Supplementary Figures

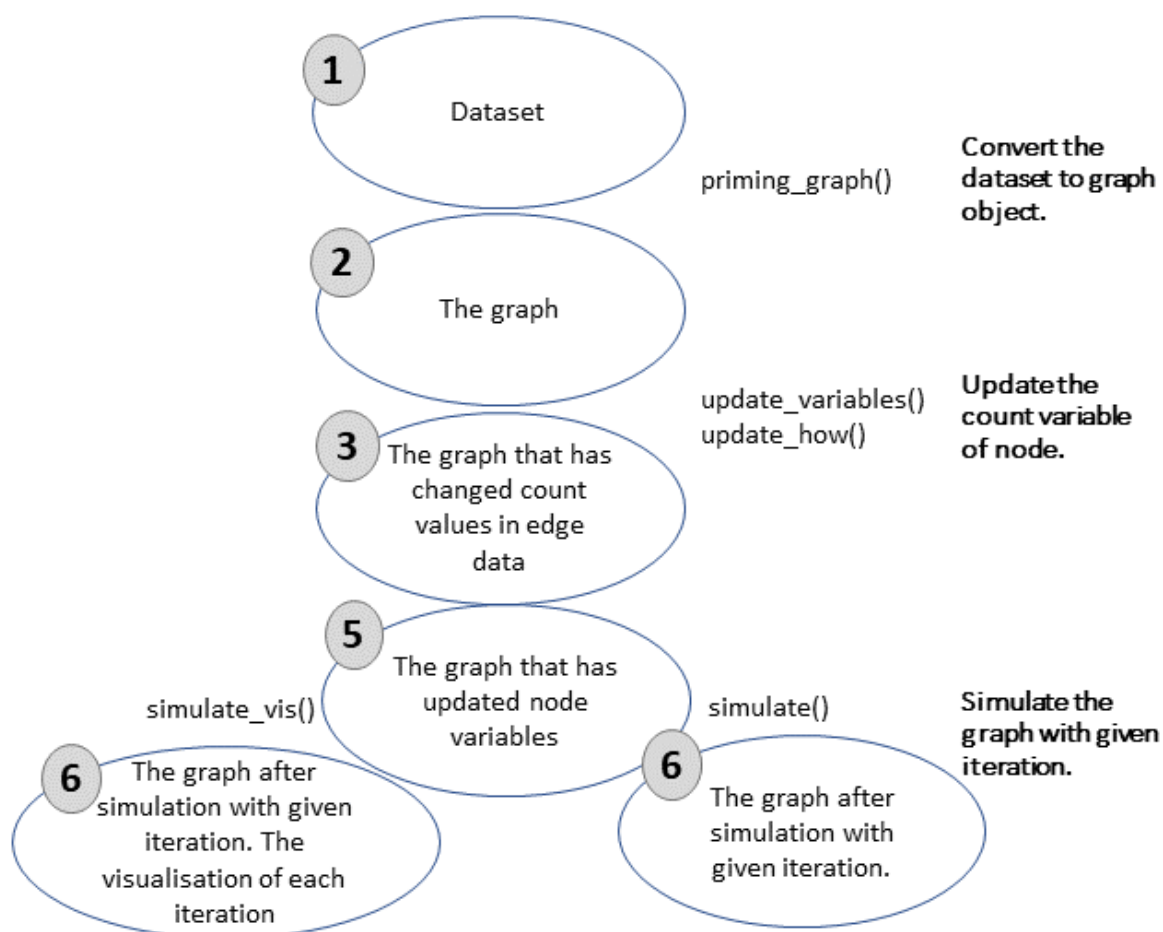*Selcen Ari*
Alper Yilmaz

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Figure S1: Workflow for simulation of competing endogenous RNA regulations. Graph object in steps 2-6 is saved and updated continuously.

```
# install.packages('devtools')
# devtools::install_github('selcenari/ceRNAnetsim')
library(ceRNAnetsim)
```

