Assignment5 : Population substructure

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1. The file SNPChr22.rda contains genotype information of 49 individuals of unknown background. The genotype information concerns 136 SNPs on chromosome 22. Load this data into the R environment. The data file contains a matrix Y containing the allele counts (0,1 or 2) for 136 SNPs for one of the alleles of each SNP.

```
load('SNPChr22.rda')
```

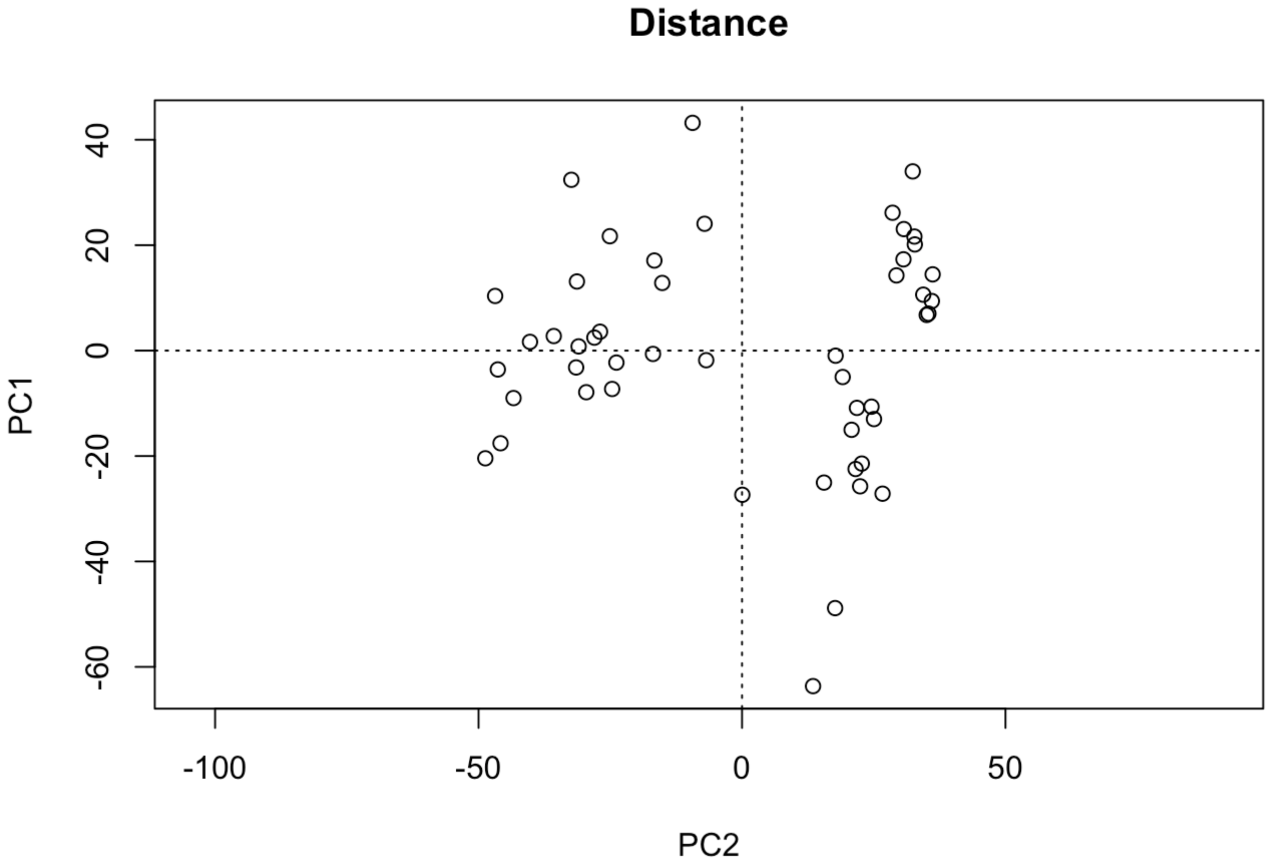
2. Compute the Manhattan distance matrix between the 49 individuals. Include a submatrix of dimension 5 by 5 with the distances between the first 5 individuals in your report.

```
md = as.matrix(dist(Y, method = "manhattan"))
md[1:5, 1:5]
```

```
##    1  2  3  4  5
## 1  0 80 49 55 65
## 2 80  0 71 77 81
## 3 49 71  0 52 54
## 4 55 77 52  0 62
## 5 65 81 54 62  0
```

