Differential cell-cell communication between SCZ and NTC using cellchat V2

Method

- A rough summary of cell chat V2.
- Rational of uisng cell chat V2: enabling the comparative comparative cell-cell communication between the diagnosis groups.
- Implementaion: It first run the cell-chat pipeline on the subset of samples from each diagnosis separately (stored), and then use `mergeCellChat` fucntion to merge the two cellchat object and identify the differential pattern and measure the strength of the evidence.
- Nuanced noted: despite cell chat V2 have spatially aware cell-cell communication analysis, we didn't use it. That's because that our objective is to identify the communication patter, or the differenital communication pattern, at the cortical layer level instead of at the spot level, and hence. We decided to use the without accounting more nuanced spatial coordinate information.

Code

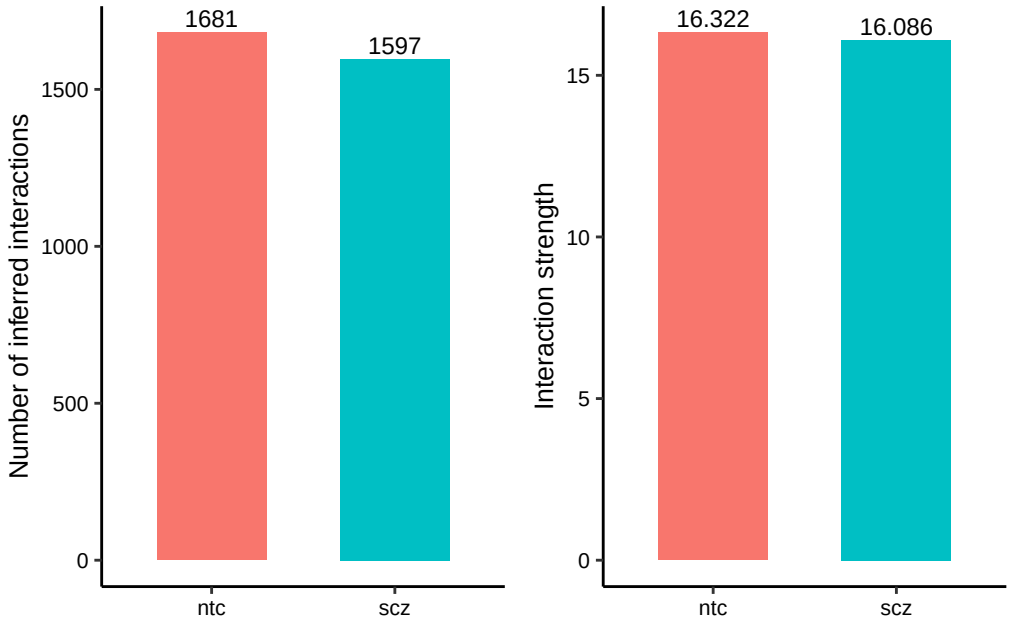
Results

Number of interaction and interaction strength

Overall levelfor SCZ and NTC respectively

- # of interaction There's more interaction among NTC group compared to SCZ group.
- The strength between the two groups seems to be equaly strong.

```
gg1 <- compareInteractions(cellchat, show.legend = F, group = c(1, 2))
gg2 <- compareInteractions(cellchat, show.legend = F, group = c(1, 2), measure = "weight")
gg1 + gg2
```



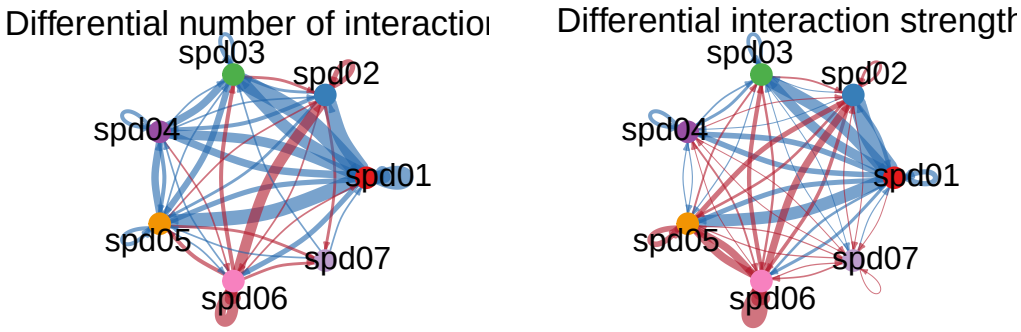
At the layer level

The differential number of interactions or interaction strength in the cell-cell communication network between two datasets can be visualized using circle plot, where red (or blue) colored edges represent increased (or decreased) signaling in the second dataset compared to the first one.

In our data anlysis, teh first data set is **NTC** and teh second data set is **SCZ**. So this would mean we see - **Increased (red) signaling in SCZ group, (in reference to NTC group) for communication between SpD02 (L3/4) -SpD06 (L2/3) and SpD06(L2/3)-06(L2/3) - Decreased (blue) signaling in SCZ grup, (in reference to NTC group), for communication between spd01 and the rest of SpDs (SpD05, SpD 02, SpD 03, SpD 04)** Among NTC, there's more communication between SPD02 and SpD06 (can't see the directionality), and among SCZ group

Note: left is # of interaction and right is strength of the interaction.

```
par(mfrow = c(1,2), xpd=TRUE)
netVisual_diffInteraction(cellchat, weight.scale = T)
netVisual_diffInteraction(cellchat, weight.scale = T, measure = "weight")
```



Heat map visualization of this. Same conclusion holds as the above.

```
gg1 <- netVisual_heatmap(cellchat)
```

```
Do heatmap based on a merged object
```

```
#> Do heatmap based on a merged object
gg2 <- netVisual_heatmap(cellchat, measure = "weight")
```

```
Do heatmap based on a merged object
```

```
#> Do heatmap based on a merged object
gg1 + gg2
```

Compare major sources and targets

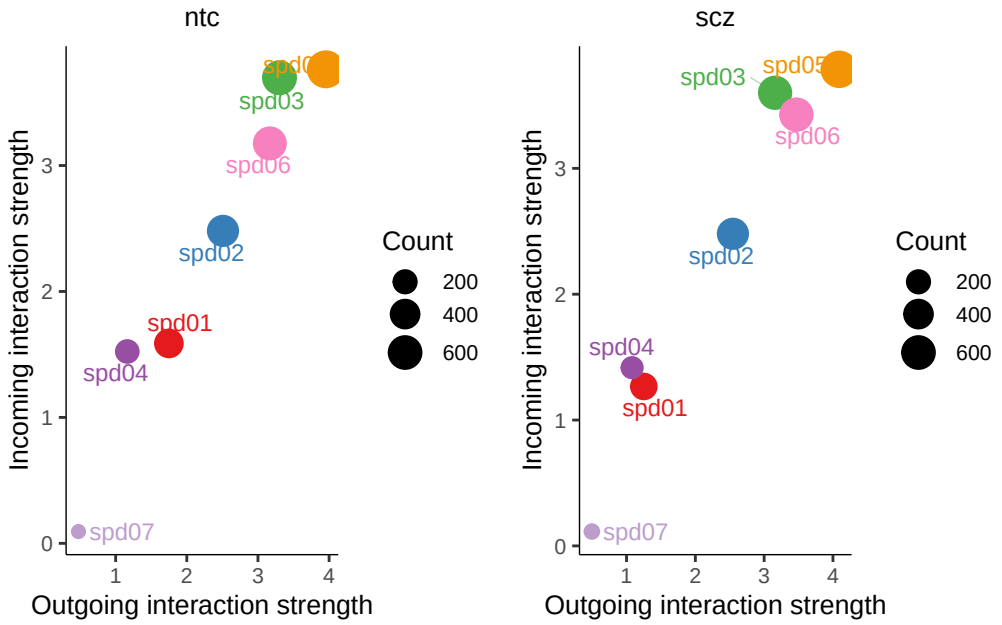
These plots also suggest that spd01 (L6/WM) have larger outgoing interaction strenth in SCZ, and SpD06 (L2/3) have both larger outgoing interaction and more incoming interaction strenth in SCZ.

```
ntc_cellchat <- readRDS(here(
  "processed-data/layer_layer_comm",
  "ntc_cellchat.rds"
))
scz_cellchat <- readRDS(
  here(
    "processed-data/layer_layer_comm",
    "scz_cellchat.rds"
  )
)

object.list <- list(ntc = ntc_cellchat, scz = scz_cellchat)

num.link <- sapply(object.list, function(x) {rowSums(x@net$count) + colSums(x@net$count)-dia
weight.MinMax <- c(min(num.link), max(num.link)) # control the dot size in the different data
```

```
gg <- list()
for (i in 1:length(object.list)) {
  gg[[i]] <- object.list[[i]] |>
  #netAnalysis_computeCentrality(slot.name = "netP") |>
   netAnalysis_signalingRole_scatter(title = names(object.list)[i], weight.MinMax = weight.Mi
}
```

```
Signaling role analysis on the aggregated cell-cell communication network from all signaling
Signaling role analysis on the aggregated cell-cell communication network from all signaling
```

```
#> Signaling role analysis on the aggregated cell-cell communication network from all signali
#> Signaling role analysis on the aggregated cell-cell communication network from all signali
patchwork::wrap_plots(plots = gg)
```



