

Week 1

Data filtering

Only use day 32.

Prevalence threshold. Only include taxa with more than 1 read in at least 30% of samples. This results in 39 taxa and 68 samples. The percent of the data is 46.3.

Then calculate absolute abundance.

The current covariate being used is

Current code decisions

- X is just the normal dataframe, so work needs to be done for each β_j . Should save on space and computation time.
- Currently beta loop has 1 iteration.
- Update is `beta.new = beta.old - .1update`
- V inv is `phi A -1/2 r inv A -1/2`

Trying to locate code error

- Maybe revisit
- First loop: R inv Min. 1st Qu. Median Mean 3rd Qu. Max. -0.5101610 0.0000000 0.0000000 0.0000554 0.0000000 1.7355810
- Getting an error first go: (in update beta function)

```
Error in h(simpleError(msg, call)) :
  error in evaluating the argument 'x' in selecting a method for function 'print': error in eval
In addition: Warning message:
In paste0("beta ", rep(ASV_id, each = q), " = ", beta.new) :
  restarting interrupted promise evaluation Haven't seen before
```

FIXED. This was a problem with the ASV id argument having an old object.

- Check to make sure update items match the beta items they are subtracting? Yes.
- Check to make sure update items match the beta items they are subtracting? Yes.
-
- Try with more iterations. 2nd iteration
- Third iteration. Seems to be diverging.

It seems like the 'update' value isn't changing at all? Check this.

So one problem is that it doesn't change within loops. Does it change after calculating phi and rho? Check.

This is definitely some sort of problem.

Current value for update

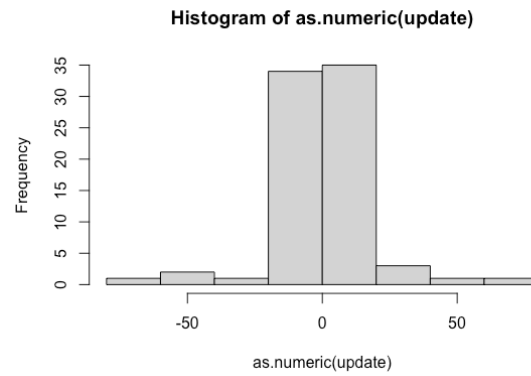


Figure 1: Histogram of update on first iteration

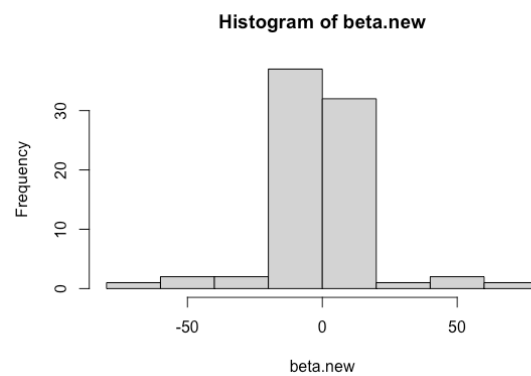


Figure 2: Histogram of first betas

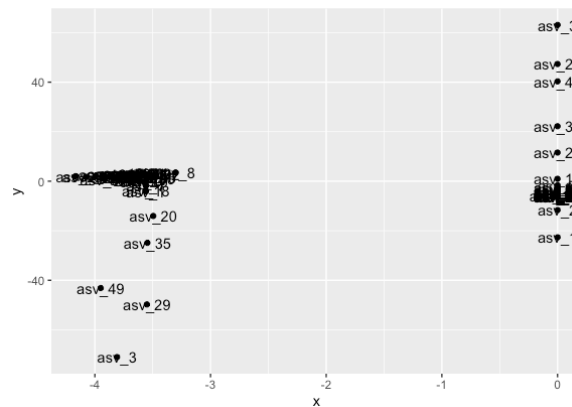


Figure 3:

```
[1] 46.2016753 -47.3258792 -6.1901234 11.6566619 -4.7021419 3.6183032 -6.3952101
[8] 6.3162696 -5.3106373 4.4185593 -6.6760288 5.7370180 -6.1907947 5.1419914
[15] -6.6558117 5.5859662 -5.5437446 4.4394525 -6.7754318 5.6839888 21.3286876
[22] -22.2086941 -6.8085055 5.6762828 -5.1983832 4.4678220 -6.6312077 5.5477890
[29] -3.3886343 2.5882506 -6.7459322 6.1195971 -4.4694171 3.4240657 -6.5218785
[36] 6.1263917 10.5371811 -11.5680454 -5.1779672 4.0250935 -6.2453704 5.1017399
[43] -6.8097845 5.7015088 -6.1182510 4.9906303 -6.6345801 5.5203673 39.1947088
```

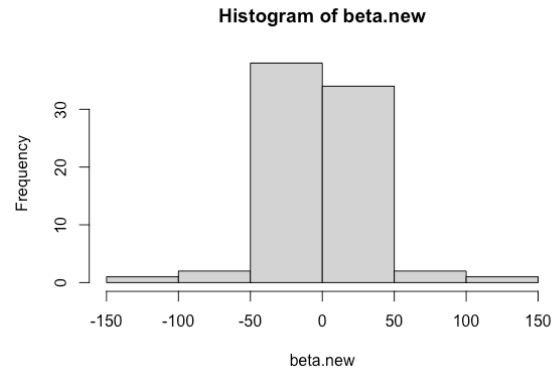


Figure 4:

