Supplementary Figures

Selcen Arı

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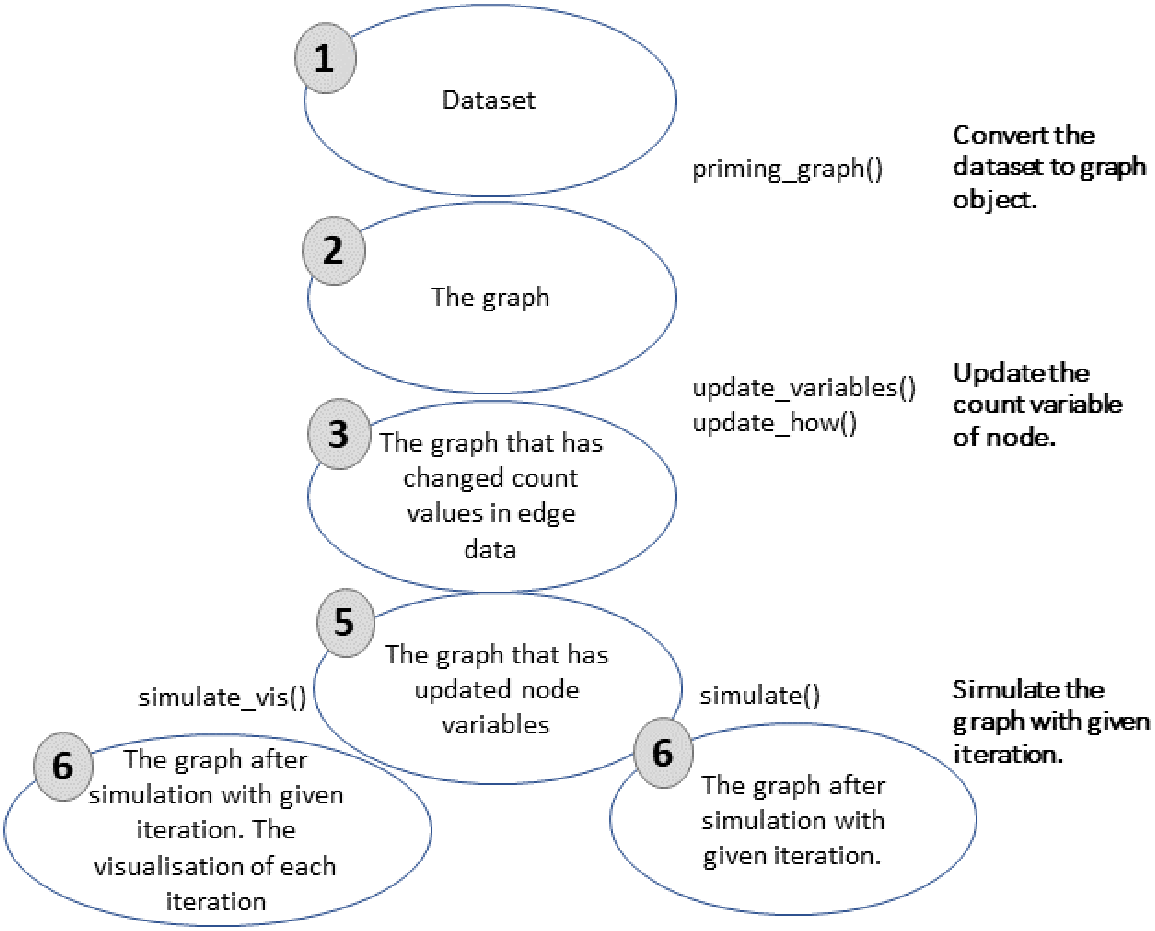
1
Dataset
priming_graph()
Convert the dataset to graph object.
2
The graph
update_variables()
update_how()
Update the count variable of node.
3
The graph that has changed count values in edge data
5
The graph that has updated node variables
simulate_vis()
simulate()
Simulate the graph with given iteration.
6
The graph after simulation with given iteration. The visualisation of each iteration
6
The graph after simulation with given iteration.

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.