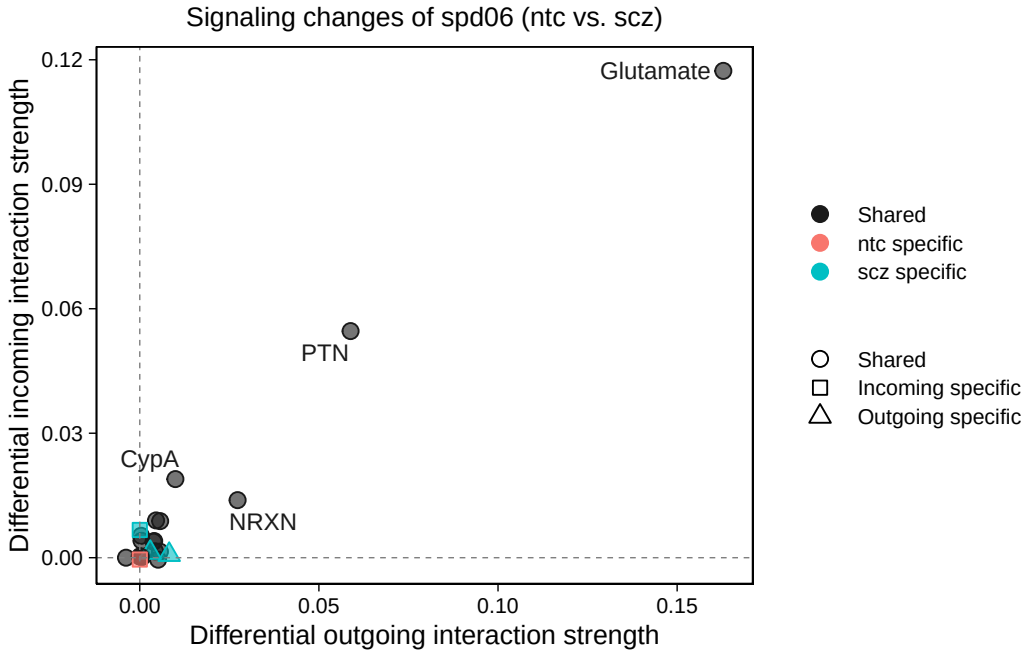
signaling changes in spd 06(L2/3)

```
gg1 <- netAnalysis_signalingChanges_scatter(cellchat, idents.use = "spd06")
```

```
Visualizing differential outgoing and incoming signaling changes from ntc to scz
```

```
The following `from` values were not present in `x`: 2
```

```
gg1
```




```
gg1$data
```

	outgoing	incoming	specificity.out.in	specificity	labels
Glutamate	0.1628860063	0.1173254985	Shared	Shared	Glutamate
NRXN	0.0273036735	0.0138742238	Shared	Shared	NRXN
PTN	0.0588416225	0.0546160810	Shared	Shared	PTN
NCAM	0.0056871196	0.0088169080	Shared	Shared	NCAM
APP	0.0003601754	0.0052816739	Shared	Shared	APP
CypA	0.0099379832	0.0189491836	Shared	Shared	CypA
CNTN	0.0056232663	0.0014650739	Shared	Shared	CNTN
GABA-A	0.0045407605	0.0089869611	Shared	Shared	GABA-A
PSAP	-0.0038462473	0.0000000000	Shared	Shared	PSAP
NEGR	0.0038433194	0.0038433194	Shared	Shared	NEGR
ADGRL	0.0051194705	-0.0004743843	Shared	Shared	ADGRL
GABA-B	0.0042473264	0.0015515012	Shared	Shared	GABA-B
CADM	0.0004940774	0.0040691409	Shared	Shared	CADM
GAP	0.0040250561	0.0040250561	Shared	Shared	GAP
FGF	0.0000000000	0.0066848294	Incoming specific	scz specific	FGF

```
SLITRK      0.0006976941  0.0001657942              Shared       Shared    SLITRK
PTPR        0.0082028892  0.0007133601  Outgoing specific scz specific      PTPR
FLRT        0.0002493161  0.0002493161              Shared       Shared      FLRT
EPHB        0.0000000000  0.0003131917              Shared       Shared      EPHB
NGL         0.0029108618  0.0012269029  Outgoing specific scz specific       NGL
L1CAM       0.0002399292  0.0002399292              Shared       Shared     L1CAM
GAS         0.0000000000 -0.0004427115  Incoming specific ntc specific       GAS
```

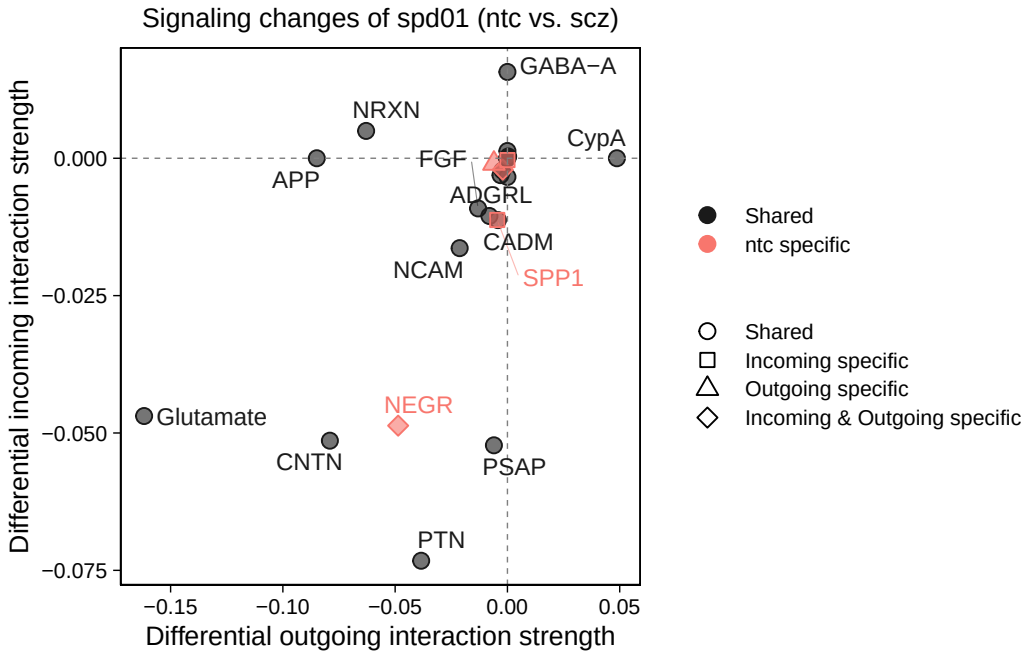
signaling changes in spd 01(L6/WM)

```
gg2 <- netAnalysis_signalingChanges_scatter(cellchat, idents.use = "spd01")
```

```
Visualizing differential outgoing and incoming signaling changes from ntc to scz
```

```
The following `from` values were not present in `x`: 1
```

```
gg2
```



```
gg2$data
```

```
              outgoing      incoming           specificity.out.in  specificity
Glutamate -0.1617970795 -4.691516e-02                       Shared       Shared
NRXN      -0.0629311461  4.972700e-03                       Shared       Shared
PTN       -0.0384131674 -7.325429e-02                       Shared       Shared
NCAM      -0.0212743857 -1.635939e-02                       Shared       Shared
APP       -0.0848937899  0.000000e+00                       Shared       Shared
CypA       0.0487483835  0.000000e+00                       Shared       Shared
CNTN      -0.0790635572 -5.140388e-02                       Shared       Shared
GABA-A     0.0000000000  1.570825e-02                       Shared       Shared
PSAP      -0.0060177202 -5.224473e-02                       Shared       Shared
NEGR      -0.0486665396 -4.866654e-02 Incoming & Outgoing specific ntc specific
ADGRL     -0.0080336543 -1.050539e-02                       Shared       Shared
GABA-B     0.0000000000 -3.403509e-03                       Shared       Shared
CADM      -0.0042067294 -1.125570e-02                       Shared       Shared
CLDN      -0.0022416517 -2.241652e-03                       Shared       Shared
GAP       -0.0030743274 -3.074327e-03                       Shared       Shared
FGF       -0.0130715661 -9.131264e-03                       Shared       Shared
MAG        0.0003238194  3.238194e-04                       Shared       Shared
SPP1      -0.0045359847 -1.123409e-02            Incoming specific ntc specific
SLITRK    -0.0060226707 -9.672523e-04            Outgoing specific ntc specific
PTPR       0.0000000000  1.320990e-03                       Shared       Shared
EPHB       0.0000000000  3.192213e-05                       Shared       Shared
JAM       -0.0020759655 -2.075965e-03 Incoming & Outgoing specific ntc specific
SEMA4     -0.0001057011  0.000000e+00                       Shared       Shared
GAS        0.0000000000 -3.316159e-04            Incoming specific ntc specific
             labels
Glutamate Glutamate
NRXN           NRXN
PTN             PTN
NCAM           NCAM
APP             APP
CypA           CypA
CNTN           CNTN
GABA-A       GABA-A
PSAP           PSAP
NEGR           NEGR
ADGRL         ADGRL
GABA-B       GABA-B
CADM           CADM
CLDN           CLDN
```

```
GAP              GAP
FGF              FGF
MAG              MAG
SPP1            SPP1
SLITRK       SLITRK
PTPR            PTPR
EPHB            EPHB
JAM              JAM
SEMA4         SEMA4
GAS              GAS
```