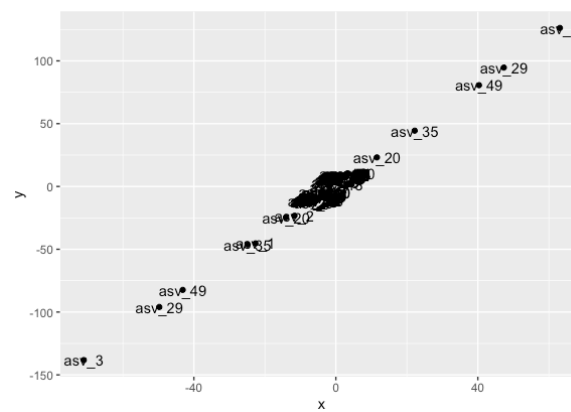


Figure 5: 2nd iteration

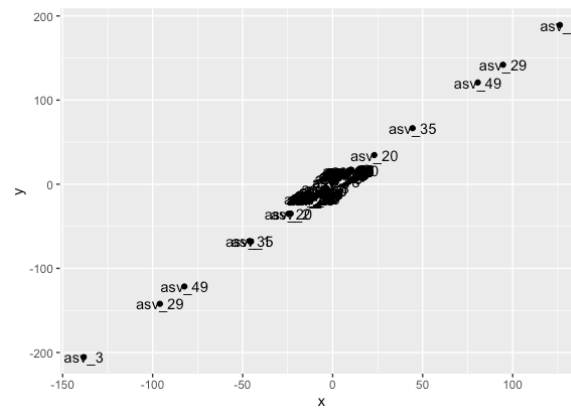
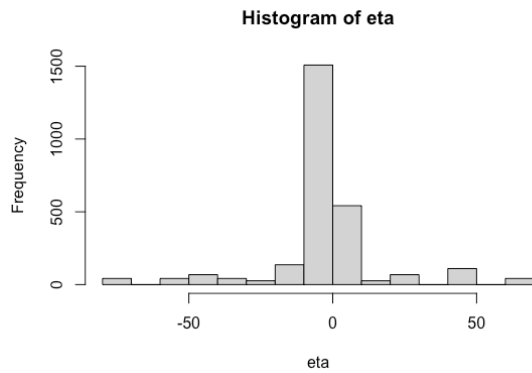


Figure 6: 3rd iteration

[50]	-40.3184609	0.6062871	22.6626964	-3.7255341	2.6365179	-6.7033879	5.6927960
[57]	67.2184146	-63.0972211	-6.8193206	5.7064405	-4.9738631	3.8700908	-6.7519904
[64]	5.6536608	-4.7809281	3.7102062	-6.7036938	6.0152241	0.2275543	-0.9651037
[71]	-6.7608940	5.6802879	-5.8318696	4.7273785	-5.3378333	5.6281093	-1.7353577
[78]	1.6122465						

- Now in Update ϕ r inv step



```

Browse[2]> summary(alpha)
      Min.   1st Qu.   Median     Mean   3rd Qu.    Max.
0.000e+00 0.000e+00 0.000e+00 7.977e+26 4.000e+00 5.037e+28

```

This is already a huge problem, and looks to be from only one ASV.

(check if hessian and EEs are same?)

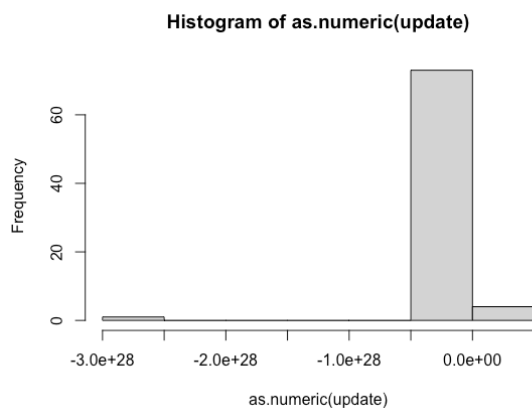
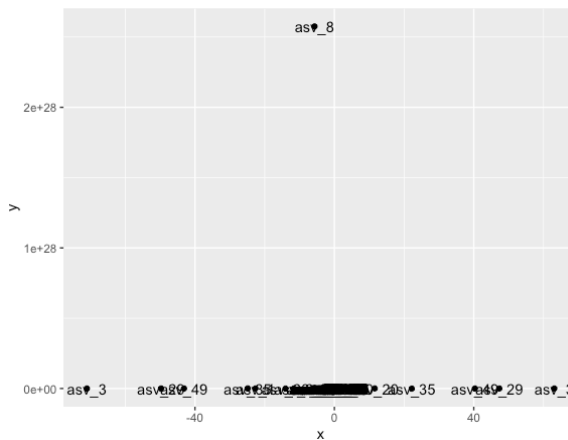
Again all the alphas are the same across samples. Why? Is this correct? Sort of. Since X is either 0 or 1.

- Back to beta loop.

Seems like a bug was found; get_eta step had beta, not beta.new. Try now.

Still think like I will need to recalculate A.

– 2nd iteration



- On third loop, update is NaN. So is hessian. Probably because Vinv is now either 0 or NaN. Probably because of alpha. All partials are NaN.

What is the cause of this? Is this because phi is just 1? should we loop back?

Should do some checking about the partials.

Should test the

The gradient to find the direction towards zero of steepest decent which would be where zero would be? Confusion how this is the same as the estimating equations equaling zero.

And also that the sum is equal to zero, vs the matrix form.

Am i forgetting an X term??? in the hessian and GEE equations... ? No, this the X values are incorporated in the partials. But are they in both the partials AND the GEE equations? No. So GEE is correct?

Is hessian a correct block matrix?

- Now try constant times update. Trying $\text{beta.new} = \text{beta.old} - .1 \text{ update}$

Somehow always gets a huge value? On like the second iteration. Range of beta values always goes up by a factor of 10 at least.