3. Use metric multidimensional scaling to obtain a map of the individuals, and include your map in your report. Do you think the data come from one homogeneous population?

```
n = nrow(md)
md_out = cmdscale(md, k = n-1, eig=TRUE)
X = md_out$points[,1:2]
plot(X[,1], X[,2],type="p", ylab="PC1",
     xlab="PC2", main="Distance", asp = 1)
abline(v=0,lty=3)
abline(h=0,lty=3)
```



According to out plot we see two distinct set of popuation. In a homogeneous population all the individuals belong to the same group and are of the same type.

4. Report the eigenvalues of the solution.

```
md_out$eig
```

```
##  [1]  4.151272e+04  2.076796e+04  1.020205e+04  8.114257e+03  7.942764e+03
##  [6]  6.369659e+03  5.378938e+03  4.935698e+03  4.208222e+03  3.895748e+03
## [11]  3.353511e+03  3.030022e+03  2.469254e+03  1.830817e+03  1.695681e+03
## [16]  1.353295e+03  1.232518e+03  1.156127e+03  8.546821e+02  6.821345e+02
## [21]  5.811545e+02  4.845013e+02  2.249721e+02  1.698057e+02  4.795882e+01
## [26]  1.823470e+01 -2.273737e-12 -1.674019e+01 -5.842130e+01 -8.544354e+01
## [31] -2.535464e+02 -2.828951e+02 -3.452678e+02 -3.894639e+02 -4.051893e+02
## [36] -5.065839e+02 -5.378960e+02 -6.817495e+02 -7.244295e+02 -8.140500e+02
## [41] -9.313391e+02 -1.054480e+03 -1.108750e+03 -1.237461e+03 -1.357667e+03
## [46] -1.461376e+03 -1.695883e+03 -1.926193e+03 -2.175898e+03
```

5. Is the distance matrix you have used an Euclidean distance matrix?.

No, the distance matrix used was Manhattan distance.

$$|x_1 - x_2| + |y_1 - y_2|$$

This is the L_1 norm, where as the Euclidean distance is the L_2 norm.

6. What is the goodness-of-fit of a two-dimensional approximation to your distance matrix?

```
md_out$GOF[1]
```

```
## [1] 0.8801121
```

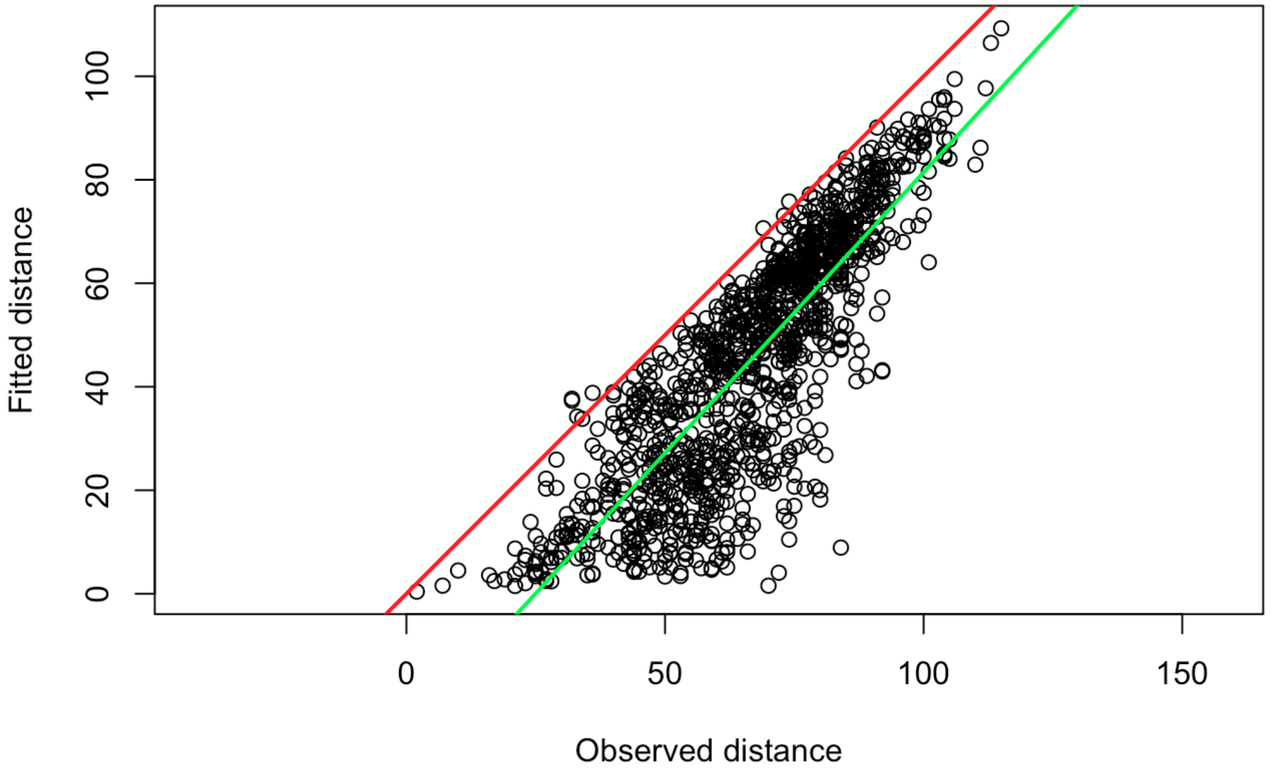
`GOF` is the amount of variance explained by our model. This value is usually represented by out eigenvaules sorted in descending order.