Compare outgoing (or incoming) signaling patterns associated with each cell population

- There are some overlapping genes in the lay-layer analysis, for example the PTN, PYAP
- The gene **APP** stands out

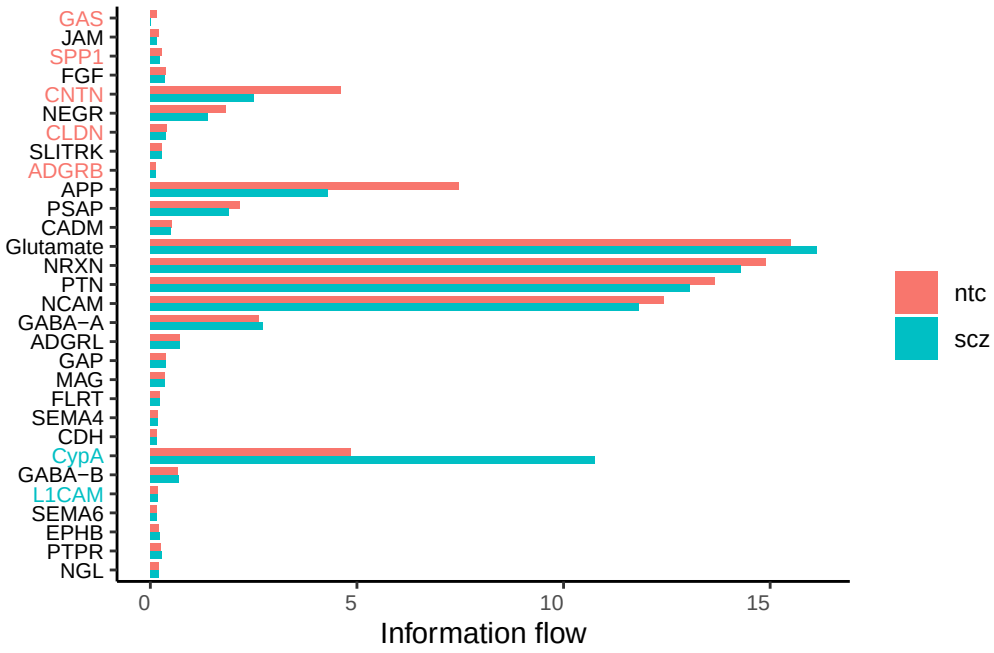
functional similarity

TODO: need to install python packag `pip install umap-learn`

```
cellchat <- computeNetSimilarityPairwise(cellchat, type = "functional")
cellchat <- netEmbedding(cellchat, type = "functional")
cellchat <- netClustering(cellchat, type = "functional")
netVisual_embeddingPairwise(cellchat, type = "functional", label.size = 3.5)
```

overall information flow of each signaling pathway or ligand-receptor pair

```
# gg1 <- rankNet(cellchat, mode = "comparison", measure = "weight", sources.use = NULL, targ
gg2 <- rankNet(cellchat, mode = "comparison", measure = "weight", sources.use = NULL, target

# gg1 + gg2
gg2
```



- There are some overlapping genes in the lay-layer analysis, for example the PTN, PYAP
- The gene **APP** stands out

I think overall plot seems to match with previously plots better.

Outgoing

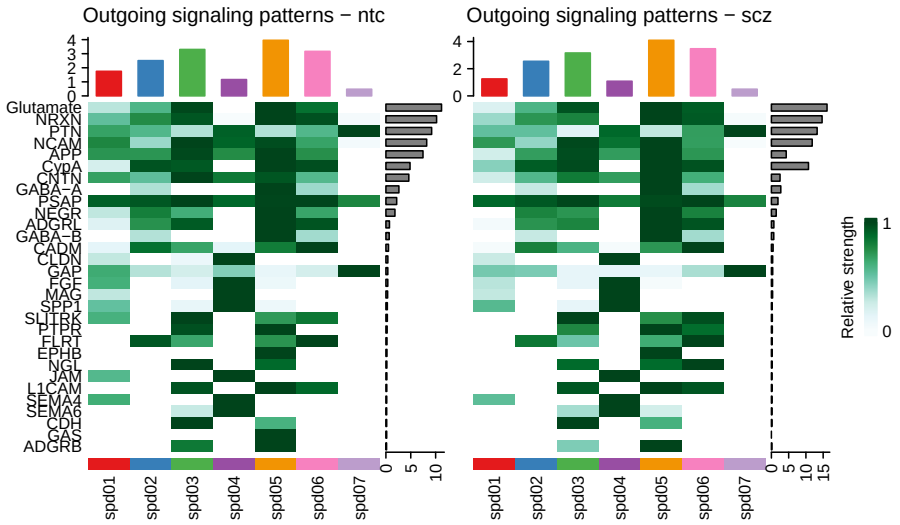
```
library(ComplexHeatmap)
```

```
Loading required package: grid
```

```
========================================
ComplexHeatmap version 2.20.0
Bioconductor page: http://bioconductor.org/packages/ComplexHeatmap/
Github page: https://github.com/jokergoo/ComplexHeatmap
Documentation: http://jokergoo.github.io/ComplexHeatmap-reference

If you use it in published research, please cite either one:
- Gu, Z. Complex Heatmap Visualization. iMeta 2022.
- Gu, Z. Complex heatmaps reveal patterns and correlations in multidimensional
    genomic data. Bioinformatics 2016.
```

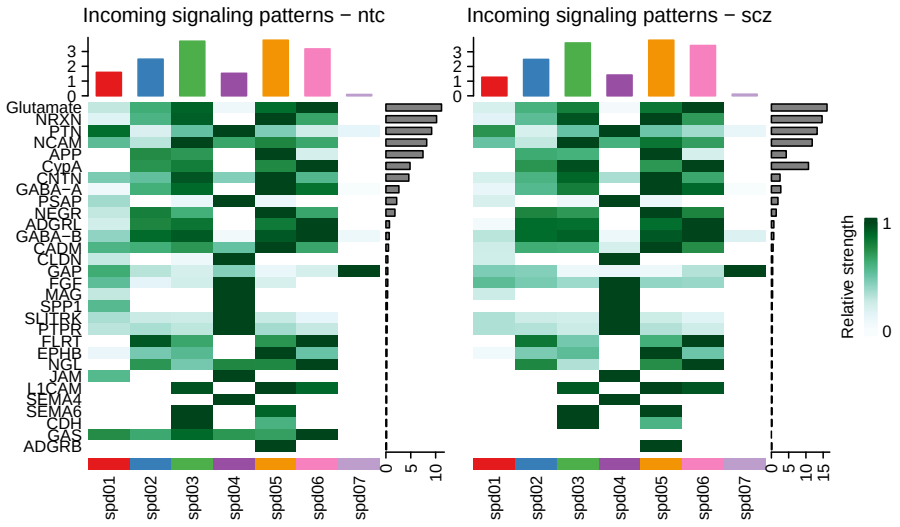
```
The new InteractiveComplexHeatmap package can directly export static
complex heatmaps into an interactive Shiny app with zero effort. Have a try!

This message can be suppressed by:
  suppressPackageStartupMessages(library(ComplexHeatmap))
========================================
```

```r
i = 1
pathway.union <- union(object.list[[i]]@netP$pathways, object.list[[i+1]]@netP$pathways)
ht1 = netAnalysis_signalingRole_heatmap(object.list[[i]], pattern = "outgoing", signaling = p
ht2 = netAnalysis_signalingRole_heatmap(object.list[[i+1]], pattern = "outgoing", signaling =
draw(ht1 + ht2, ht_gap = unit(0.5, "cm"))
```