First run through:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
0.01549	0.02411	0.02804	0.20715	0.03035	1.00000

After only 1 beta iteration

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
0.00002	0.02163	0.03603	1.85100	0.10781	113.58914

After 2:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
0.000e+00	0.000e+00	2.000e+01	1.439e+26	3.080e+03	9.087e+27

- test one more time if it should be +? No. even quicker huge. Actually is this correct? Geem code uses +. How is it different? Should try again with loops.
- Try going back and forth. At least one loop of going back to phi and rho estimating. With only one beta iteration.
- R inv should change right? It does depend on rho and w, but it also depends on alpha. So it needs to change each iteration.
Also change R inv function to depend on alpha and alpha0 instead of X and beta. Change R inv section of update phi R inv to call fxn.
But this shouldnt be the problems, since we still get the problem when the beta loops just once.
- Try setting R -inv to be the identity matrix?
- Check that hessian and estimating equations are correct and solve is doing what we think it is.
- Code rearranging. Move partials calculation to separate function. Update phi rho omega function no longer returns R inv since it is calculated in Beta step as needed depending on alpha values. DONE code runs. Still problem if multiple beta loops.
- Things seem correct except one or two ASVs.
- Going back to +. Try multiple beta loops (5) Then try (1) and back and forth with phi.
- Look at residuals. At begining very right skewed. doing resid * phi results in larger numbers as phi starts off as 1.

- Trying on simulated dataset from orig paper. 45 percent prevalence.
Still problems. 2nd iteration already 10x9
- Try going back and forth now. One beta iteration

```
[1] "Iteration: 1"
[1] "unstandardized residuals"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
-0.32868 -0.17361 -0.15113  0.07366 -0.03836 13.36048
[1] "phi = 0.939547462231508, omega = 0.935468698041697 , rho = 3.17044241846978"
[1] "Beta iteration 1"
[1] "alpha"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.01549 0.02411 0.02804 0.20715 0.03035 1.00000
[1] "update"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
-61.9698 -6.3523  0.3406  0.0000  5.5856  66.1109
[1] "beta"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
-6.1970 -4.2508 -1.8167 -1.8396  0.5397  2.8024
Called from: update_beta(Y = Y, X = X, beta = beta, R_inv = R_inv, phi = phi,
      n_iter = 1, n = n, p = p, q = q, ASV_id, rho, omega, D = distance_matrix)
Browse[1]> Q
> # model!
> source(here::here("R","dm_cor_gee_clean.R"))
> zebra_res <- dm_cor_gee(Y = dat$Y, X = group, sample_id = dat$sampleID,
+       ASV_id = taxa_names(zebrafish_ps), distance_matrix = D)
[1] "Iteration: 1"
[1] "unstandardized residuals"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
-0.32868 -0.17361 -0.15113  0.07366 -0.03836 13.36048
[1] "standardized residuals"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
-0.30881 -0.16312 -0.14199  0.06921 -0.03604 12.55280
[1] "phi = 0.939547462231508, omega = 0.935468698041697 , rho = 3.17044241846978"
[1] "Beta iteration 1"
[1] "alpha"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.01549 0.02411 0.02804 0.20715 0.03035 1.00000
[1] "update"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
-61.9698 -6.3523  0.3406  0.0000  5.5856  66.1109
[1] "beta"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
-6.1970 -4.2508 -1.8167 -1.8396  0.5397  2.8024
Called from: update_beta(Y = Y, X = X, beta = beta, R_inv = R_inv, phi = phi,
      n_iter = 1, n = n, p = p, q = q, ASV_id, rho, omega, D = distance_matrix)
Browse[1]> c
[1] "Difference = 73.1214064026175"
[1] "Iteration: 2"
[1] "unstandardized residuals"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
-9.8986  -0.0543  -0.0203  1.7148  0.1129 386.2322
[1] "standardized residuals"
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
```

```

-0.0293348 -0.0001610 -0.0000601 0.0050819 0.0003345 1.1446128
[1] "phi = 0.00296353515610966, omega = 0.983583744233043 , rho = 0.308232522541486"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
0.000024 0.015260 0.024415 0.833407 0.158479 25.868966
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-19.0617 -2.4970 -1.3329 0.0000 -0.1486 55.5879
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-6.4988 -4.4549 -1.7234 -1.8396 0.3347 7.8160
Called from: update_beta(Y = Y, X = X, beta = beta, R_inv = R_inv, phi = phi,
  n_iter = 1, n = n, p = p, q = q, ASV_id, rho, omega, D = distance_matrix)
Browse[1]> c
[1] "Difference = 30.5331749772207"
[1] "Iteration: 3"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-24.2972 -0.0415 -0.0078 9.9096 0.2748 2818.1882
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-1.413e-03 -2.410e-06 -4.500e-07 5.762e-04 1.598e-05 1.639e-01
[1] "phi = 5.81411712568661e-05, omega = 0.984549152947368 , rho = 0.614651231064176"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
0.00001 0.01081 0.01766 3.53512 0.32766 157.38310
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-12.58427 0.01956 0.06204 0.00000 0.17577 7.83440
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-5.9998 -4.4254 -2.1959 -1.8396 0.3538 7.9364
Called from: update_beta(Y = Y, X = X, beta = beta, R_inv = R_inv, phi = phi,
  n_iter = 1, n = n, p = p, q = q, ASV_id, rho, omega, D = distance_matrix)
Browse[1]> c
[1] "Difference = 8.61011875874332"
[1] "Iteration: 4"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-23.9501 -0.0401 -0.0070 7.4950 0.2938 1796.3779
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-3.337e-03 -5.590e-06 -9.700e-07 1.044e-03 4.094e-05 2.503e-01
[1] "phi = 0.00013933155067034, omega = 0.984796476225481 , rho = 0.440094621222131"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
0.00003 0.01035 0.01816 3.84221 0.32776 168.00334
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-14.033385 0.004312 0.053323 0.000000 0.271548 7.106205
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-7.0599 -4.4007 -1.9964 -1.8396 0.3889 8.2196