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

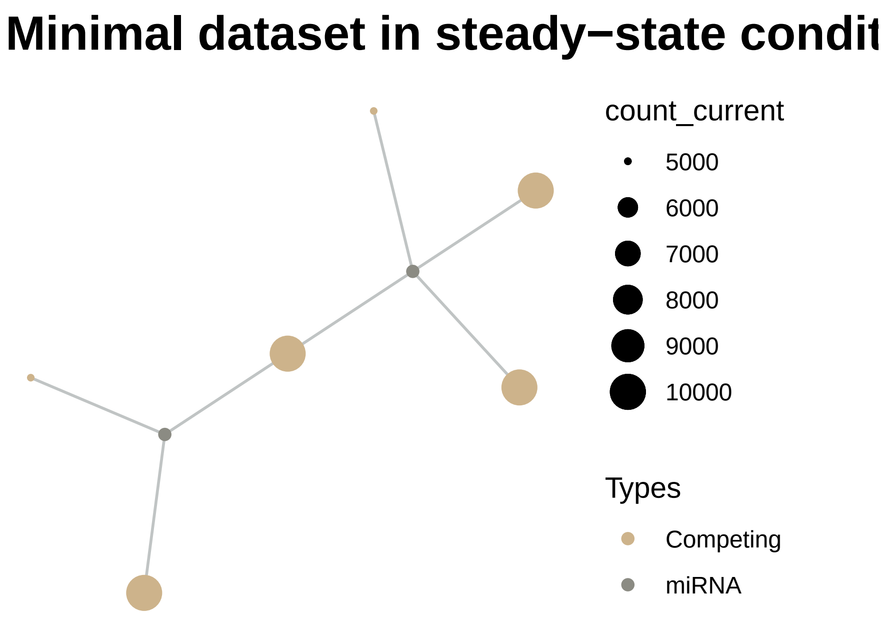

Figure S2: Minimal Dataset in Steady-state

```
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 = "Ge
```

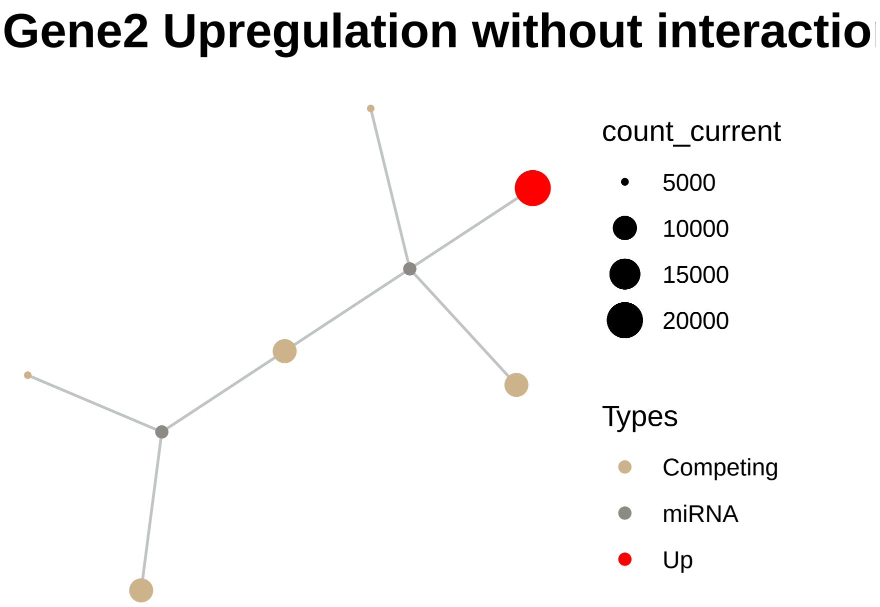

Figure S3: Gene2 Upregulation on Minimal Dataset

```
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", Downregulati

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", Downregulati
```