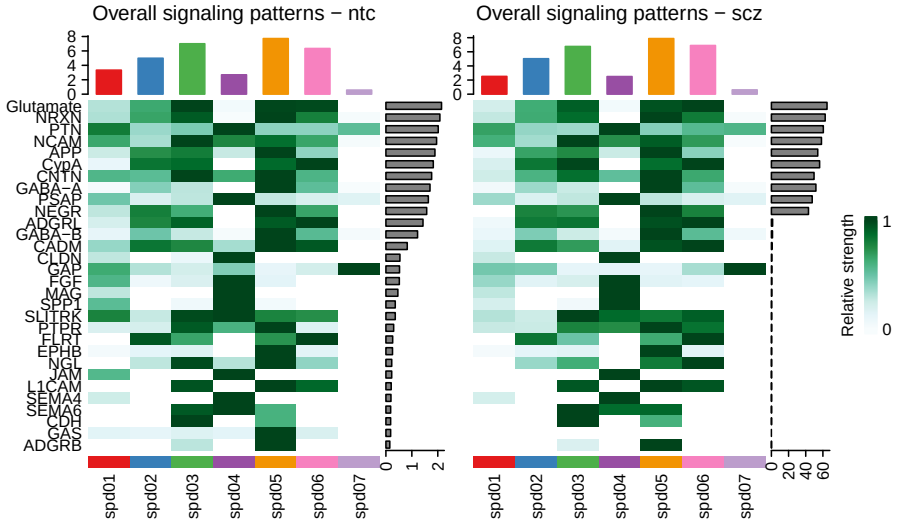
Incoming

```r
library(ComplexHeatmap)
i = 1
pathway.union <- union(object.list[[i]]@netP$pathways, object.list[[i+1]]@netP$pathways)
ht1 = netAnalysis_signalingRole_heatmap(object.list[[i]], pattern = "incoming", signaling = p
ht2 = netAnalysis_signalingRole_heatmap(object.list[[i+1]], pattern = "incoming", signaling =
draw(ht1 + ht2, ht_gap = unit(0.5, "cm"))
```



Overall

```
library(ComplexHeatmap)
i = 1
pathway.union <- union(object.list[[i]]@netP$pathways, object.list[[i+1]]@netP$pathways)
ht1 = netAnalysis_signalingRole_heatmap(object.list[[i]], pattern = "all", signaling = pathwa
ht2 = netAnalysis_signalingRole_heatmap(object.list[[i+1]], pattern = "all", signaling = patl
draw(ht1 + ht2, ht_gap = unit(0.5, "cm"))
```

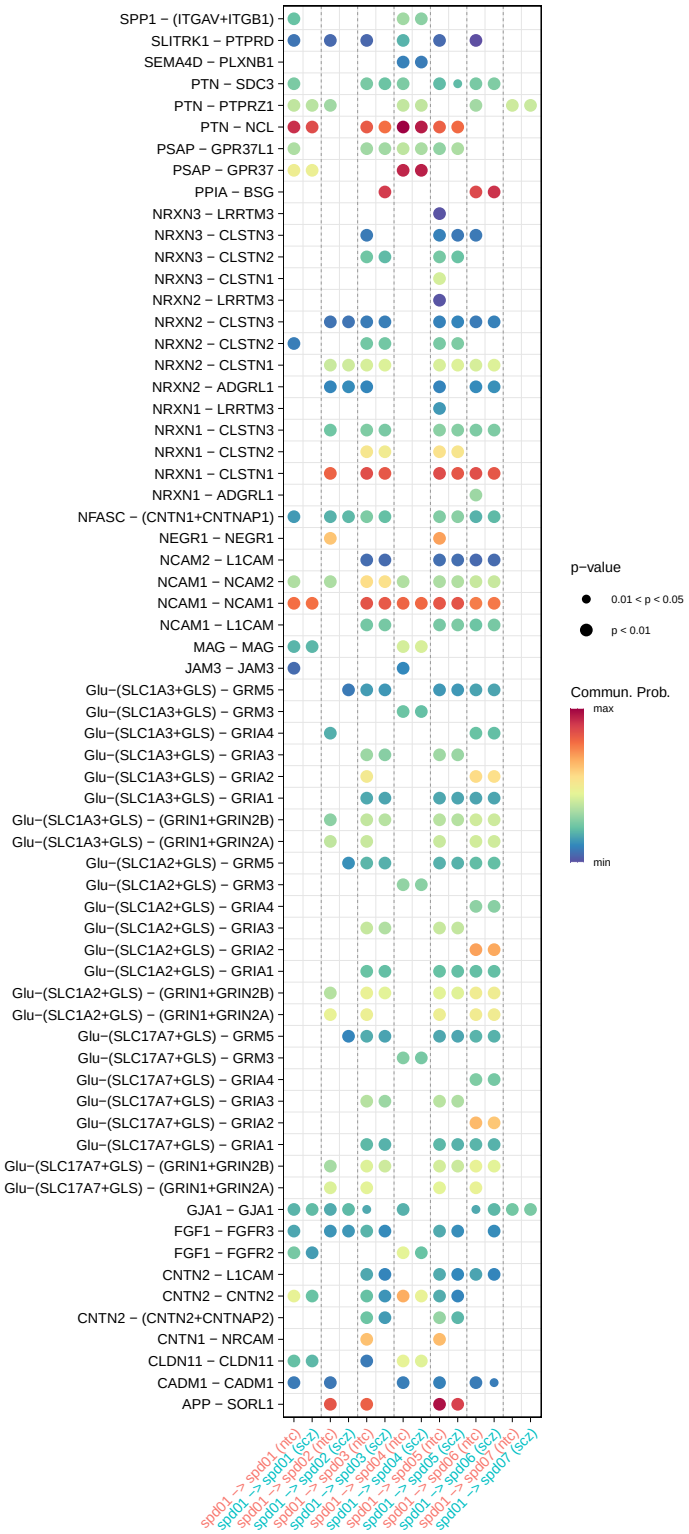


Upregulated and downregulated signaling LR apris

Note: it is possible to make the following plot more succinct by only showing differential LR pairs with regulation. https://htmlpreview.github.io/?https://github.com/jinworks/CellChat/blob/master/tuto dysfunctional-signaling-by-comparing-the-communication-probabities ## SpD1

```
netVisual_bubble(cellchat, sources.use = 1,  comparison = c(1, 2), angle.x = 45)
```

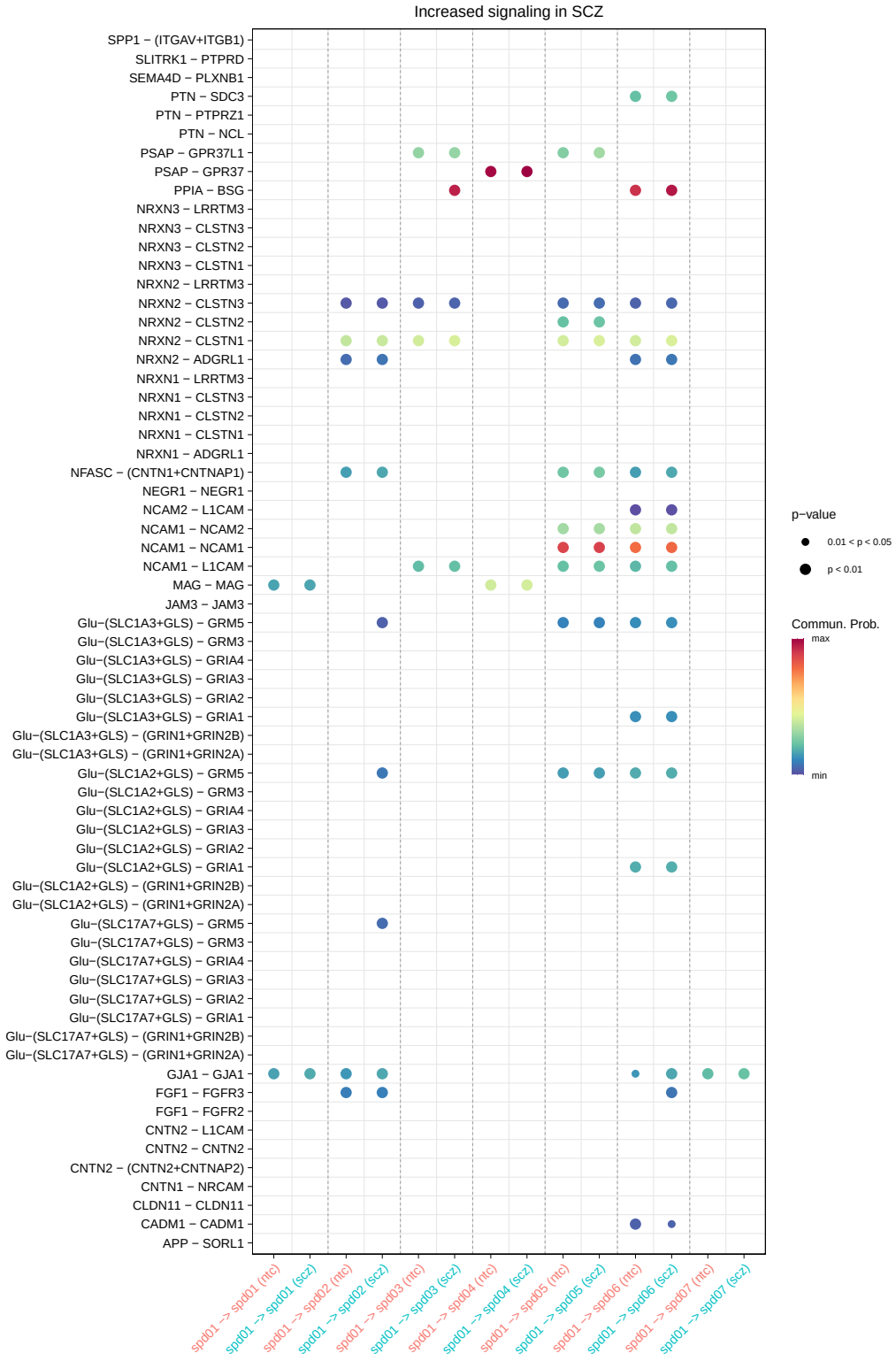
```
Comparing communications on a merged object
```