7. Make a plot of the estimated distances (according to your map of individuals) versus the observed distances. Regress estimated distances on observed distances and report the coefficient of determination of the regression.

```
D.fitted = as.matrix(dist(X))
D.obs = md[lower.tri(md)]
D.fit <- D.fitted[lower.tri(D.fitted)]
plot(D.obs,D.fit,asp=1,xlab="Observed distance",ylab="Fitted distance")
abline(0,1,col="red",lw=2)
out.lm <- lm(D.fit~D.obs)
summary(out.lm)$coef
```

```
##               Estimate Std. Error   t value      Pr(>|t|)
## (Intercept) -27.071800 1.40731276 -19.23652  6.730527e-72
## D.obs         1.085097 0.02037819  53.24795 2.153915e-315
```

```
abline(summary(out.lm)$coef[1,1],summary(out.lm)$coef[2,1],col="green",lw=2)
```

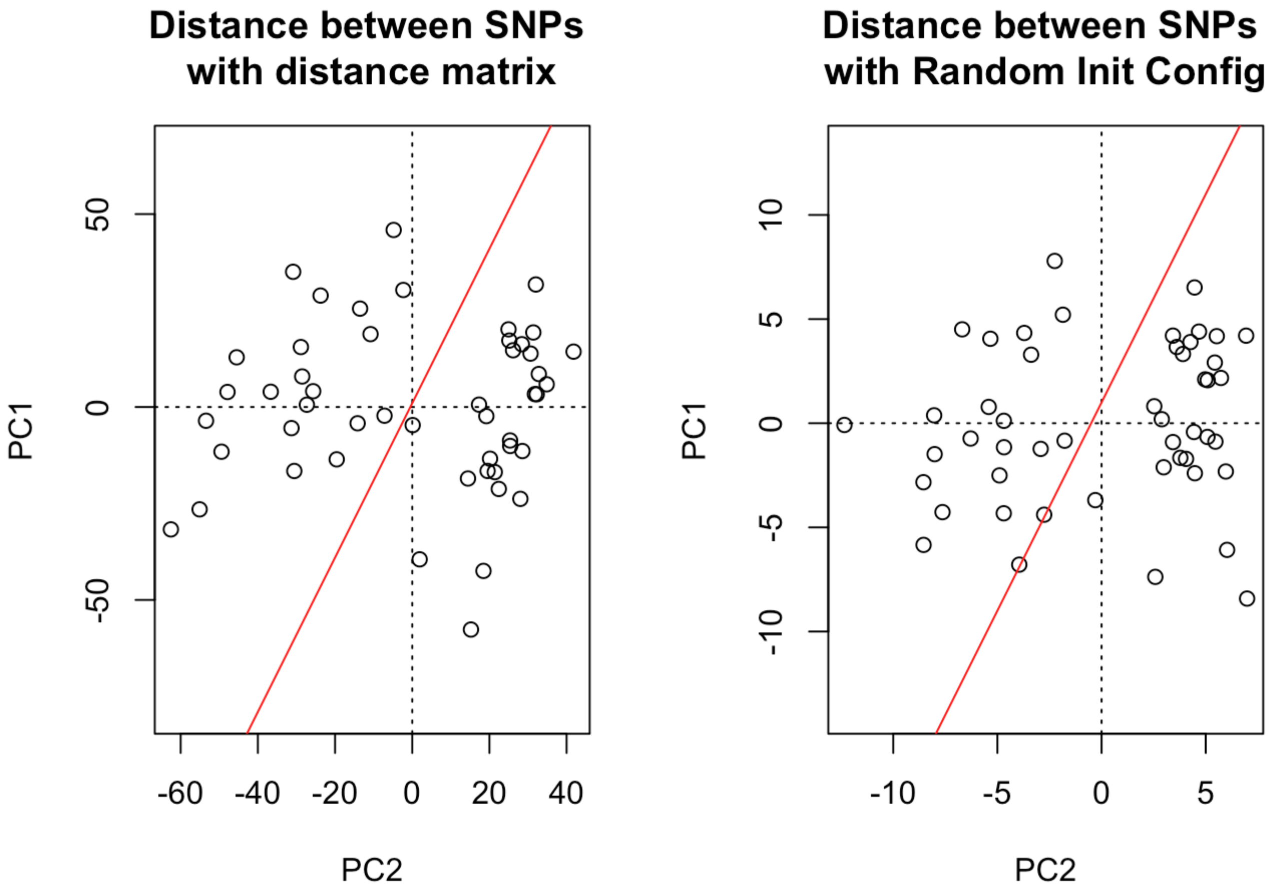


```
(R_sq= summary(out.lm)$adj.r.squared)
```

```
## [1] 0.7069346
```

8. Try now non-metric multidimensional scaling with your distance matrix. Use both a random initial configuration as well as the classical metric solution as an initial solution. Make a plot of the two-dimensional solution. Do the results support that the data come from one homogeneous population?

```
par(mfrow=c(1,2))
out.nmds.1 = isoMDS(md,k=2, trace = F)
X.nmds.1 = out.nmds.1$points
plot(X.nmds.1[,1],X.nmds.1[,2],asp=1, ylab="PC1",
     xlab="PC2",
     main="Distance between SNPs \nwith distance matrix")
abline(v=0,lty=3)
abline(h=0,lty=3)
abline(1,2, col="red")
x.init <- scale(matrix(runif(2*nrow(Y)),ncol=2))
out.nmds.2 <- isoMDS(md,y=x.init)
X.nmds.2 <- out.nmds.2$points
plot(X.nmds.2[,1],X.nmds.2[,2],asp=1, ylab="PC1",
     xlab="PC2",
     main="Distance between SNPs \nwith Random Init Config")
abline(v=0,lty=3)
abline(h=0,lty=3)
abline(1,2, col="red")
```