minsamp dataset analysis at lack of interaction factors.

```
minsamp <- readRDS("data/minsamp.RDS")
```

```
priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", title = "Minimal dataset in steady-state conditions")
```
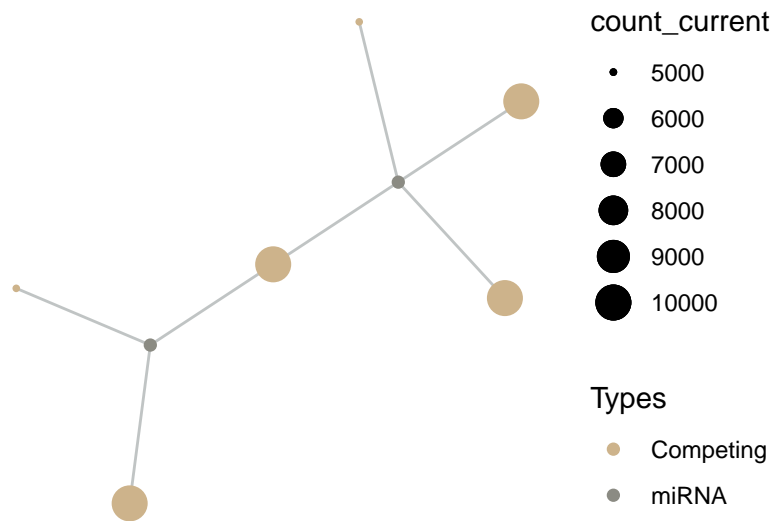

Figure S2: Minimal Dataset in Steady-state

```
priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression) %>% update_how("Gene2",
    2) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", title = "Gene2 Upregulation without interaction facto
```
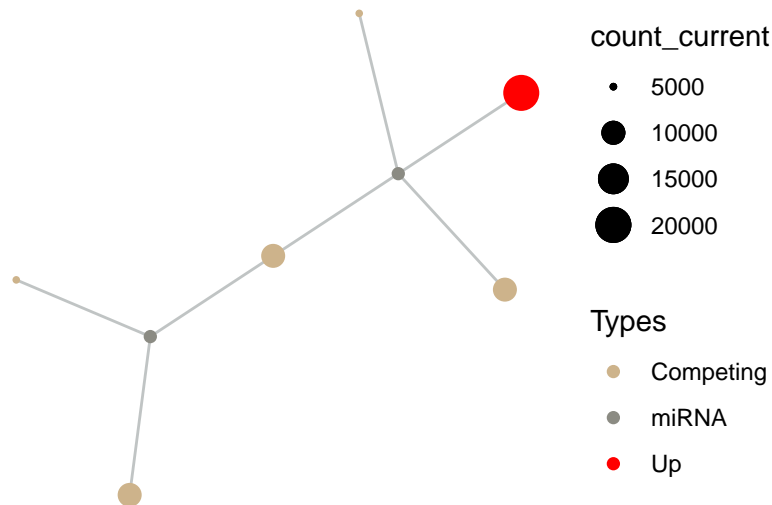
Gene2 Upregulation without interaction

Figure S3: Gene2 Upregulation on Minimal Dataset

```
priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression) %>% update_how("Gene2",
    2) %>% simulate(cycle = 1) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", Downregulation = "blue",
    title = "a)")

priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression) %>% update_how("Gene2",
    2) %>% simulate(2) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", Downregulation = "blue",
    title = "b)")
```
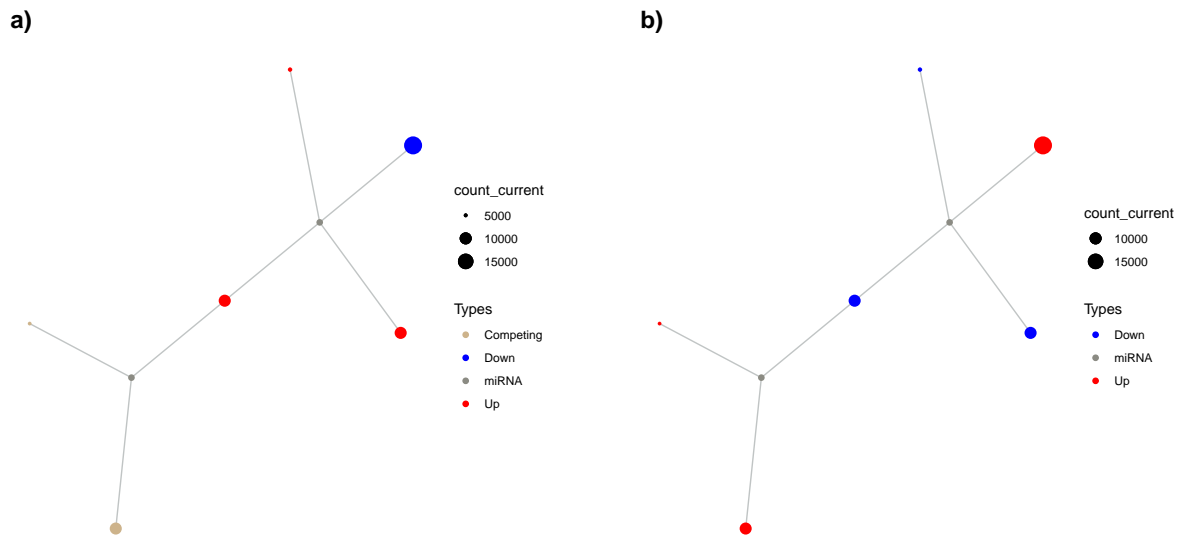
a)