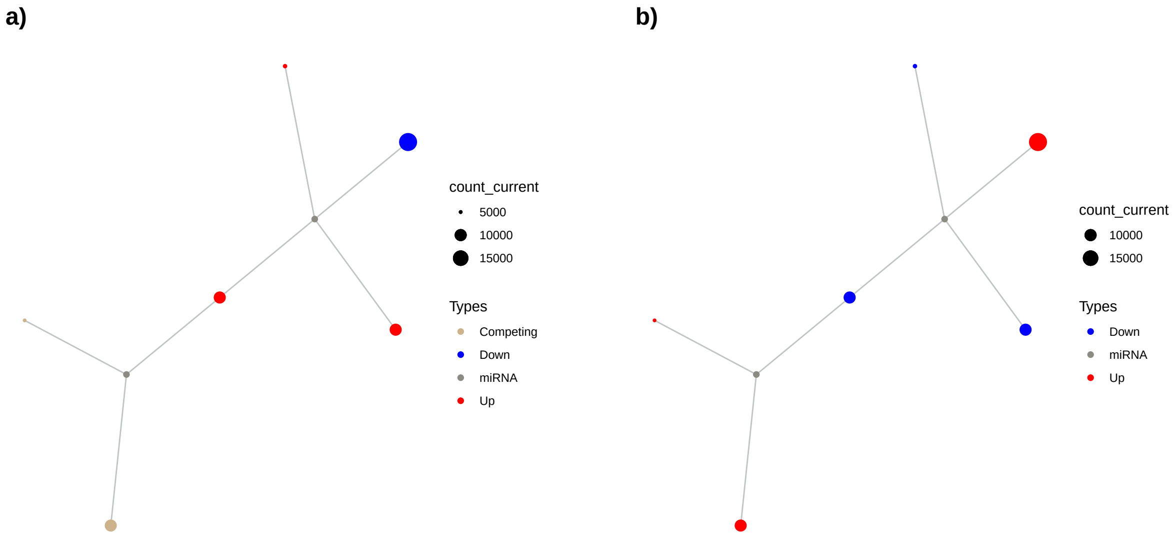

Figure S4: Sequential iteration of minsamp data. a) First response of system to Gene2 upregulation (2nd iteration). b) Spreading of perturbation on system (3th iteration)

minsamp dataset analysis with interaction factors.

```
priming_graph(minsamp, competing_count = Competing_expression, miRNA_count = miRNA_expression, aff_facto
  vis_graph(Competing_color = "navajowhite3", mirna_color = "ivory4", title = "Minimal dataset with inte
```

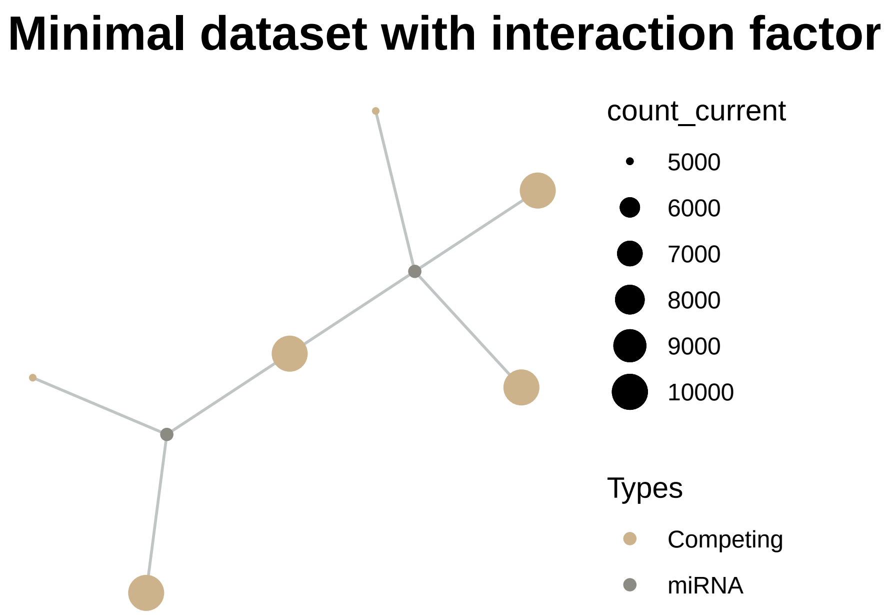

Figure S5: Minimal Dataset with interaction factors in Steady-state

```
priming_graph(minsamp, competing_count = Competing_expression, miRNA_count = miRNA_expression, aff_facto
  update_how("Gene2", 2)%>%
  vis_graph(Competing_color = "navajowhite3", mirna_color = "ivory4", Upregulation = "red", title = "Ge
```