SPP1 − (ITGAV+ITGB1)
SLITRK1 − PTPRD
SEMA4D − PLXNB1
PTN − SDC3
PTN − PTPRZ1
PTN − NCL
PSAP − GPR37L1
PSAP − GPR37
PPIA − BSG
NRXN3 − LRRTM3
NRXN3 − CLSTN3
NRXN3 − CLSTN2
NRXN3 − CLSTN1
NRXN2 − LRRTM3
NRXN2 − CLSTN3
NRXN2 − CLSTN2
NRXN2 − CLSTN1
NRXN2 − ADGRL1
NRXN1 − LRRTM3
NRXN1 − CLSTN3
NRXN1 − CLSTN2
NRXN1 − CLSTN1
NRXN1 − ADGRL1
NFASC − (CNTN1+CNTNAP1)
NEGR1 − NEGR1
NCAM2 − L1CAM
NCAM1 − NCAM2
NCAM1 − NCAM1
NCAM1 − L1CAM
MAG − MAG
JAM3 − JAM3
Glu−(SLC1A3+GLS) − GRM5
Glu−(SLC1A3+GLS) − GRM3
Glu−(SLC1A3+GLS) − GRIA4
Glu−(SLC1A3+GLS) − GRIA3
Glu−(SLC1A3+GLS) − GRIA2
Glu−(SLC1A3+GLS) − GRIA1
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2A)
Glu−(SLC1A2+GLS) − GRM5
Glu−(SLC1A2+GLS) − GRM3
Glu−(SLC1A2+GLS) − GRIA4
Glu−(SLC1A2+GLS) − GRIA3
Glu−(SLC1A2+GLS) − GRIA2
Glu−(SLC1A2+GLS) − GRIA1
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2A)
Glu−(SLC17A7+GLS) − GRM5
Glu−(SLC17A7+GLS) − GRM3
Glu−(SLC17A7+GLS) − GRIA4
Glu−(SLC17A7+GLS) − GRIA3
Glu−(SLC17A7+GLS) − GRIA2
Glu−(SLC17A7+GLS) − GRIA1
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2B)
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2A)
GJA1 − GJA1
FGF1 − FGFR3
FGF1 − FGFR2
CNTN2 − L1CAM
CNTN2 − CNTN2
CNTN2 − (CNTN2+CNTNAP2)
CNTN1 − NRCAM
CLDN11 − CLDN11
CADM1 − CADM1
APP − SORL1
spd01 -> spd01 (ntc)
spd01 -> spd01 (scz)
spd01 -> spd02 (ntc)
spd01 -> spd02 (scz)
spd01 -> spd03 (ntc)
spd01 -> spd03 (scz)
spd01 -> spd04 (ntc)
spd01 -> spd04 (scz)
spd01 -> spd05 (ntc)
spd01 -> spd05 (scz)
spd01 -> spd06 (ntc)
spd01 -> spd06 (scz)
spd01 -> spd07 (ntc)
spd01 -> spd07 (scz)
p−value
0.01 < p < 0.05
p < 0.01
Commun. Prob.
max
min

Only differential ones in SpD1

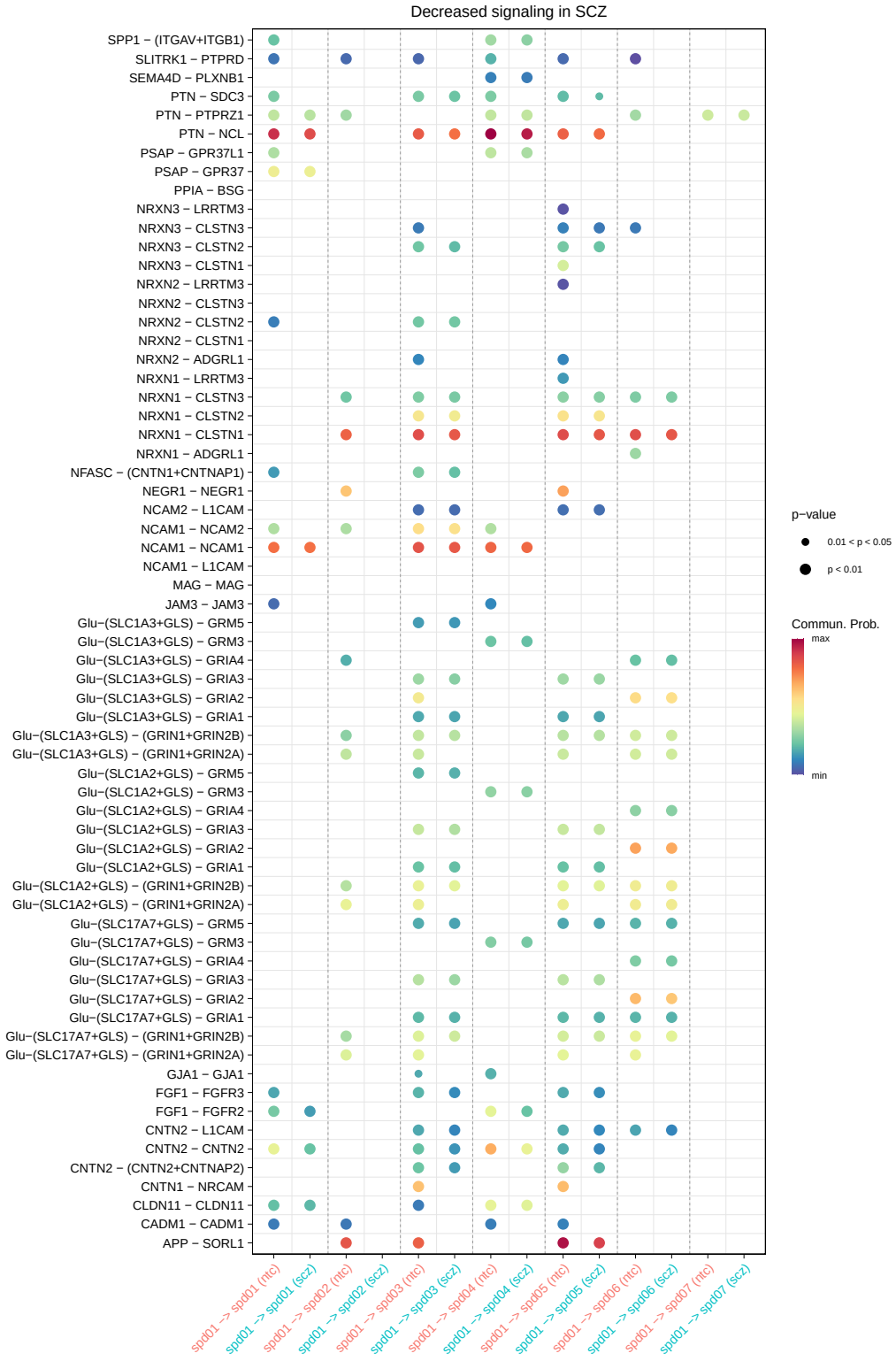
```
netVisual_bubble(cellchat, sources.use = 1,  comparison = c(1, 2), angle.x = 45,
title.name = "Increased signaling in SCZ",
max.dataset = 2)
```

```
Comparing communications on a merged object
```


Increased signaling in SCZ
SPP1 − (ITGAV+ITGB1)
SLITRK1 − PTPRD
SEMA4D − PLXNB1
PTN − SDC3
PTN − PTPRZ1
PTN − NCL
PSAP − GPR37L1
PSAP − GPR37
PPIA − BSG
NRXN3 − LRRTM3
NRXN3 − CLSTN3
NRXN3 − CLSTN2
NRXN3 − CLSTN1
NRXN2 − LRRTM3
NRXN2 − CLSTN3
NRXN2 − CLSTN2
NRXN2 − CLSTN1
NRXN2 − ADGRL1
NRXN1 − LRRTM3
NRXN1 − CLSTN3
NRXN1 − CLSTN2
NRXN1 − CLSTN1
NRXN1 − ADGRL1
NFASC − (CNTN1+CNTNAP1)
NEGR1 − NEGR1
NCAM2 − L1CAM
NCAM1 − NCAM2
NCAM1 − NCAM1
NCAM1 − L1CAM
MAG − MAG
JAM3 − JAM3
Glu−(SLC1A3+GLS) − GRM5
Glu−(SLC1A3+GLS) − GRM3
Glu−(SLC1A3+GLS) − GRIA4
Glu−(SLC1A3+GLS) − GRIA3
Glu−(SLC1A3+GLS) − GRIA2
Glu−(SLC1A3+GLS) − GRIA1
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2A)
Glu−(SLC1A2+GLS) − GRM5
Glu−(SLC1A2+GLS) − GRM3
Glu−(SLC1A2+GLS) − GRIA4
Glu−(SLC1A2+GLS) − GRIA3
Glu−(SLC1A2+GLS) − GRIA2
Glu−(SLC1A2+GLS) − GRIA1
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2A)
Glu−(SLC17A7+GLS) − GRM5
Glu−(SLC17A7+GLS) − GRM3
Glu−(SLC17A7+GLS) − GRIA4
Glu−(SLC17A7+GLS) − GRIA3
Glu−(SLC17A7+GLS) − GRIA2
Glu−(SLC17A7+GLS) − GRIA1
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2B)
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2A)
GJA1 − GJA1
FGF1 − FGFR3
FGF1 − FGFR2
CNTN2 − L1CAM
CNTN2 − CNTN2
CNTN2 − (CNTN2+CNTNAP2)
CNTN1 − NRCAM
CLDN11 − CLDN11
CADM1 − CADM1
APP − SORL1
spd01 --> spd01 (ntc)
spd01 --> spd01 (scz)
spd01 --> spd02 (ntc)
spd01 --> spd02 (scz)
spd01 --> spd03 (ntc)
spd01 --> spd03 (scz)
spd01 --> spd04 (ntc)
spd01 --> spd04 (scz)
spd01 --> spd05 (ntc)
spd01 --> spd05 (scz)
spd01 --> spd06 (ntc)
spd01 --> spd06 (scz)
spd01 --> spd07 (ntc)
spd01 --> spd07 (scz)
p−value
0.01 < p < 0.05
p < 0.01
Commun. Prob.
max
min

```
netVisual_bubble(cellchat, sources.use = 1,  comparison = c(1, 2), angle.x = 45,
title.name = "Decreased signaling in SCZ",
max.dataset = 1)
```