b)

Figure S4: Sequential iteration of minsamp data. a) First response of system to Gene2 upregulation (2nd iteration). b) Spreading of perturbation on system (3th iteration)

minsamp dataset analysis with interaction factors.

```
priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression, aff_factor = c(energy,
        seed_type), deg_factor = region) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", title = "Minimal dataset with interaction factors in steady-state conditions
```

Minimal dataset with interaction factor
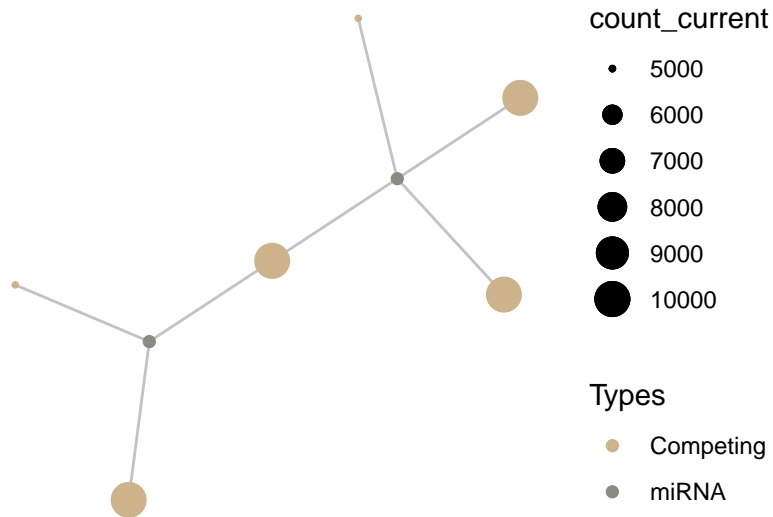

Figure S5: Minimal Dataset with interaction factors in Steady-state

```r
priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression, aff_factor = c(energy,
        seed_type), deg_factor = region) %>% update_how("Gene2",
    2) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", title = "Gene2 Upregulation with interaction factors")
```
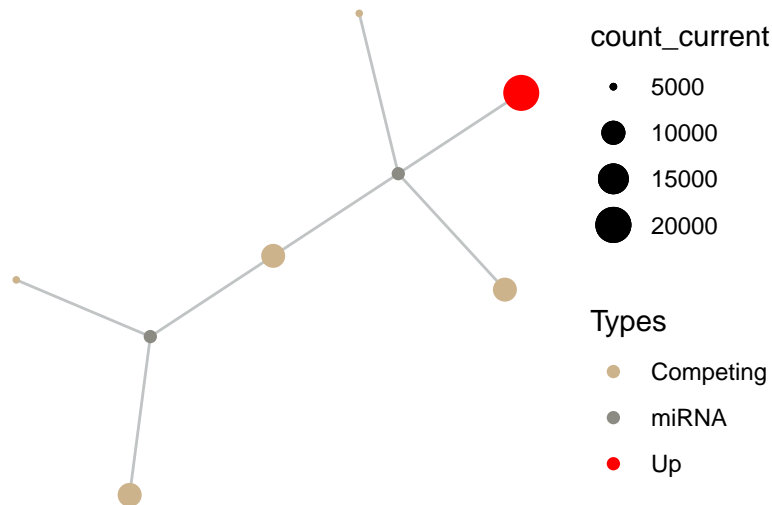
Gene2 Upregulation with interaction fa