```

```

Called from: update_beta(Y = Y, X = X, beta = beta, R_inv = R_inv, phi = phi,
  n_iter = 1, n = n, p = p, q = q, ASV_id, rho, omega, D = distance_matrix)
Browse[1]> c
[1] "Difference = 9.72467917960964"
[1] "Iteration: 5"
[1] "unstandardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-24.1412  -0.0376  -0.0064   7.4793   0.3330 1292.1849
[1] "standardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-5.580e-03 -8.680e-06 -1.480e-06  1.729e-03  7.697e-05  2.987e-01
[1] "phi = 0.000231139860008589, omega = 0.981520887502283 , rho = 0.369866079073633"
[1] "Beta iteration 1"
[1] "alpha"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
 0.00006   0.01129   0.01979   4.49665   0.29609 192.75334
[1] "update"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-18.66292  -0.03128   0.04199   0.00000   0.41205  10.10912
[1] "beta"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-8.3170 -4.3644 -2.1857 -1.8396  0.3966  8.6902
Called from: update_beta(Y = Y, X = X, beta = beta, R_inv = R_inv, phi = phi,
  n_iter = 1, n = n, p = p, q = q, ASV_id, rho, omega, D = distance_matrix)
Browse[1]> Q
> # model!
> source(here::here("R","dm_cor_gee_clean.R"))
> zebra_res <- dm_cor_gee(Y = dat$Y, X = group, sample_id = dat$sampleID,
+                        ASV_id = taxa_names(zebrafish_ps), distance_matrix = D)
[1] "Iteration: 1"
[1] "unstandardized residuals"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-0.32868 -0.17361 -0.15113  0.07366 -0.03836 13.36048
[1] "standardized residuals"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-0.30881 -0.16312 -0.14199  0.06921 -0.03604 12.55280
[1] "phi = 0.939547462231508, omega = 0.935468698041697 , rho = 3.17044241846978"
[1] "Beta iteration 1"
[1] "alpha"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
0.01549 0.02411 0.02804 0.20715 0.03035 1.00000
[1] "update"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-61.9698 -6.3523  0.3406  0.0000  5.5856  66.1109
[1] "beta"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-6.1970 -4.2508 -1.8167 -1.8396  0.5397  2.8024
[1] "Difference = 73.1214064026175"
[1] "Iteration: 2"
[1] "unstandardized residuals"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-9.8986  -0.0543  -0.0203  1.7148  0.1129 386.2322
[1] "standardized residuals"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-0.0293348 -0.0001610 -0.0000601  0.0050819  0.0003345  1.1446128
[1] "phi = 0.00296353515610966, omega = 0.983583744233043 , rho = 0.308232522541486"

```



```

[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
0.000024 0.015260 0.024415 0.833407 0.158479 25.868966
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-19.0617 -2.4970 -1.3329  0.0000 -0.1486 55.5879
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-6.4988 -4.4549 -1.7234 -1.8396  0.3347  7.8160
[1] "Difference = 30.5331749772207"
[1] "Iteration: 3"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-24.2972 -0.0415 -0.0078  9.9096  0.2748 2818.1882
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-1.413e-03 -2.410e-06 -4.500e-07  5.762e-04  1.598e-05  1.639e-01
[1] "phi = 5.81411712568661e-05, omega = 0.984549152947368 , rho = 0.614651231064176"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
0.00001 0.01081 0.01766 3.53512 0.32766 157.38310
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-12.58427 0.01956 0.06204 0.00000 0.17577 7.83440
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-5.9998 -4.4254 -2.1959 -1.8396  0.3538 7.9364
[1] "Difference = 8.61011875874332"
[1] "Iteration: 4"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-23.9501 -0.0401 -0.0070  7.4950  0.2938 1796.3779
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-3.337e-03 -5.590e-06 -9.700e-07  1.044e-03  4.094e-05  2.503e-01
[1] "phi = 0.00013933155067034, omega = 0.984796476225481 , rho = 0.440094621222131"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
0.00003 0.01035 0.01816 3.84221 0.32776 168.00334
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-14.033385 0.004312 0.053323 0.000000 0.271548 7.106205
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-7.0599 -4.4007 -1.9964 -1.8396  0.3889 8.2196
[1] "Difference = 9.72467917960964"
[1] "Iteration: 5"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-24.1412 -0.0376 -0.0064  7.4793  0.3330 1292.1849
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-5.580e-03 -8.680e-06 -1.480e-06  1.729e-03  7.697e-05  2.987e-01

