \( Q^T X \cdot Q^T X \).
4. In parallel, compute \( \hat{\beta} \) and \( \hat{\sigma} \) as in Lemma 2.1.

Computing \( Q \) and \( Q^T X \) dominate the computational complexity as

\[ O \left( NK^2 + \frac{NM}{C} \right) \] (4)

In practice we consider \( K \) as a small constant so the complexity is

\[ O \left( \frac{NM}{C} \right) \] (5)

i.e. that of reading the data and therefore best possible with no further assumptions on the entropy of \( X \). For further gains, QR decomposition can also be parallelized\(^2\) and the columns of \( X \) can be packed sparsely so that the flop count for \( Q^T X \) is reduced in proportion to the sparsity of \( X \).

3 Secure multi-party association scan

Now suppose the \( N \) samples are divided among \( P \) parties who are not willing or able to share their data. For simplicity of notation, we will suppose \( P = 3 \), with Alice, Bob, and Carla holding \( N_a, N_b, \) and \( N_c \) samples, respectively.

\[ y = \begin{pmatrix} y_a \\ y_b \\ y_c \end{pmatrix}, \quad X = \begin{pmatrix} X_a \\ X_b \\ X_c \end{pmatrix}, \quad C = \begin{pmatrix} C_a \\ C_b \\ C_c \end{pmatrix} \]

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\(^2\) Tall and skinny QR factorizations in MapReduce architectures, [https://pdfs.semanticscholar.org/747c/a08cbf258da8d2b89ba31f24bdb17d7132bb.pdf](https://pdfs.semanticscholar.org/747c/a08cbf258da8d2b89ba31f24bdb17d7132bb.pdf)
We also assume $C_a$, $C_b$, and $C_c$ have full column-rank.

In such situations, analysts typically have no recourse but to meta-analyze within-party estimates, with loss of power due to noisy standard errors as well as between-group heterogeneity (c.f. Simpson’s paradox). Being power hungry, we instead solve the:

**Secure multi-party association scan problem:** securely determine the vectors $\hat{\beta} = (\hat{\beta}_1, \ldots, \hat{\beta}_M)$ and $\hat{\sigma} = (\hat{\sigma}_1, \ldots, \hat{\sigma}_M)$ efficiently and scalably while communicating only $O(M)$ bits inter-party.

Note that $O(M)$ is best possible since all parties must receive the results. In fact, our secure algorithm has the same distributed computational complexity as before.

**QR algorithm:** The first aim is to securely provide Alice, Bob, and Carla with their respective rows of

$$Q = \begin{pmatrix} Q_a \\ Q_b \\ Q_c \end{pmatrix}$$

where

$$C = \begin{pmatrix} C_a \\ C_b \\ C_c \end{pmatrix} = \begin{pmatrix} Q_a R \\ Q_b R \\ Q_c R \end{pmatrix} = QR.$$ 

First Alice, Bob, and Carla simultaneously compute $R_a$, $R_b$, and $R_c$ in the QR decomposition of $C_a$, $C_b$, and $C_c$, respectively. The resulting matrices depend only on the orbit of $C$ under product-preserving isometry of $\mathbb{R}^{N_a} \times \mathbb{R}^{N_b} \times \mathbb{R}^{N_c}$.

Furthermore, each upper triangular matrix contains only $\binom{K}{2}$ real numbers, independent of $N$; these effectively describe the angles between pairs of permanent covariates.

So we assume that $N_A$, $N_B$, and $N_C$ are sufficiently large relative to $K$ that Alice, Bob, and Carla are perfectly happy to disclose $R_a$, $R_b$, and $R_c$.

\[3\]For greater security, one could employ a binary tree with $\log_2 P$ levels such that parties only share their $K \times K$ matrix directly in pairs (see first footnote). With $S$ so small, it’s also feasible to use SMC to compute $R$ without leaking any additional information.
$R_c$ in order to compute $R$ in the QR decomposition of the (tiny) $PK \times K$ matrix

$$S = \begin{pmatrix} R_a \\ R_b \\ R_c \end{pmatrix}.$$ 

The $R$ for $S$ coincides with that for $C$, so now the parties can privately compute:

$$Q_a = C_a R^{-1}$$
$$Q_b = C_b R^{-1}$$
$$Q_c = C_c R^{-1}$$

By Lemma 2.1, it now suffices to compute the following six quantities (those in the first row are numbers, the rest are $M$-vectors):

$$y \cdot y, \quad Q^T y \cdot Q^T y$$
$$X \cdot y, \quad Q^T X \cdot Q^T y$$
$$X \cdot X, \quad Q^T X \cdot Q^T X$$

Since

$$\mathbb{R}^{N_a} \times \mathbb{R}^{N_b} \times \mathbb{R}^{N_c}$$

is an orthogonal decomposition of $\mathbb{R}^N$, Alice, Bob, and Carla can compute the three left-hand quantities by computing their internal summands and then either sharing them to sum or or applying an SMC sum protocol which only reveals the overall sum:

$$y \cdot y = y_a \cdot y_a + y_b \cdot y_b + y_c \cdot y_c$$
$$X \cdot y = X_a \cdot y_a + X_b \cdot y_b + X_c \cdot y_c$$
$$X \cdot X = X_a \cdot X_a + X_b \cdot X_b + X_c \cdot X_c$$