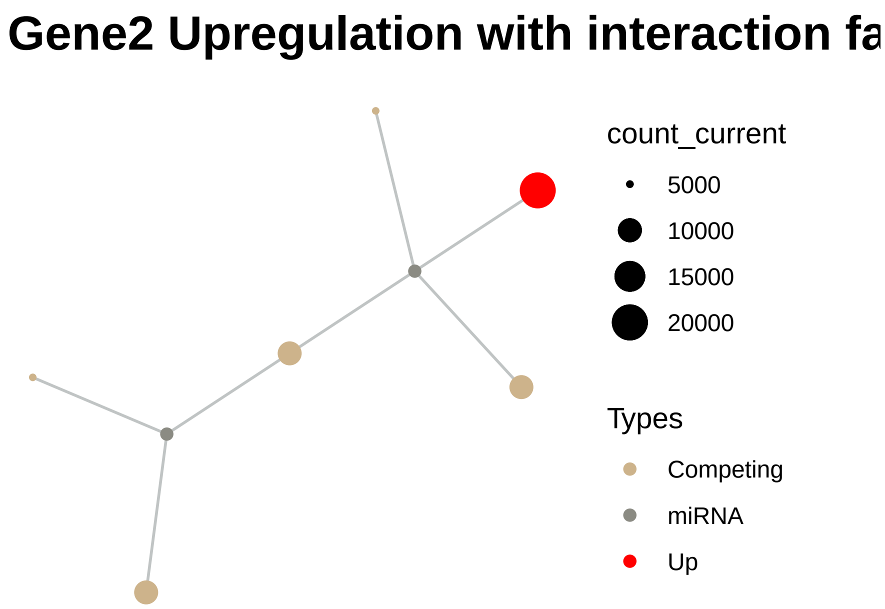

Figure S6: When Gene2 is upregulated on Minimal Dataset with interaction factors

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

priming_graph(minsamp, competing_count = Competing_expression, miRNA_count = miRNA_expression, aff_facto
  update_how("Gene2", 2)%>%
  simulate(cycle = 2)%>%
  vis_graph(Competing_color = "navajowhite3", mirna_color = "ivory4", Upregulation = "red", Downregulati
```

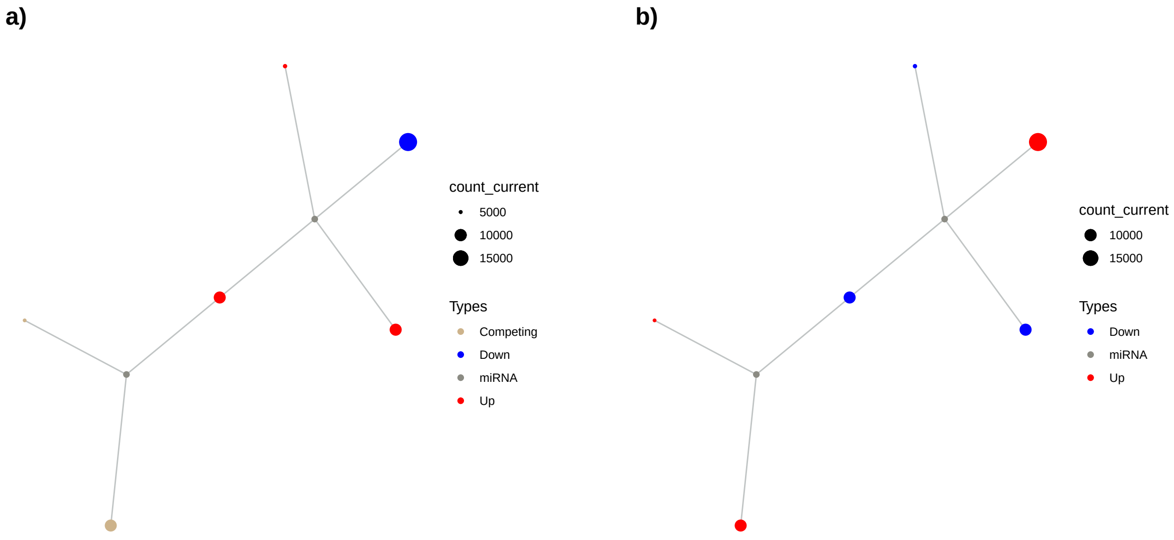

Figure S7: Sequential iteration of minsamp data with interaction factors a)First response of system to Gene2 upregulation (2nd iteration). b)Spreading of perturbation on system (3th iteration)

Common target perturbation in *minsamp* dataset.