```

```

[1] "phi = 0.000231139860008589, omega = 0.981520887502283 , rho = 0.369866079073633"
[1] "Beta iteration 1"
[1] "alpha"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
0.00006  0.01129   0.01979   4.49665   0.29609  192.75334
[1] "update"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-18.66292 -0.03128   0.04199   0.00000   0.41205   10.10912
[1] "beta"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-8.3170 -4.3644 -2.1857 -1.8396  0.3966   8.6902
[1] "Difference = 12.9032787639054"
[1] "Iteration: 6"
[1] "unstandardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-24.3482  -0.0361  -0.0057   11.0754   0.3874  1013.8554
[1] "standardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-3.938e-03 -5.840e-06 -9.200e-07  1.791e-03  6.266e-05  1.640e-01
[1] "phi = 0.000161748619031987, omega = 0.977301954235005 , rho = 0.426519229141335"
[1] "Beta iteration 1"
[1] "alpha"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
0.00011  0.01054   0.02011   5.82520   0.35510  239.40531
[1] "update"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-23.72076 -0.03532   0.06225   0.00000   0.88363   12.20260
[1] "beta"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-10.0963 -4.2798 -2.0745 -1.8396  0.3993   9.0211
[1] "Difference = 17.0379943115704"
[1] "Iteration: 7"
[1] "unstandardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-24.0014  -0.0324  -0.0046   24.7836   0.4011  2630.8079
[1] "standardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-6.732e-04 -9.100e-07 -1.300e-07  6.952e-04  1.125e-05  7.379e-02
[1] "phi = 2.80500340906498e-05, omega = 0.979940749278977 , rho = 0.767286381667904"
[1] "Beta iteration 1"
[1] "alpha"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
0.00001  0.01153   0.02309   7.19580   0.36725  277.28483
[1] "update"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-20.567520  0.006673   0.049880   0.000000   0.864810   18.328470
[1] "beta"
      Min. 1st Qu.  Median     Mean 3rd Qu.     Max.
-12.0073 -4.2858 -1.5401 -1.8396  0.4062   9.0784
[1] "Difference = 15.8878677458046"
[1] "Iteration: 8"
[1] "unstandardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-22.289   -0.035   -0.005   60.270   0.406  6753.782
[1] "standardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.

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-9.624e-05 -1.490e-07 -2.000e-08 2.602e-04 1.753e-06 2.916e-02
[1] "phi = 4.31785512143427e-06, omega = 0.981709982661524 , rho = 0.961916134714736"
[1] "Beta iteration 1"
[1] "alpha"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
0.00000  0.01248   0.02315   8.25611   0.51991 286.74174
[1] "update"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-14.016899  0.004457   0.025964   0.000000   0.518477 14.558641
[1] "beta"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-13.3450 -4.2257  -1.0646  -1.8396   0.4119   9.0873
[1] "Difference = 9.80437753991997"
[1] "Iteration: 9"
[1] "unstandardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-19.672   -0.030   -0.005  101.003   0.438 11249.150
[1] "standardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-3.053e-05 -4.700e-08 -7.000e-09 1.568e-04 6.800e-07 1.746e-02
[1] "phi = 1.55207729785946e-06, omega = 0.983803047522562 , rho = 0.868270247649568"
[1] "Beta iteration 1"
[1] "alpha"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
0.00000  0.01256   0.02430   9.55604   0.65224 289.15841
[1] "update"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-15.37337  0.00853   0.03123   0.00000   0.46301 11.10487
[1] "beta"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-14.8315 -4.1920  -1.0642  -1.8396   0.4288   9.0904
[1] "Difference = 7.98261948839764"
[1] "Iteration: 10"
[1] "unstandardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-18.309   -0.029   -0.004  129.332   0.434 13959.282
[1] "standardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-1.833e-05 -2.900e-08 -4.000e-09 1.295e-04 4.340e-07 1.397e-02
[1] "phi = 1.00102793904902e-06, omega = 0.983523869706203 , rho = 0.773146920273194"
[1] "Beta iteration 1"
[1] "alpha"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
0.0000  0.0136   0.0256  10.5181   1.0068 291.3046
[1] "update"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-18.19715  0.01472   0.03910   0.00000   0.50783  7.87463
[1] "beta"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-16.6097 -4.1478  -1.0636  -1.8396   0.4337   9.0925
[1] "Difference = 7.70284144296252"
[1] "Iteration: 11"
[1] "unstandardized residuals"
      Min.   1st Qu.   Median     Mean   3rd Qu.     Max.
-17.543   -0.031   -0.004  138.071   0.431 13422.175
[1] "standardized residuals"

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      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-1.812e-05 -3.200e-08 -4.000e-09  1.426e-04  4.450e-07  1.386e-02
[1] "phi = 1.032894614361e-06, omega = 0.97736747447489 , rho = 0.74371714175976"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
  0.00000  0.01464  0.02724  11.27012  1.10443 293.65488
[1] "update"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-20.73626  0.01951  0.04600  0.00000  0.58505  4.40622
[1] "beta"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-18.6416  -4.1024 -1.0627 -1.8396  0.4474  9.0946
[1] "Difference = 9.52078537828392"
[1] "Iteration: 12"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
   -17.379   -0.036   -0.004  155.679    0.433 19057.502
[1] "standardized residuals"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-1.720e-05 -3.600e-08 -4.000e-09  1.541e-04  4.280e-07  1.886e-02
[1] "phi = 9.8959962990127e-07, omega = 0.942937105631337 , rho = 1.16337548753744"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
  0.00000  0.01520  0.02992  11.77454  1.11314 296.63069
[1] "update"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-18.936152  0.003131  0.038862  0.000000  0.499806  4.293101
[1] "beta"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-20.4962  -4.0756 -1.0616 -1.8396  0.4721  9.0966
[1] "Difference = 9.14039783751598"
[1] "Iteration: 13"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
   -15.77   -0.03    0.00  245.13    0.46 51778.12
[1] "standardized residuals"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-4.615e-06 -1.000e-08 -1.000e-09  7.172e-05  1.350e-07  1.515e-02
[1] "phi = 2.92597293152538e-07, omega = 0.87531027288368 , rho = 2.48890365167915"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
  0.00000  0.01679  0.03344  13.39275  1.12181 298.59983
[1] "update"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-6.136997 -0.003978  0.008558  0.000000  0.149141  4.202295
[1] "beta"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
-21.0967  -4.0554 -1.0611 -1.8396  0.4762  9.0972
[1] "Difference = 3.67821574427527"
[1] "Iteration: 14"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median    Mean    3rd Qu.    Max.
   -15.62   -0.03    0.00  294.70    0.47 72050.71

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[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-2.590e-06 -6.000e-09  0.000e+00  4.886e-05  7.800e-08  1.195e-02
[1] "phi = 1.65792585919558e-07, omega = 0.839776237723401 , rho = 3.4180370064409"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.00000  0.01796  0.03444  14.00361  1.12401 298.63102
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-2.977099 -0.003386  0.003406  0.000000  0.064081  2.237480
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-21.3456  -4.0503  -1.0609  -1.8396   0.4774   9.0976
[1] "Difference = 1.799666661543"
[1] "Iteration: 15"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
   -15.91    -0.03     0.00   321.93     0.47 82856.93
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-2.040e-06 -4.000e-09  0.000e+00  4.129e-05  6.100e-08  1.063e-02