The three right-hand quantities are trickier because the orthogonal projection

$$Q^T : \mathbb{R}^N \rightarrow \mathbb{R}^K$$

does not preserve orthogonality between vectors. Hence the $K$-vector decompositions

$$Q^T y = Q_a^T y_a + Q_b^T y_b + Q_c^T y_c$$
$$Q^T X = Q_a^T X_a + Q_b^T X_b + Q_c^T X_c$$
are not orthogonal decompositions. So instead the parties can compute the $K$-vector $Q^T y$ and the $M \times K$ matrix $Q^T X$ by computing their internal summands and either sharing them to sum or by applying an SMC sum protocol which only reveals the overall sum (for even greater security, they can use a more sophisticated SMC algorithm to only share the three right-hand quantities (two dot products of $K$-vectors for each $m$)). In all cases, these SMC protocols (if needed at all!) are fast because they require only simple secret sharing on tiny data, parallelize over $M$, and are independent of $N$.

Note that adding an intercept covariate is equivalent to translating $y$ and each column of $C$ to have zero mean. Adding an intercept for each party (i.e., $P$ indicator covariates to control for batch effects) is equivalent to mean centering $y$ and each column of $C_a$, $C_b$, and $C_c$ independently.

4 R demo

The following R code demonstrates our scheme, which we call the Distributed Association Scan Hammer (DASH). This code is also available at https://github.com/jbloom22/DASH/

```r
set.seed(0)

dot <- function(x){
  return(sum(x * x))
}

# Public
N1 = 1000
N2 = 2000
N3 = 1500
M = 10000
K = 3

D = N1 + N2 + N3 - K - 1

# Alice
y1 = rnorm(N1)
X1 = matrix(rnorm(N1 * M), N1, M)
C1 = matrix(rnorm(N1 * K), N1, K)
R1 = qr.R(qr(C1))
```
# Bob
y2 = rnorm(N2)
X2 = matrix(rnorm(N2 * M), N2, M)
C2 = matrix(rnorm(N2 * K), N2, K)
R2 = qr.R(qr(C2))

# Carla
y3 = rnorm(N3)
X3 = matrix(rnorm(N3 * M), N3, M)
C3 = matrix(rnorm(N3 * K), N3, K)
R3 = qr.R(qr(C3))

# Public or tree or SMC
invR = solve(qr.R(qr(rbind(R1, R2, R3))))

# Alice
Q1 = C1 %*% invR
Qty1 = t(Q1) %*% y1
QtX1 = t(Q1) %*% X1

yy1 = dot(y1)
Xy1 = t(X1) %*% y1
XX1 = apply(X1, 2, dot)

# Bob
Q2 = C2 %*% invR
Qty2 = t(Q2) %*% y2
QtX2 = t(Q2) %*% X2

yy2 = dot(y2)
Xy2 = t(X2) %*% y2
XX2 = apply(X2, 2, dot)

# Carla
Q3 = C3 %*% invR
Qty3 = t(Q3) %*% y3
QtX3 = t(Q3) %*% X3

yy3 = dot(y3)
Xy3 = t(X3) %*% y3
XX3 = apply(X3, 2, dot)

# Public or SMC
yy = yy1 + yy2 + yy3
Xy = Xy1 + Xy2 + Xy3
XX = XX1 + XX2 + XX3

Qty = Qty1 + Qty2 + Qty3
QtX = QtX1 + QtX2 + QtX3

QtXQty = t(QtX) %*% Qty
QtXQtX = apply(QtX, 2, dot)

yyq = yy - QtyQty
Xyq = Xy - QtXQty
XXq = XX - QtXQtX

# Public
beta = Xyq / XXq
sigma = sqrt((yyq / XXq - beta^2) / D)
tstat = beta / sigma
pval = 2 * pt(-abs(tstat), D)

df = data.frame(beta=beta, sigma=sigma, tstat=tstat, pval=pval)

# Compare to primary analysis for first M0 columns of $X$
M0 = 5

y = c(y1, y2, y3)
X = rbind(X1, X2, X3)
C = rbind(C1, C2, C3)

res = matrix(nrow=0, ncol=4)
for (m in 1:M0) {
    fit = lm(y ~ X[,m] + C - 1)
    res = rbind(res, as.vector(summary(fit)$coefficients[1,]))
}
df2 = data.frame(beta=res[,1], sigma=res[,2], tstat=res[,3], pval=res[,4])

all.equal(df[1:M0,],df2) # Returns TRUE

5 Generalizations

This approach efficiently generalizes to the case of multiple transient co-
variants (such as interaction terms) or multiple phenotypes (such as will
biobanks or eQTL studies). If an (eigendecomposition of) the kinship ker-
nel can be shared, then the approach extends to linear mixed models as
well. Gene burden tests (where linear combination of genotypes become
gene scores) also play well with this approach, since they involve linear pro-
jection on the variant axis rather than the sample axis. Thankfully, matrix
multiplication is associative.

Note also that one can alternatively compress using $C^T$ rather than $Q^T$
to preserve the ability to select phenotypes and covariates post-compression.

6 Acknowledgements

I am grateful to Alex Bloemendal who helped me derive Lemma 2.1 (a classic
result) as we sought to optimize linear regression for GWAS in the open-
source, distributed system Hail (www.hail.is). Without our intensive linear
algebra discussions, I would not have recognized the relevance of Lemma 2.1
combined with TSQR for defining a “doubly-distributed” linear regression
algorithm that plays well with privacy preservation.