Distance between SNPs
with distance matrix

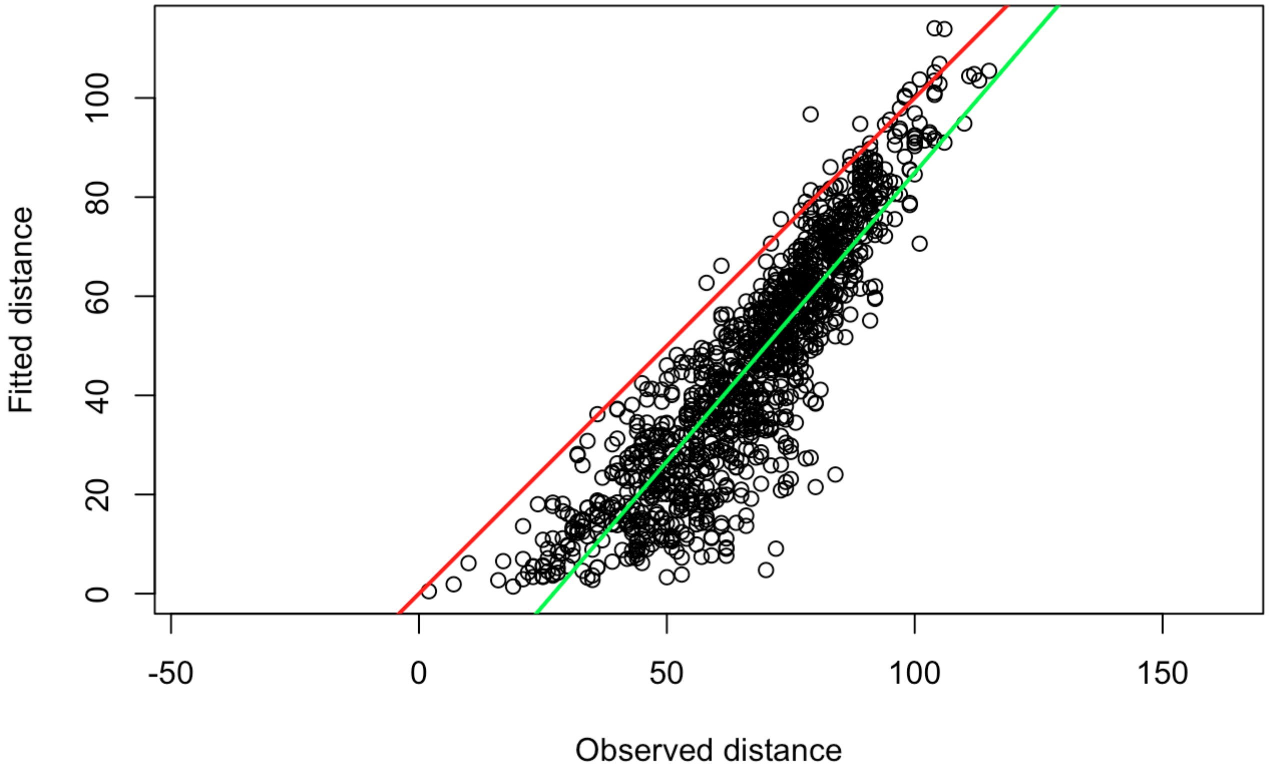
Distance between SNPs
with Random Init Config

Both the plots have 2 divided populations and divided groups.

9. Make again a plot of the estimated distances (according to your map of individuals) versus the observed distances, now for the two-dimensional solution of non-metric MDS. Regress estimated distances on observed distances and report the coefficient of determination of the regression. Is the fit better or worse than with metric MDS?

```
D.Fitted <- as.matrix(dist(X.nmds.1))
D.fit2 <- D.Fitted[lower.tri(D.Fitted)]

plot(D.obs,D.fit2,asp=1,xlab="Observed distance",ylab="Fitted distance")
abline(0,1,col="red",lw=2)
out.lm <- lm(D.fit2~D.obs)
abline(summary(out.lm)$coef[1,1],summary(out.lm)$coef[2,1],col="green",lw=2)
```



```
summary(out.lm)$coef
```

```
##                Estimate Std. Error   t value      Pr(>|t|)
## (Intercept) -31.601203 1.20788657 -26.16239 3.048145e-119
## D.obs         1.165212 0.01749046  66.61984  0.000000e+00
```

```
(R_sq1= summary(out.lm)$adj.r.squared)
```