```
priming_graph(minsamp, competing_count = Competing_expression, miRNA_count = miRNA_expression, aff_facto
  vis_graph(Competing_color = "navajowhite3", mirna_color = "ivory4", Upregulation = "red", title = "a)

priming_graph(minsamp, competing_count = Competing_expression, miRNA_count = miRNA_expression, aff_facto
  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_facto
  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_facto
  update_how("Gene4", 2)%>%
  simulate(cycle=2)%>%
  vis_graph(Competing_color = "navajowhite3", mirna_color = "ivory4", Upregulation = "red", title = "d)
```

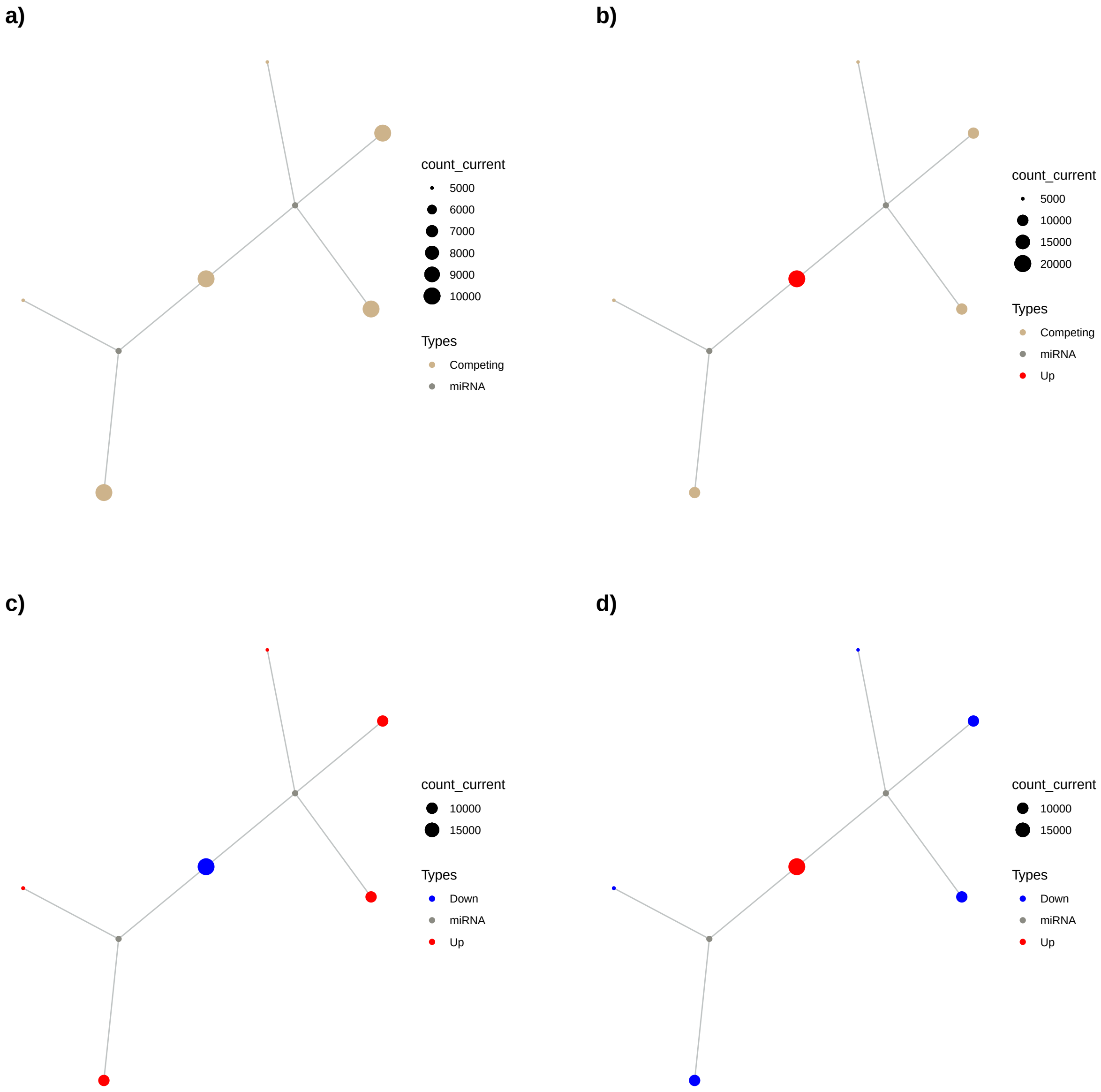

Figure S8: Perturbation of Gene4 on minsamp data with interaction factors. a) Netwrk at steady-state. b) Upregulation of Gene4. c) Primary response of network to upregulation of Gene4. d) Re-regulation of whole nodes on system (3th iteration)

Determination of iteration for Upregulation of ANO6 gene from Breast cancer patient dataset

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