Figure S6: When Gene2 is upregulated on Minimal Dataset with interaction factors

```r
priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression, aff_factor = c(energy,
        seed_type), deg_factor = region) %>% update_how("Gene2",
    2) %>% simulate(cycle = 1) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", Downregulation = "blue",
    title = "a)")

priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression, aff_factor = c(energy,
        seed_type), deg_factor = region) %>% update_how("Gene2",
    2) %>% simulate(cycle = 2) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", Downregulation = "blue",
    title = "b)")
```
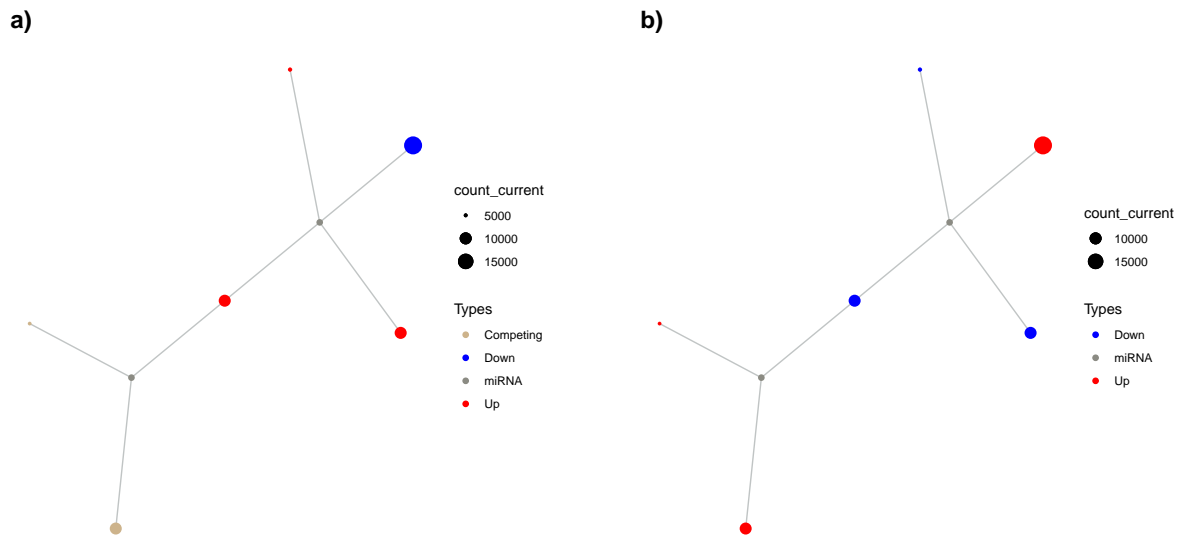
Figure S7: Sequential iteration of minsamp data with interaction factors a)First response of system to Gene2 upregulation (2nd iteration). b)Spreading of perturbation on system (3th iteration)