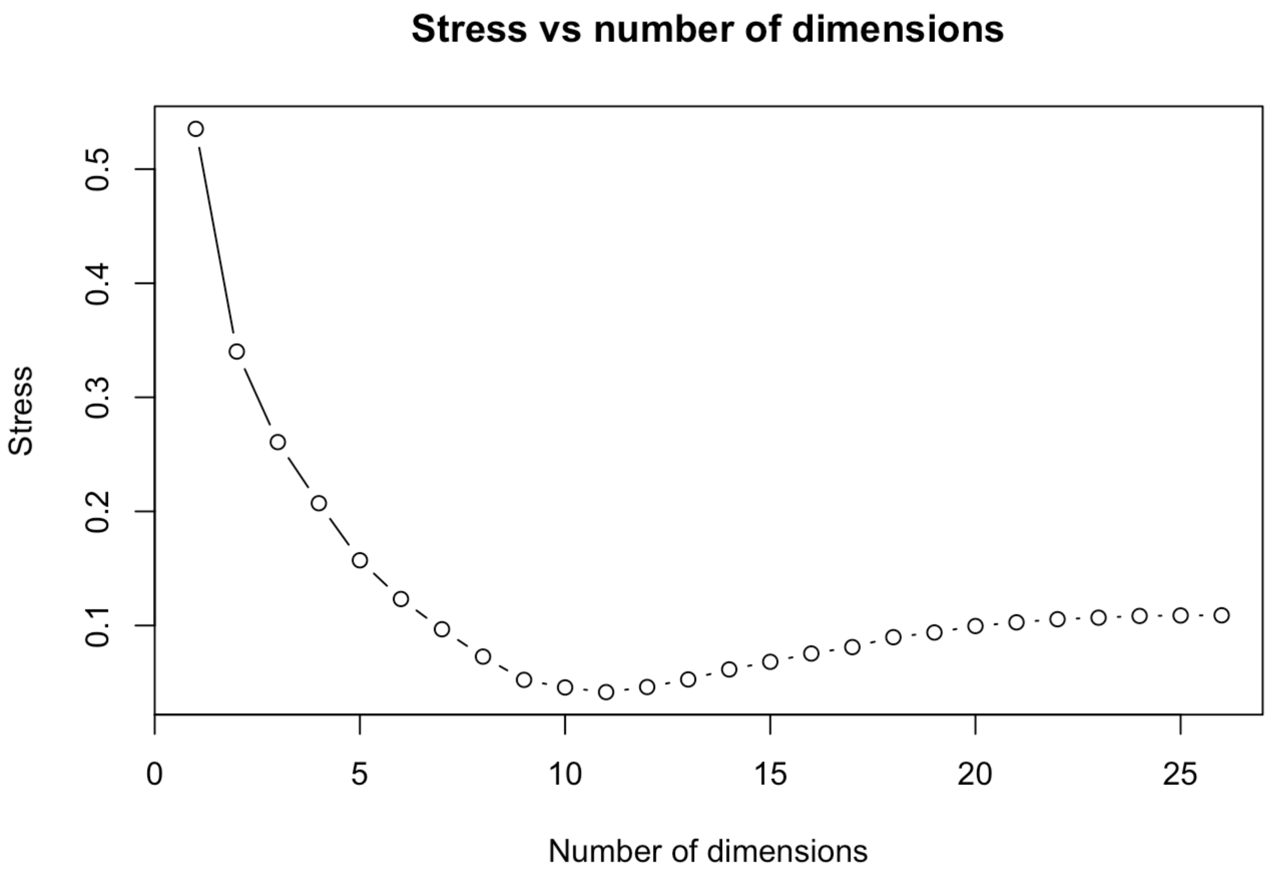
```
## [1] 0.7906348
```

The fit is slightly better as the adjusted R^2 value is `0.79` which is better than `0.70` .

10. Compute the stress for a 1, 2, 3, 4, . . . , n-dimensional solution, always using the classical MDS solution as an initial configuration. How many dimensions are necessary to obtain a good representation? Make a plot of the stress against the number of dimensions.

```
get_stress <- function(real.dist, est.dist){
  diag(est.dist) <- 0
  diag(real.dist) <- 0
  stress <- sapply(1:length(real.dist),
                   function (x) (real.dist[x] - est.dist[x])^2)
  stress <- sqrt(sum(stress)/sum((real.dist)^2))
  return(stress)
}
get_nm_mds <- function(k, dist_mat){
  out_nmds <- isoMDS(dist_mat,k=k, trace = F)
 return(as.matrix(dist(out_nmds$points)))
}

stress <- sapply(1:26, function(x)
  get_stress(md, get_nm_mds(x, md)))
plot(1:26, stress, type = 'b', main = 'Stress vs number of dimensions',
     ylab = 'Stress', xlab = 'Number of dimensions')
```



```
which.min(stress)
```

```
## [1] 11
```

Minimum stress is achieved at `11th` dimension. We can say than based on stress level of 0.1 we can choose dimensions between `6 to 11`.