[1] "phi = 1.28248839357702e-07, omega = 0.828273602668781 , rho = 3.7252933030863"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.00000  0.01818  0.03485  14.29110  1.12504 298.59553
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-2.350114 -0.002299  0.002545  0.000000  0.044816  1.784247
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-21.5192  -4.0463  -1.0608  -1.8396   0.4782   9.0978
[1] "Difference = 1.36297655529556"
[1] "Iteration: 16"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
   -16.13    -0.03     0.00   343.41     0.48 91301.89
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.724e-06 -4.000e-09  0.000e+00  3.671e-05  5.100e-08  9.760e-03
[1] "phi = 1.06895154366371e-07, omega = 0.821954985685942 , rho = 3.89260965287554"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.00000  0.01834  0.03513  14.46801  1.12580 298.57293
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-2.009067 -0.001680  0.002094  0.000000  0.034465  1.545656
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-21.6570  -4.0429  -1.0606  -1.8396   0.4788   9.0981
[1] "Difference = 1.14164129574494"
[1] "Iteration: 17"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.

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-16.33    -0.03     0.00   362.13     0.48 98572.87
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.509e-06 -3.000e-09  0.000e+00  3.346e-05  4.400e-08  9.109e-03
[1] "phi = 9.24101535408146e-08, omega = 0.817752143524932 , rho = 4.001984252125"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.000000  0.01848   0.03537  14.59056   1.12642  298.55984
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.783508 -0.001677  0.001754  0.000000  0.029174  1.387214
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-21.7730 -4.0400  -1.0605  -1.8396   0.4793   9.0982
[1] "Difference = 1.00252084244208"
[1] "Iteration: 18"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
   -16.50    -0.03     0.00    379.18     0.48 105113.72
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.348e-06 -3.000e-09  0.000e+00  3.098e-05  4.000e-08  8.588e-03
[1] "phi = 8.17024565180398e-08, omega = 0.81512168259833 , rho = 4.07040272560558"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.000000  0.01860   0.03557  14.68128   1.12696  298.55321
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.624484 -0.001357  0.001587  0.000000  0.025886  1.275652
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-21.875  -4.037  -1.060  -1.840   0.480   9.098
[1] "Difference = 0.909333461307958"
[1] "Iteration: 19"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
   -16.67    -0.03     0.00    395.15     0.49 111172.40
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.222e-06 -2.000e-09  0.000e+00  2.898e-05  3.600e-08  8.152e-03
[1] "phi = 7.33305412394345e-08, omega = 0.81275529367871 , rho = 4.13181563693982"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.000000  0.01871   0.03574  14.75118   1.12743  298.55116
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.496403 -0.001123  0.001456  0.000000  0.023598  1.182527
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-21.9653 -4.0348  -1.0603  -1.8396   0.4807   9.0986
[1] "Difference = 0.834171847811243"
[1] "Iteration: 20"
[1] "unstandardized residuals"

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      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-16.82    -0.03     0.00    410.29     0.49 116852.54
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.120e-06 -2.000e-09  0.000e+00  2.732e-05  3.300e-08  7.780e-03
[1] "phi = 6.65784120493533e-08, omega = 0.81109333216788 , rho = 4.17480938728343"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.00000    0.01882    0.03671   14.80723    1.12785  298.55240
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.3961088 -0.0009499  0.0013521  0.0000000  0.0218359  1.1091146
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-22.0476   -4.0324   -1.0603   -1.8396    0.4813    9.0987
[1] "Difference = 0.775798299095333"
[1] "Iteration: 21"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-16.96    -0.03     0.00    424.84     0.49 122251.16
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.034e-06 -2.000e-09  0.000e+00  2.591e-05  3.000e-08  7.454e-03
[1] "phi = 6.09768859792844e-08, omega = 0.809388414671349 , rho = 4.21959678375907"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.00000    0.01891    0.03676   14.85325    1.12823  298.55606
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.3088934 -0.0008111  0.0011964  0.0000000  0.0203318  1.0435144
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-22.1231   -4.0303   -1.0602   -1.8396    0.4818    9.0988
[1] "Difference = 0.724929256292401"
[1] "Iteration: 22"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-17.10    -0.03     0.00    438.86     0.49 127406.42
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-9.620e-07 -2.000e-09  0.000e+00  2.469e-05  2.700e-08  7.167e-03
[1] "phi = 5.6253998469363e-08, omega = 0.808112293735121 , rho = 4.2508573317048"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
 0.00000    0.01900    0.03677   14.89208    1.12858  298.56155
[1] "update"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-1.2376627 -0.0007025  0.0010839  0.0000000  0.0191143  0.9896530
[1] "beta"
      Min.    1st Qu.    Median      Mean    3rd Qu.      Max.
-22.1930   -4.0282   -1.0601   -1.8396    0.4823    9.0989
[1] "Difference = 0.683596353407489"
[1] "Iteration: 23"

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[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-17.22    -0.03     0.00    452.49     0.49 132372.85
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-8.990e-07 -2.000e-09  0.000e+00  2.362e-05  2.500e-08  6.910e-03
[1] "phi = 5.21985800496743e-08, omega = 0.807087454024426 , rho = 4.27629557449581"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
 0.00000   0.01909   0.03677  14.92542   1.12890  298.56839
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-1.1767636 -0.0006142  0.0010144  0.0000000  0.0180836  0.9431323
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-22.2583   -4.0263   -1.0600   -1.8396    0.4828    9.0990
[1] "Difference = 0.648328105483543"
[1] "Iteration: 24"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-17.35     -0.03     0.00    465.79     0.49 137182.89
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-8.440e-07 -2.000e-09  0.000e+00  2.267e-05  2.400e-08  6.677e-03
[1] "phi = 4.86706590722903e-08, omega = 0.806196366262477 , rho = 4.29792968866025"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
 0.00000   0.01909   0.03678  14.95445   1.12921  298.57626
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-1.1235722 -0.0005412  0.0009542  0.0000000  0.0171907  0.9020291
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-22.3197   -4.0244   -1.0600   -1.8396    0.4832    9.0991
[1] "Difference = 0.617539235770946"
[1] "Iteration: 25"
[1] "unstandardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-17.46     -0.03     0.00    478.83     0.49 141859.99
[1] "standardized residuals"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-7.960e-07 -2.000e-09  0.000e+00  2.182e-05  2.200e-08  6.464e-03
[1] "phi = 4.55692681244084e-08, omega = 0.80541706862667 , rho = 4.31647868718837"
[1] "Beta iteration 1"
[1] "alpha"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
 0.00000   0.01909   0.03678  14.98010   1.12949  298.58490
[1] "update"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-1.0765919 -0.0004804  0.0009014  0.0000000  0.0164077  0.8653577
[1] "beta"
      Min.    1st Qu.    Median      Mean   3rd Qu.      Max.
-22.3777   -4.0226   -1.0599   -1.8396    0.4836    9.0992
[1] "Difference = 0.590359570128033"