Common target perturbation in *minsamp* dataset.

```r
priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression, aff_factor = c(energy,
        seed_type), deg_factor = region) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", title = "a)")

priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression, aff_factor = c(energy,
        seed_type), deg_factor = region) %>% update_how("Gene4",
    2) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", title = "b)")

priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression, aff_factor = c(energy,
        seed_type), deg_factor = region) %>% update_how("Gene4",
    2) %>% simulate(cycle = 1) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", title = "c)")

priming_graph(minsamp, competing_count = Competing_expression,
    miRNA_count = miRNA_expression, aff_factor = c(energy,
        seed_type), deg_factor = region) %>% update_how("Gene4",
    2) %>% simulate(cycle = 2) %>% vis_graph(Competing_color = "navajowhite3",
    mirna_color = "ivory4", Upregulation = "red", title = "d)")
```
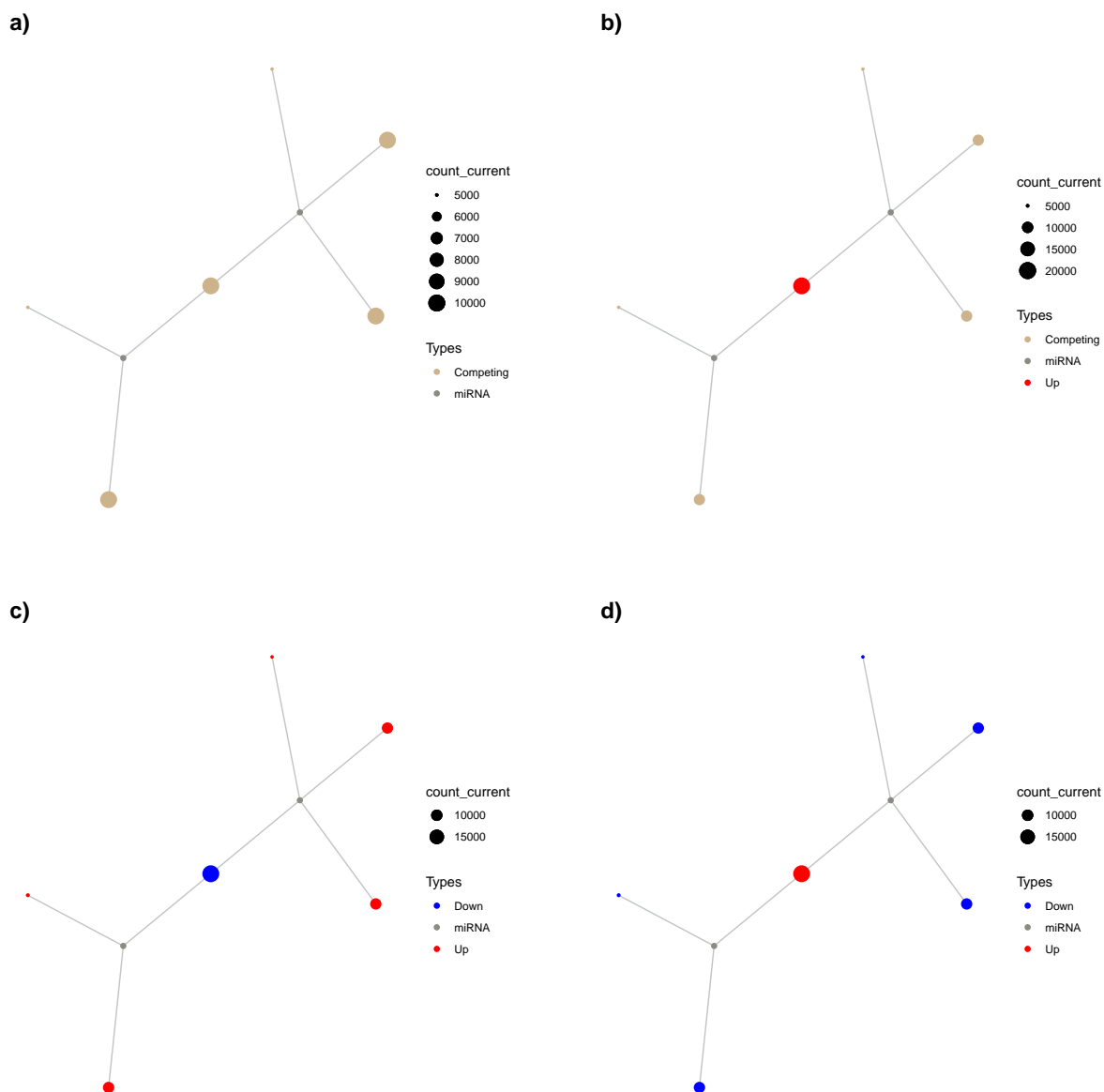
Figure S8: Perturbation of Gene4 on minsamp data with interaction factors. a) Network at steady-state. b) Upregulation of Gene4. c) Primary response of network to upregulation of Gene4. d) Re-regulation of whole nodes on system (3th iteration)