```
## # A tibble: 6 x 7
##   Hugo_Symbol miRNA_name mirna_RPM GE_normal energy seed_type_effect
##   <chr>       <chr>          <dbl>     <dbl>  <dbl>            <dbl>
## 1 ENAH        hsa-let-7~   111204.      7540  -22.7            0.01
## 2 GALNT2      hsa-let-7~   111204.      2824  -20.5            0.14
## 3 RLF         hsa-let-7~   111204.      1144  -18              0.028
## 4 MAST2       hsa-let-7~   111204.      2640  -22.6            0.24
## 5 DOCK1       hsa-let-7~   111204.      4826  -20.5            0.01
## 6 ZBTB16      hsa-let-7~   111204.       315  -24.3            0.14
## # ... 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_ef
 update_how("ANO6",3) %>%
 simulate(150) %>%
 find_iteration(limit=1, plot= TRUE) #limit=1 describes the change that is not taken into account.
```

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

```
## Warning: Removed 150 rows containing missing values (geom_path).
```

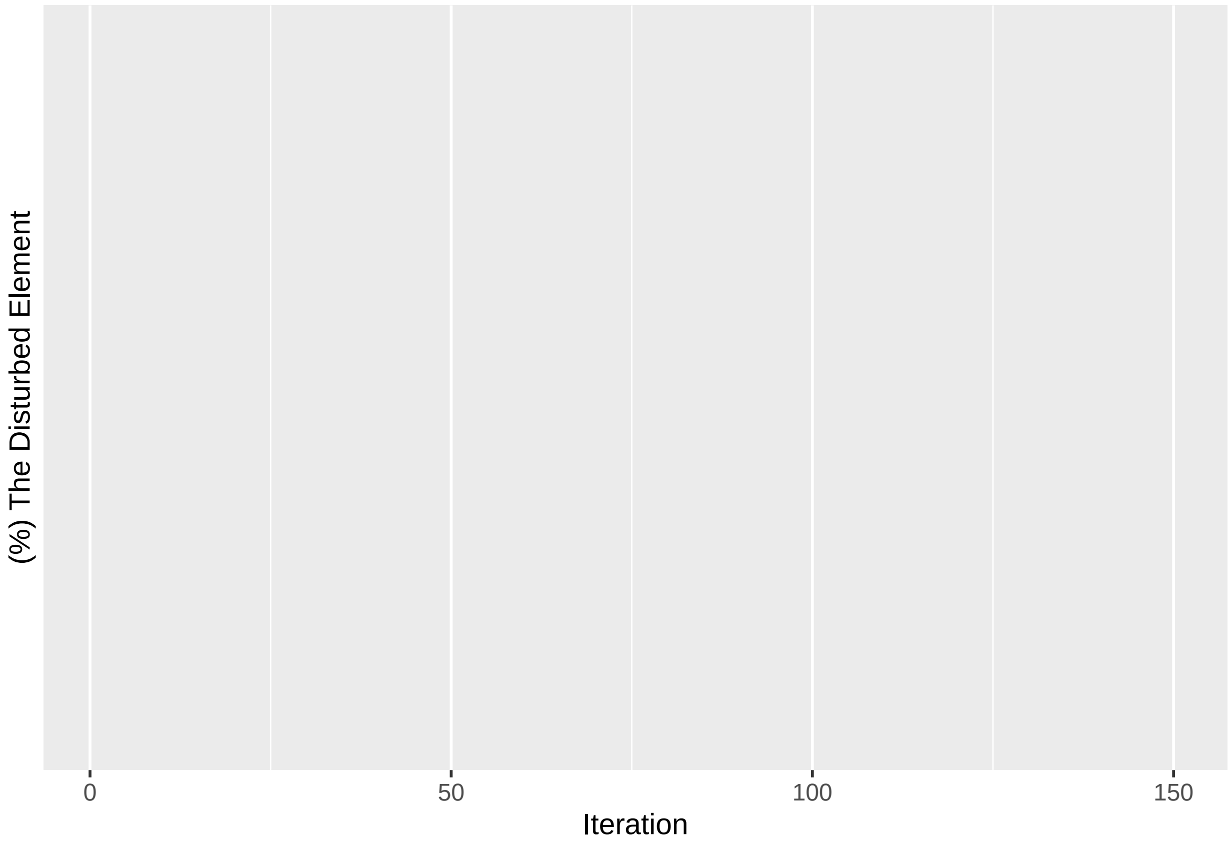

Figure S9: Percentage of affected nodes of each iteration for ANO6 Gene