```


- It looks like it is working? With +, and only 1 update each. And a small update.
- Wondering if a separate checklist and journal file would be a good idea.
- I THINK IT IS RUNNING!

Things i did:

- Change from - to +
- First do phi/rho/omega loop, then ONE beta loop. With update of .1 scaled.
- About a 2.5 min runtime with convergence defined as sum of absolute difference between beta values
j .1. 225 iterations
-

- Try removing step update.

```

–      [1] "Iteration: 1"
      [1] "phi = 0.939547462231508, omega  = 0.935468698041697 , rho = 3.17044241846978"
      [1] "Beta iteration 1"
      [1] "Difference = 731.214064026175"
      [1] "Iteration: 2"
      [1] "phi = 1.74415189832243e-55, omega  = 0 , rho = 363.857722495099"
      [1] "Beta iteration 1"
      [1] "Difference = 0"

```

- Try .5 Still only 2 loops.

- Graphs:
- **Meeting**
- Check eigenvalues of update and scalar by minimum.
- Implement line search. Numerical Optimization book ch 11.2

Week 2

Next steps (from paper)

1. Currently 39 taxa across 48 samples, Increase number of taxa, increase percent zero
2. Try increasing covariates
3. Think about genus level analysis
4. Choose α more automatically (simple line search)
5. How to test significance of β ? Role of ω in this test.
6. Simulation

Start working on presentation, which should motivate and give a good todo on the way. Going over definitions of working correlation matrix, GEE equations, and update rho and beta steps. Then will include questions (3) and (5). Include line search if implemented. Data analysis results? TBD.

Goal implement the line search: (write up)

Work on presenting the data analysis portion on the presentation.

Today's agenda and order:

- Re-do analysis: number 1 and 2: Increase number of taxa.(done) Increase covariates.
- Probably not writing this up yet, wait for line search step. But can include the data preprocessing slide
- Implement and write up line search
- Compare results for independence, different algorithm
- Calculate sandwich estimator, identify significance, figure out which ASVs corresponding to.

Meeting agenda:

Creating presentation: Did we forget that the phylogenetic portion has to be positive?

Ask about how to make presentations longer, always rushed and quick. Ask for feedback.

If I use minus hessian and minus it stalls out on 2nd iteration. Weird that this doesnt work?

What should the initial value of rho and omega be in the nls optim? Currently always .5 and 1. Would this change results?

Item 1 Increase number of taxa

Processing and filtering, and covariate information:

Still had to match tip labels. Using phyloseq object from Tom (in paireddata and ps Box folder) and tree from?

Only looking at day 32 Unfiltered day 32 has 3895 taxa across 68 samples. 98.4 percent zero entries

Keep ASV if present in at least 10 % of samples

Results in 166 taxa in 68 samples. 75% of data are zero.

Covariates. 1 if NC, 0 if ND.