Determination of iteration for Upregulation of SERPINE2 gene from Breast cancer patient dataset

```
E9GE_mirnagenenormal <- readRDS("data/E9GE_mirnagenenormal.RDS")
head(E9GE_mirnagenenormal)
```

```
## # A tibble: 6 x 7
```

```
##    hgnc_symbol miRNA_name mirna_RPM GE_normal Energy seed_type_effect
##    <chr>       <chr>          <dbl>     <dbl> <dbl>            <dbl>
## 1 CCNG1        hsa-let-7~    111204.      5245  -25.1             0.05
## 2 DICER1       hsa-let-7~    111204.      3285  -24.4             0.43
## 3 SESN1        hsa-let-7~    111204.      1179  -22.2             0.05
## 4 NIPBL        hsa-let-7~    111204.      4503  -22.1             0.05
## 5 INTS12       hsa-let-7~    111204.       600  -21.9             0.05
## 6 FNIP1        hsa-let-7~    111204.      1248  -21.8             0.43
## # ... with 1 more variable: region_effect <dbl>
```

```
as.data.frame(E9GE_mirnagenenormal) %>% priming_graph(competing_count = GE_normal,
    miRNA_count = mirna_RPM, aff_factor = c(Energy,
        seed_type_effect), deg_factor = region_effect) %>%
    update_how("SERPINE2", 2.75) %>% simulate(150) %>%
    find_iteration(limit = 1, plot = TRUE)
```

```
## Warning in priming_graph(., competing_count = GE_normal, miRNA_count = mirna_RPM, : First column is
```
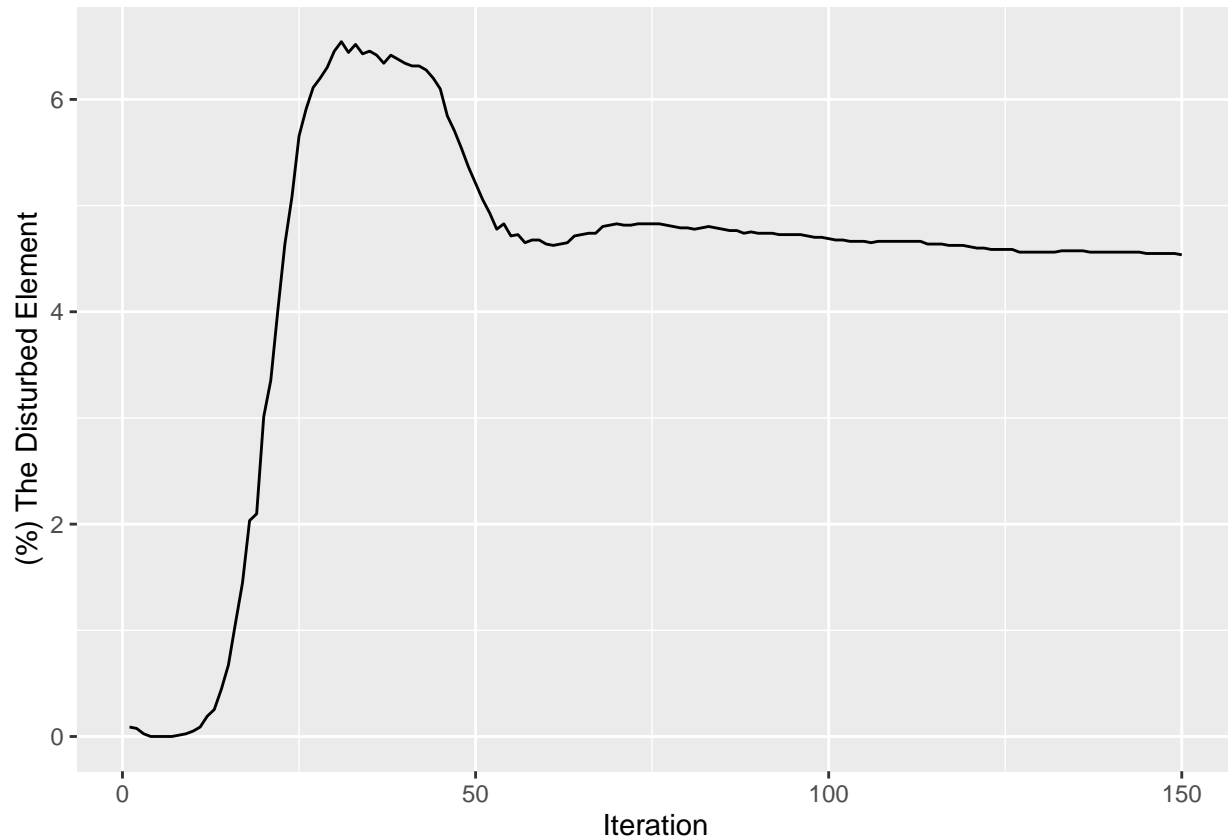

Figure S9: Percentage of affected nodes of each iteration for SERPINE2 Gene

```
# limit=0 describes the change that is not taken
# into account.
```