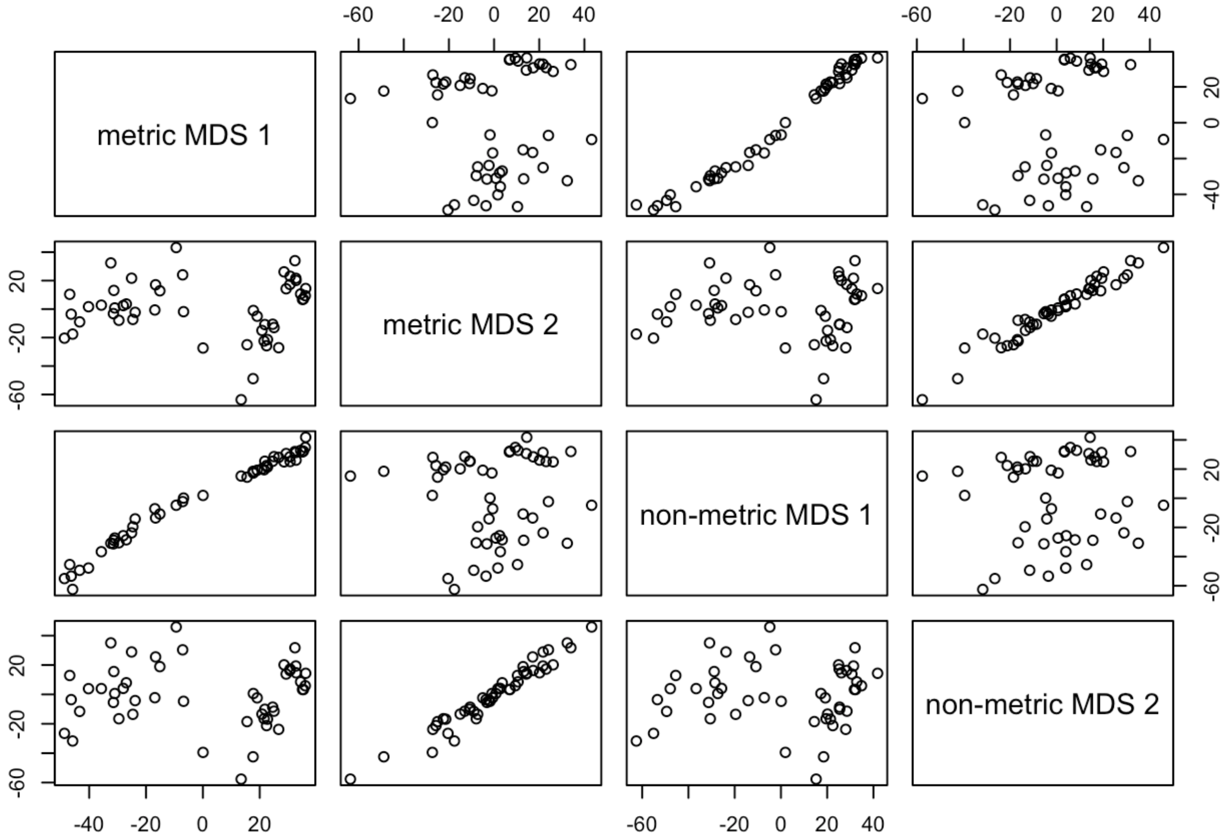
11. Compute the correlation matrix between the first two dimensions of a metric MDS and the two dimensional solution of a non-metric MDS. Make a scatterplot matrix of the 4 variables. Comment on your findings.

```
data_cor <- cor(cbind(X,X.nmds.1))
colnames(data_cor) <- c('metric MDS 1', 'metric MDS 2',
                              'non metric MDS 1', 'non metric MDS 2')
rownames(data_cor) <- c('metric MDS 1', 'metric MDS 2',
                              'non metric MDS 1', 'non metric MDS 2')

kable(data_cor, digits=3)
```

	metric MDS 1	metric MDS 2	non metric MDS 1	non metric MDS 2
metric MDS 1	1.000	0.000	0.988	0.011
metric MDS 2	0.000	1.000	0.011	0.972
non metric MDS 1	0.988	0.011	1.000	0.036
non metric MDS 2	0.011	0.972	0.036	1.000

```
pairs(cbind(X,X.nmds.1),
      labels = c('metric MDS 1', 'metric MDS 2',
          'non-metric MDS 1', 'non-metric MDS 2'))
```



We observe high correlation between the same dimension of each metric, and no correlation / little correlation between the same different dimensions as they are orthogonal to each other and uncorrelated.