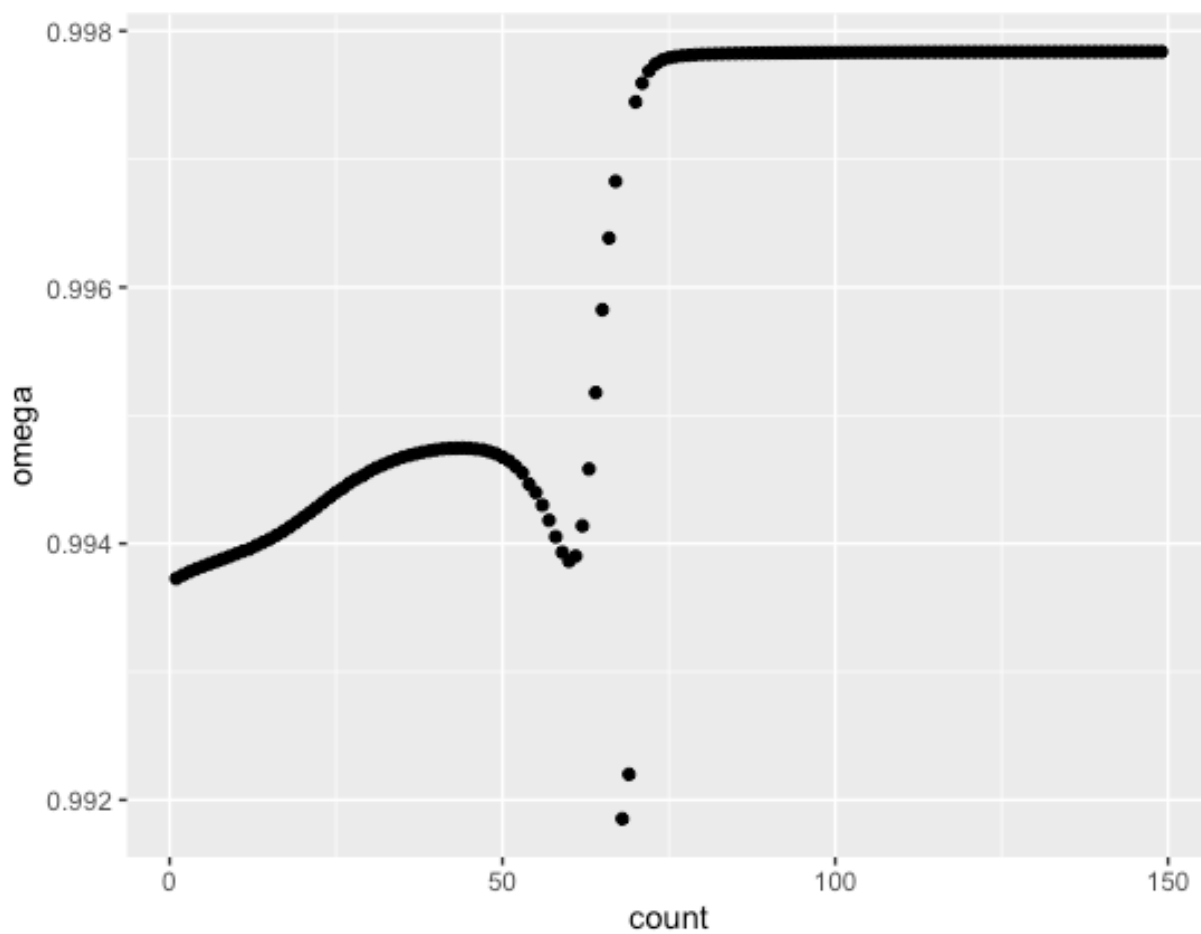
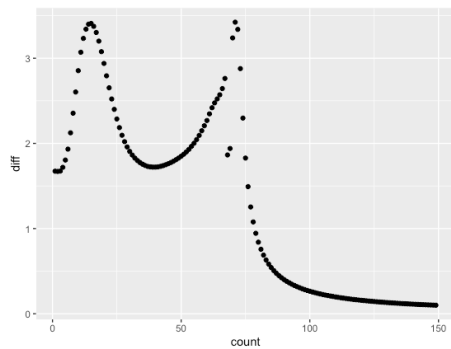
RESULTS:

```
[1] "Iteration: 149"
[1] "phi = 7.98731653686342e-12, omega = 0.997838301680261 , rho = 0.104950295482753"
[1] "Beta iteration 1"
[1] "Difference = 0.0998224219301233"
```

So not great, and very different from previous. So high an omega would mean all weight is towards the compositional correlation. So low an rho means.

Also had a slower run time. 20 minutes.

Some interesting plots! Seems like something happens around iteration 60 that completely changes the results.



Initial values of rho and omega in nlsoptim

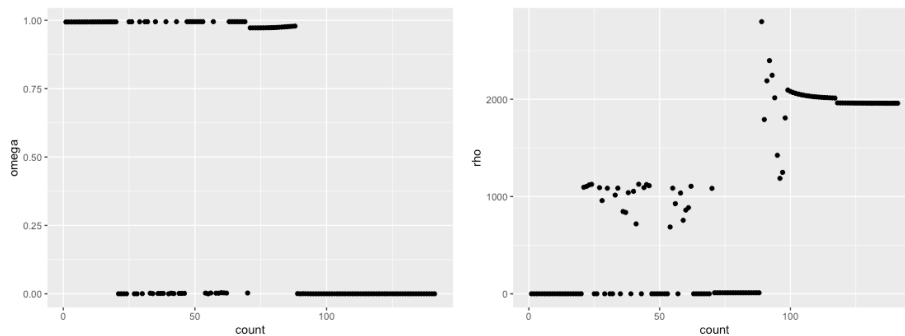
Should we use .5 and 1 or the previous iteration values?

What would happen if we used .5 and 10?

Seems like it makes it very unstable.

Stability seems to not be great. Might be finding local mins?

(Note, changing max iterations to 50)



With this last run, the last betas seem to be reasonable numbers, between -10 and 10 and roughly normally distributed, although a couple around -40 and -30

Did work on data best practices: Save all test datasets so dont have to rerun code. Currently have 10, 20 and 30 percent filtering, with the one covariate.

Filtering of 20 percent

With rho start value of 10. Difference is 0 after 2 iterations. What if stronger tolerance? try diff $\geq .01$

Should save convergence results of nls optim.

Quickly add new covariate on med dataset. Then go to line search. Hopefully will help with stability?

Still high value of omega, rho 11.

Somewhat normally distributed betas, with some very large ones, same for residuals.

Try the "larger" dataset with minus: Stop after first iteration: Infinite values due to infinite valued alpha or A.

Seems to be really popping back between omega as 0 and 1 and rho as .05 and 1000.

Back to using 30 percent Also note that gamma is at .05

When gamma is .05 and rho is 10, ends in 3 iterations...

When gamma is .1, rho 10, still get omega .9, rho small

Original omega .8, rho 4

Tried back to gamma of .05 and it works...

Line search

$G+ > G$

So we would need to calculate $G+$ using new value an G for old beta values

Currently just making an "old" version of literally all calculations in the gee equations.

I'm confused.

Stalls out on 2nd iteration... But actually the minus hess part doesnt make a difference here? Tried with

Ok, but the update is identical regardless...??

Meeting

Add more aggressive constant to hessian. E.g. Look at eigenvalues and add a fraction of the eigenvalue. largest/1000 or soemthing distribution of eigenvalues.

Would add a penalty for to account for high dimensionality. But do later.