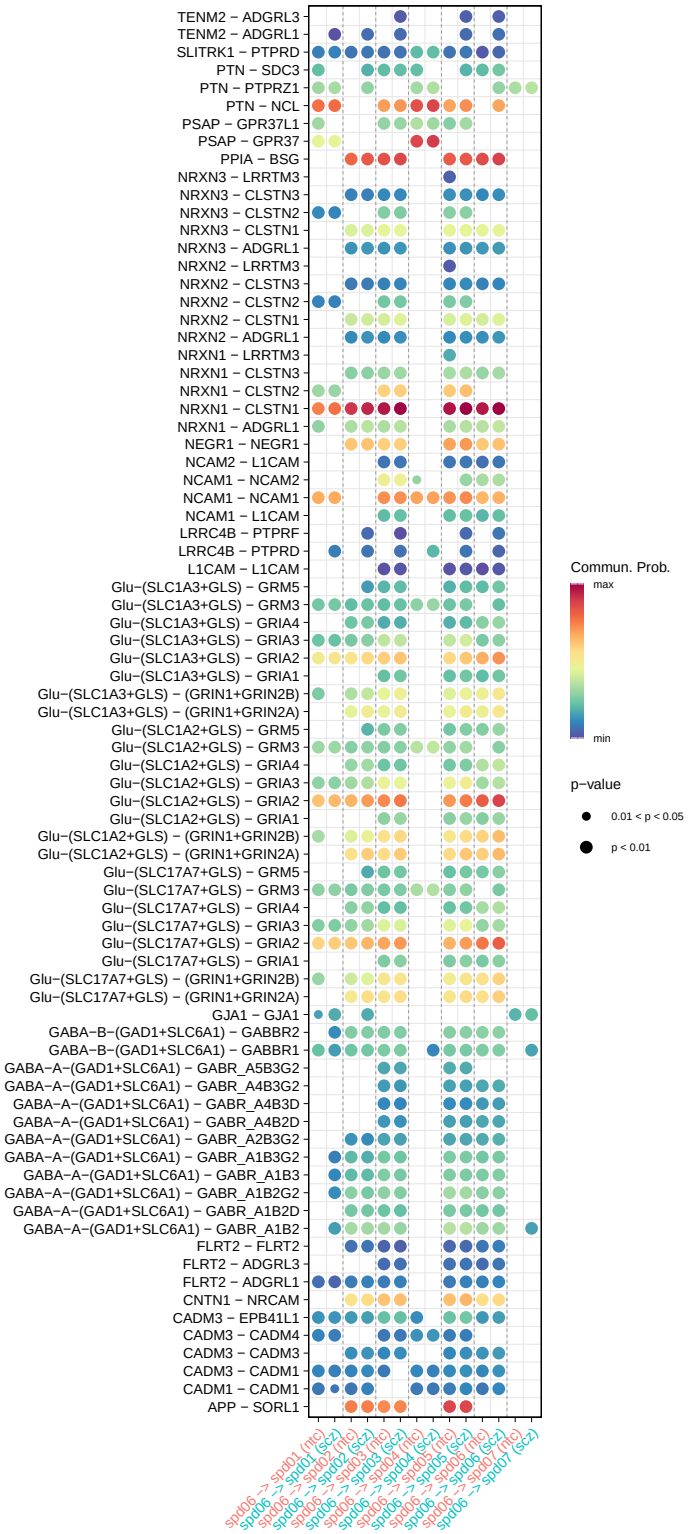
Comparing communications on a merged object


Decreased signaling in SCZ
SPP1 − (ITGAV+ITGB1)
SLITRK1 − PTPRD
SEMA4D − PLXNB1
PTN − SDC3
PTN − PTPRZ1
PTN − NCL
PSAP − GPR37L1
PSAP − GPR37
PPIA − BSG
NRXN3 − LRRTM3
NRXN3 − CLSTN3
NRXN3 − CLSTN2
NRXN3 − CLSTN1
NRXN2 − LRRTM3
NRXN2 − CLSTN3
NRXN2 − CLSTN2
NRXN2 − CLSTN1
NRXN2 − ADGRL1
NRXN1 − LRRTM3
NRXN1 − CLSTN3
NRXN1 − CLSTN2
NRXN1 − CLSTN1
NRXN1 − ADGRL1
NFASC − (CNTN1+CNTNAP1)
NEGR1 − NEGR1
NCAM2 − L1CAM
NCAM1 − NCAM2
NCAM1 − NCAM1
NCAM1 − L1CAM
MAG − MAG
JAM3 − JAM3
Glu−(SLC1A3+GLS) − GRM5
Glu−(SLC1A3+GLS) − GRM3
Glu−(SLC1A3+GLS) − GRIA4
Glu−(SLC1A3+GLS) − GRIA3
Glu−(SLC1A3+GLS) − GRIA2
Glu−(SLC1A3+GLS) − GRIA1
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2A)
Glu−(SLC1A2+GLS) − GRM5
Glu−(SLC1A2+GLS) − GRM3
Glu−(SLC1A2+GLS) − GRIA4
Glu−(SLC1A2+GLS) − GRIA3
Glu−(SLC1A2+GLS) − GRIA2
Glu−(SLC1A2+GLS) − GRIA1
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2A)
Glu−(SLC17A7+GLS) − GRM5
Glu−(SLC17A7+GLS) − GRM3
Glu−(SLC17A7+GLS) − GRIA4
Glu−(SLC17A7+GLS) − GRIA3
Glu−(SLC17A7+GLS) − GRIA2
Glu−(SLC17A7+GLS) − GRIA1
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2B)
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2A)
GJA1 − GJA1
FGF1 − FGFR3
FGF1 − FGFR2
CNTN2 − L1CAM
CNTN2 − CNTN2
CNTN2 − (CNTN2+CNTNAP2)
CNTN1 − NRCAM
CLDN11 − CLDN11
CADM1 − CADM1
APP − SORL1
spd01 --> spd01 (ntc)
spd01 --> spd01 (scz)
spd01 --> spd02 (ntc)
spd01 --> spd02 (scz)
spd01 --> spd03 (ntc)
spd01 --> spd03 (scz)
spd01 --> spd04 (ntc)
spd01 --> spd04 (scz)
spd01 --> spd05 (ntc)
spd01 --> spd05 (scz)
spd01 --> spd06 (ntc)
spd01 --> spd06 (scz)
spd01 --> spd07 (ntc)
spd01 --> spd07 (scz)
p−value
0.01 < p < 0.05
p < 0.01
Commun. Prob.
max
min

SpD06

```
netVisual_bubble(cellchat, sources.use = 6,  comparison = c(1, 2), angle.x = 45)
```

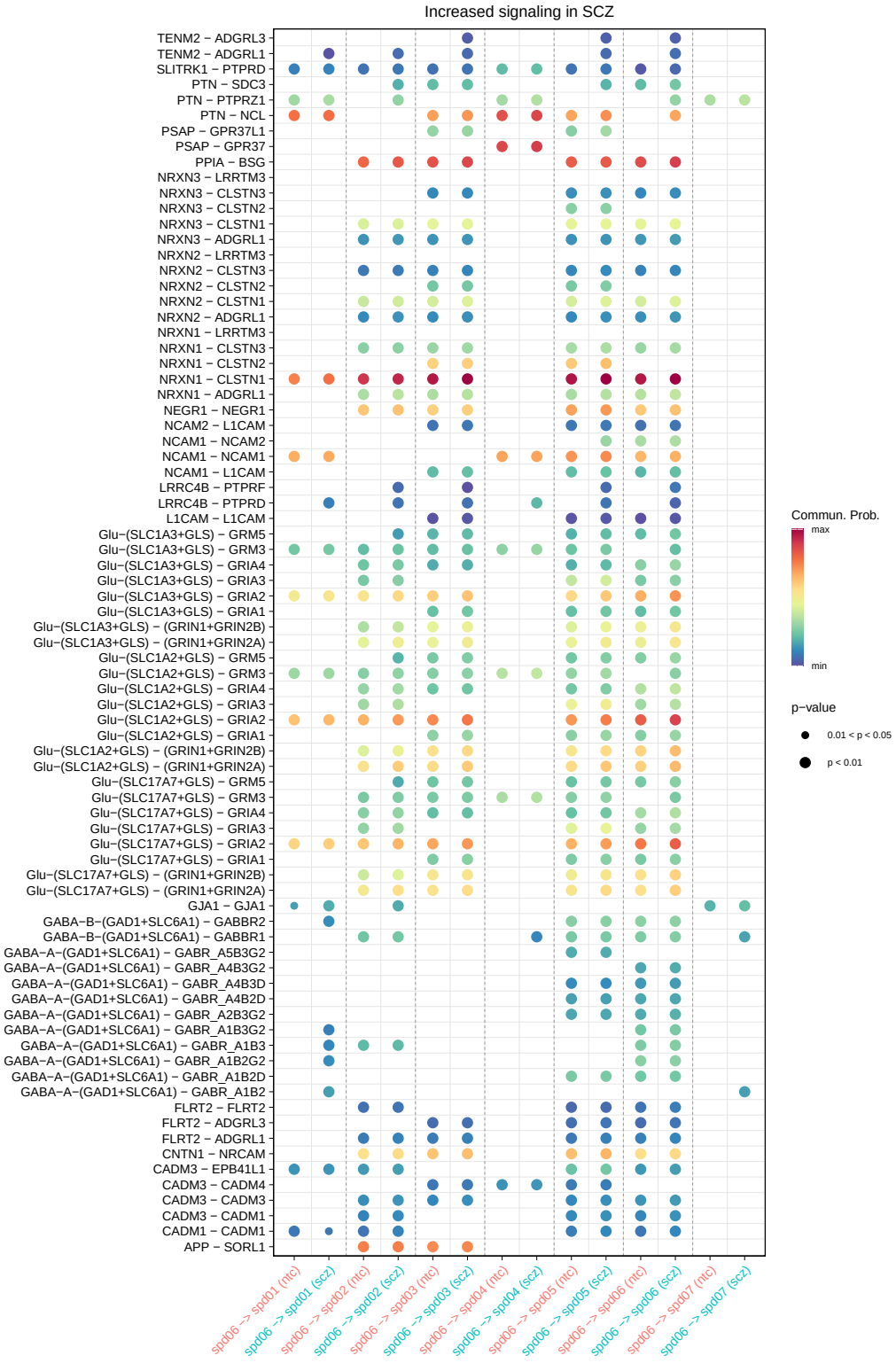
```
Comparing communications on a merged object
```


TENM2 − ADGRL3
TENM2 − ADGRL1
SLITRK1 − PTPRD
PTN − SDC3
PTN − PTPRZ1
PTN − NCL
PSAP − GPR37L1
PSAP − GPR37
PPIA − BSG
NRXN3 − LRRTM3
NRXN3 − CLSTN3
NRXN3 − CLSTN2
NRXN3 − CLSTN1
NRXN3 − ADGRL1
NRXN2 − LRRTM3
NRXN2 − CLSTN3
NRXN2 − CLSTN2
NRXN2 − CLSTN1
NRXN2 − ADGRL1
NRXN1 − LRRTM3
NRXN1 − CLSTN3
NRXN1 − CLSTN2
NRXN1 − CLSTN1
NRXN1 − ADGRL1
NEGR1 − NEGR1
NCAM2 − L1CAM
NCAM1 − NCAM2
NCAM1 − NCAM1
NCAM1 − L1CAM
LRRC4B − PTPRF
LRRC4B − PTPRD
L1CAM − L1CAM
Glu−(SLC1A3+GLS) − GRM5
Glu−(SLC1A3+GLS) − GRM3
Glu−(SLC1A3+GLS) − GRIA4
Glu−(SLC1A3+GLS) − GRIA3
Glu−(SLC1A3+GLS) − GRIA2
Glu−(SLC1A3+GLS) − GRIA1
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2A)
Glu−(SLC1A2+GLS) − GRM5
Glu−(SLC1A2+GLS) − GRM3
Glu−(SLC1A2+GLS) − GRIA4
Glu−(SLC1A2+GLS) − GRIA3
Glu−(SLC1A2+GLS) − GRIA2
Glu−(SLC1A2+GLS) − GRIA1
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2A)
Glu−(SLC17A7+GLS) − GRM5
Glu−(SLC17A7+GLS) − GRM3
Glu−(SLC17A7+GLS) − GRIA4
Glu−(SLC17A7+GLS) − GRIA3
Glu−(SLC17A7+GLS) − GRIA2
Glu−(SLC17A7+GLS) − GRIA1
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2B)
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2A)
GJA1 − GJA1
GABA−B−(GAD1+SLC6A1) − GABBR2
GABA−B−(GAD1+SLC6A1) − GABBR1
GABA−A−(GAD1+SLC6A1) − GABR_A5B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3D
GABA−A−(GAD1+SLC6A1) − GABR_A4B2D
GABA−A−(GAD1+SLC6A1) − GABR_A2B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3
GABA−A−(GAD1+SLC6A1) − GABR_A1B2G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B2D
GABA−A−(GAD1+SLC6A1) − GABR_A1B2
FLRT2 − FLRT2
FLRT2 − ADGRL3
FLRT2 − ADGRL1
CNTN1 − NRCAM
CADM3 − EPB41L1
CADM3 − CADM4
CADM3 − CADM3
CADM3 − CADM1
CADM1 − CADM1
APP − SORL1
spd06 -> spd01 (mic)
spd06 -> spd01 (scz)
spd06 -> spd02 (mic)
spd06 -> spd02 (scz)
spd06 -> spd03 (mic)
spd06 -> spd03 (scz)
spd06 -> spd04 (mic)
spd06 -> spd04 (scz)
spd06 -> spd05 (mic)
spd06 -> spd05 (scz)
spd06 -> spd06 (mic)
spd06 -> spd06 (scz)
spd06 -> spd07 (mic)
spd06 -> spd07 (scz)
Commun. Prob.
max
min
p−value
0.01 < p < 0.05
p < 0.01

Only differential ones in SpD06

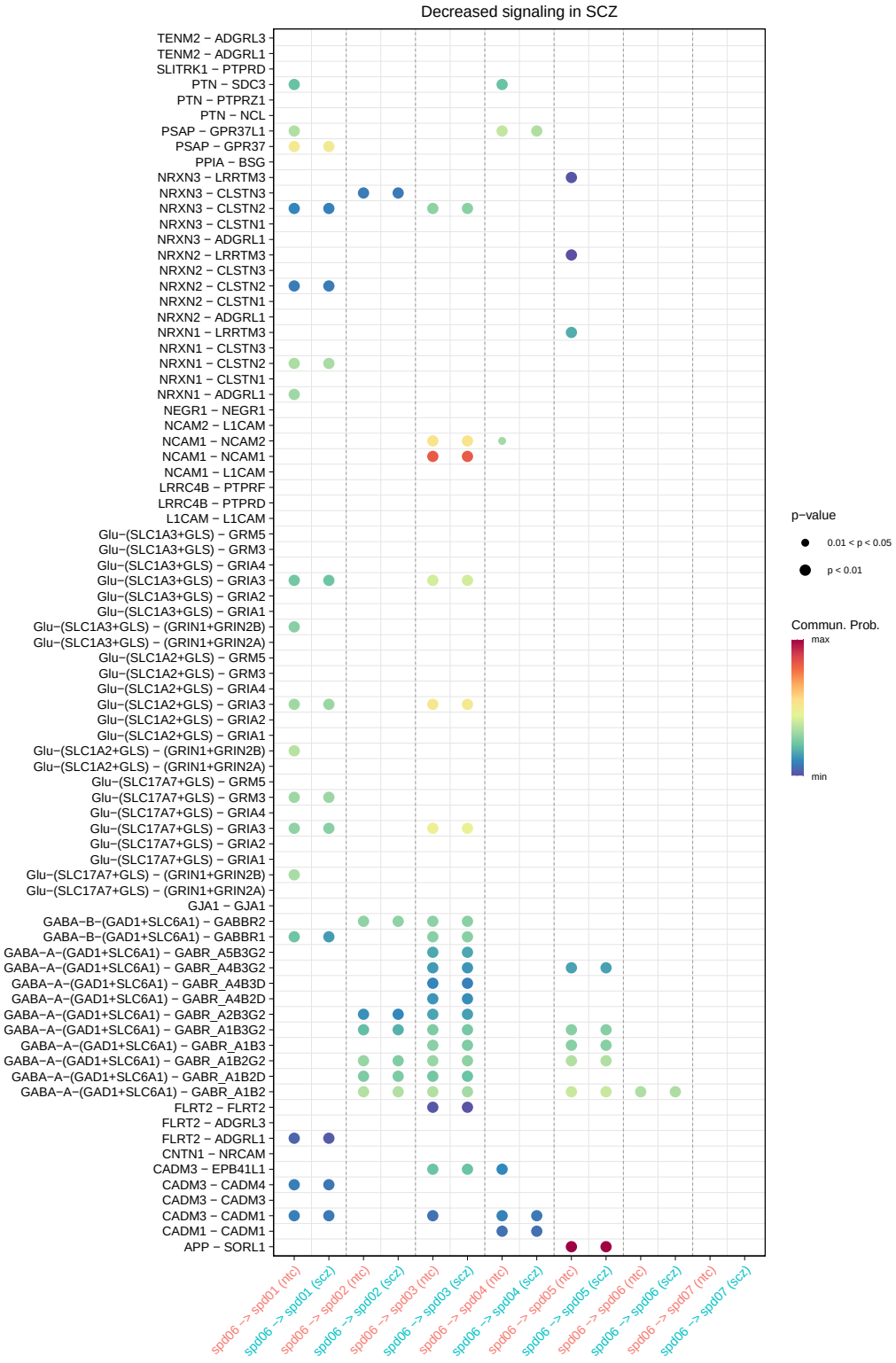
```
netVisual_bubble(cellchat, sources.use = 6,  comparison = c(1, 2), angle.x = 45,
title.name = "Increased signaling in SCZ",
max.dataset = 2)
```

```
Comparing communications on a merged object
```


Increased signaling in SCZ
TENM2 − ADGRL3
TENM2 − ADGRL1
SLITRK1 − PTPRD
PTN − SDC3
PTN − PTPRZ1
PTN − NCL
PSAP − GPR37L1
PSAP − GPR37
PPIA − BSG
NRXN3 − LRRTM3
NRXN3 − CLSTN3
NRXN3 − CLSTN2
NRXN3 − CLSTN1
NRXN3 − ADGRL1
NRXN2 − LRRTM3
NRXN2 − CLSTN3
NRXN2 − CLSTN2
NRXN2 − CLSTN1
NRXN2 − ADGRL1
NRXN1 − LRRTM3
NRXN1 − CLSTN3
NRXN1 − CLSTN2
NRXN1 − CLSTN1
NRXN1 − ADGRL1
NEGR1 − NEGR1
NCAM2 − L1CAM
NCAM1 − NCAM2
NCAM1 − NCAM1
NCAM1 − L1CAM
LRRC4B − PTPRF
LRRC4B − PTPRD
L1CAM − L1CAM
Glu−(SLC1A3+GLS) − GRM5
Glu−(SLC1A3+GLS) − GRM3
Glu−(SLC1A3+GLS) − GRIA4
Glu−(SLC1A3+GLS) − GRIA3
Glu−(SLC1A3+GLS) − GRIA2
Glu−(SLC1A3+GLS) − GRIA1
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2A)
Glu−(SLC1A2+GLS) − GRM5
Glu−(SLC1A2+GLS) − GRM3
Glu−(SLC1A2+GLS) − GRIA4
Glu−(SLC1A2+GLS) − GRIA3
Glu−(SLC1A2+GLS) − GRIA2
Glu−(SLC1A2+GLS) − GRIA1
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2A)
Glu−(SLC17A7+GLS) − GRM5
Glu−(SLC17A7+GLS) − GRM3
Glu−(SLC17A7+GLS) − GRIA4
Glu−(SLC17A7+GLS) − GRIA3
Glu−(SLC17A7+GLS) − GRIA2
Glu−(SLC17A7+GLS) − GRIA1
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2B)
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2A)
GJA1 − GJA1
GABA−B−(GAD1+SLC6A1) − GABBR2
GABA−B−(GAD1+SLC6A1) − GABBR1
GABA−A−(GAD1+SLC6A1) − GABR_A5B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3D
GABA−A−(GAD1+SLC6A1) − GABR_A4B2D
GABA−A−(GAD1+SLC6A1) − GABR_A2B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3
GABA−A−(GAD1+SLC6A1) − GABR_A1B2G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B2D
GABA−A−(GAD1+SLC6A1) − GABR_A1B2
FLRT2 − FLRT2
FLRT2 − ADGRL3
FLRT2 − ADGRL1
CNTN1 − NRCAM
CADM3 − EPB41L1
CADM3 − CADM4
CADM3 − CADM3
CADM3 − CADM1
CADM1 − CADM1
APP − SORL1
spd06 –> spd01 (ntc)
spd06 –> spd01 (scz)
spd06 –> spd02 (ntc)
spd06 –> spd02 (scz)
spd06 –> spd03 (ntc)
spd06 –> spd03 (scz)
spd06 –> spd04 (ntc)
spd06 –> spd04 (scz)
spd06 –> spd05 (ntc)
spd06 –> spd05 (scz)
spd06 –> spd06 (ntc)
spd06 –> spd06 (scz)
spd06 –> spd07 (ntc)
spd06 –> spd07 (scz)
Commun. Prob.
max
min
p−value
0.01 < p < 0.05
p < 0.01

```
netVisual_bubble(cellchat, sources.use = 6,  comparison = c(1, 2), angle.x = 45,
title.name = "Decreased signaling in SCZ",
max.dataset = 1)
```

Comparing communications on a merged object


Decreased signaling in SCZ
TENM2 − ADGRL3
TENM2 − ADGRL1
SLITRK1 − PTPRD
PTN − SDC3
PTN − PTPRZ1
PTN − NCL
PSAP − GPR37L1
PSAP − GPR37
PPIA − BSG
NRXN3 − LRRTM3
NRXN3 − CLSTN3
NRXN3 − CLSTN2
NRXN3 − CLSTN1
NRXN3 − ADGRL1
NRXN2 − LRRTM3
NRXN2 − CLSTN3
NRXN2 − CLSTN2
NRXN2 − CLSTN1
NRXN2 − ADGRL1
NRXN1 − LRRTM3
NRXN1 − CLSTN3
NRXN1 − CLSTN2
NRXN1 − CLSTN1
NRXN1 − ADGRL1
NEGR1 − NEGR1
NCAM2 − L1CAM
NCAM1 − NCAM2
NCAM1 − NCAM1
NCAM1 − L1CAM
LRRC4B − PTPRF
LRRC4B − PTPRD
L1CAM − L1CAM
Glu−(SLC1A3+GLS) − GRM5
Glu−(SLC1A3+GLS) − GRM3
Glu−(SLC1A3+GLS) − GRIA4
Glu−(SLC1A3+GLS) − GRIA3
Glu−(SLC1A3+GLS) − GRIA2
Glu−(SLC1A3+GLS) − GRIA1
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2A)
Glu−(SLC1A2+GLS) − GRM5
Glu−(SLC1A2+GLS) − GRM3
Glu−(SLC1A2+GLS) − GRIA4
Glu−(SLC1A2+GLS) − GRIA3
Glu−(SLC1A2+GLS) − GRIA2
Glu−(SLC1A2+GLS) − GRIA1
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2A)
Glu−(SLC17A7+GLS) − GRM5
Glu−(SLC17A7+GLS) − GRM3
Glu−(SLC17A7+GLS) − GRIA4
Glu−(SLC17A7+GLS) − GRIA3
Glu−(SLC17A7+GLS) − GRIA2
Glu−(SLC17A7+GLS) − GRIA1
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2B)
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2A)
GJA1 − GJA1
GABA−B−(GAD1+SLC6A1) − GABBR2
GABA−B−(GAD1+SLC6A1) − GABBR1
GABA−A−(GAD1+SLC6A1) − GABR_A5B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3D
GABA−A−(GAD1+SLC6A1) − GABR_A4B2D
GABA−A−(GAD1+SLC6A1) − GABR_A2B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3
GABA−A−(GAD1+SLC6A1) − GABR_A1B2G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B2D
GABA−A−(GAD1+SLC6A1) − GABR_A1B2
FLRT2 − FLRT2
FLRT2 − ADGRL3
FLRT2 − ADGRL1
CNTN1 − NRCAM
CADM3 − EPB41L1
CADM3 − CADM4
CADM3 − CADM3
CADM3 − CADM1
CADM1 − CADM1
APP − SORL1
spd06 –> spd01 (ntc)
spd06 –> spd01 (scz)
spd06 –> spd02 (ntc)
spd06 –> spd02 (scz)
spd06 –> spd03 (ntc)
spd06 –> spd03 (scz)
spd06 –> spd04 (ntc)
spd06 –> spd04 (scz)
spd06 –> spd05 (ntc)
spd06 –> spd05 (scz)
spd06 –> spd06 (ntc)
spd06 –> spd06 (scz)
spd06 –> spd07 (ntc)
spd06 –> spd07 (scz)
p−value
0.01 < p < 0.05
p < 0.01
Commun. Prob.
max
min

Note: It is possible to do with only the DEG's we identified, but it takes much longer to figure our the timeline.