



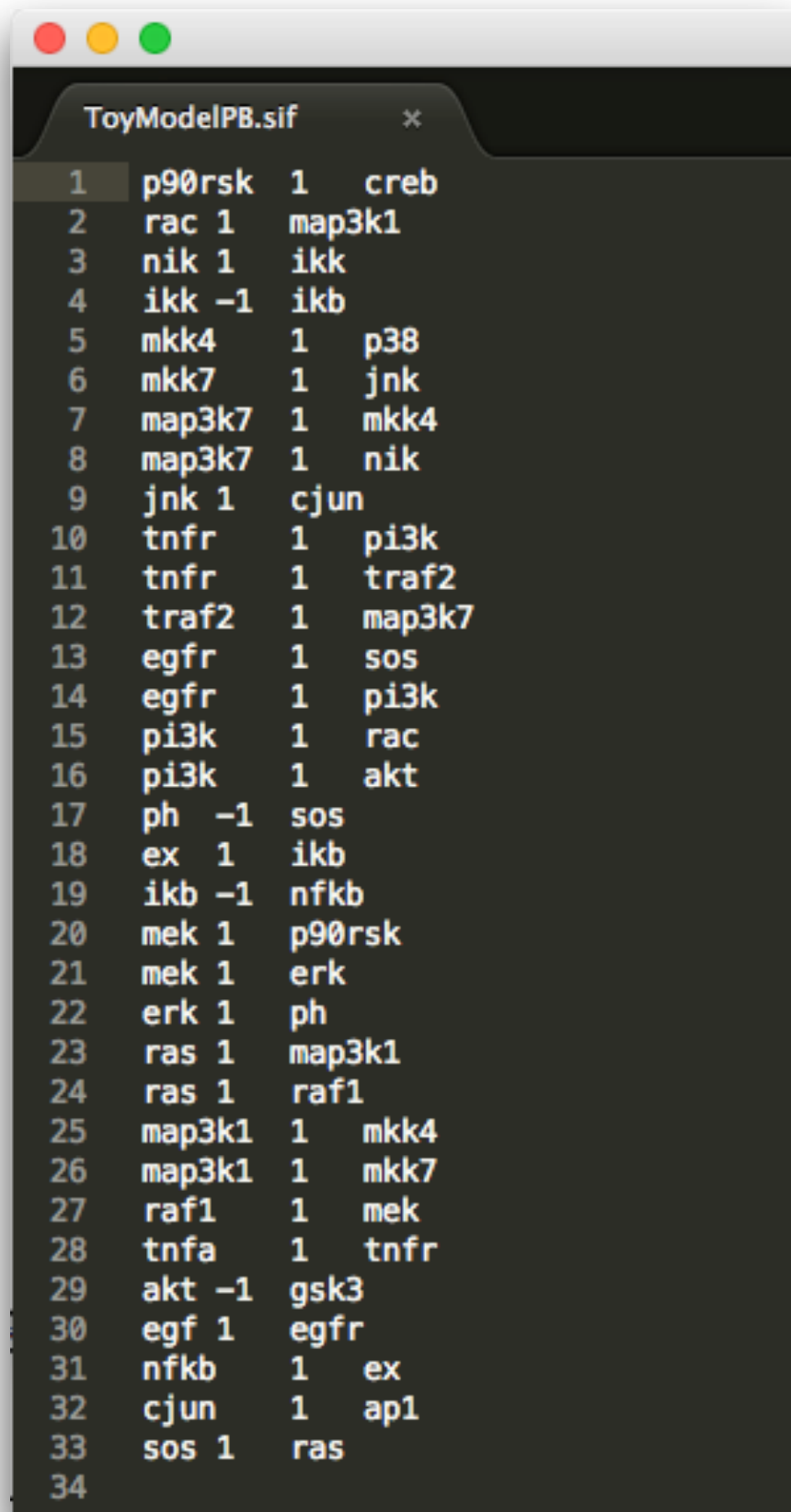
IO17 | Large Scale Bioinformatics for Immuno-Oncology

Signaling pathways with Omnipath

Francesca Finotello, Federica Eduati, and Pedro L. Fernandes

GTPB | The Gulbenkian Training Programme in Bioinformatics
Instituto Gulbenkian de Ciência, Oeiras, Portugal | Sept 19th-22nd, 2017

Prior Knowledge Network (PKN)



1	p90rsk	1	creb
2	rac	1	map3k1
3	nik	1	ikk
4	ikk	-1	ikb
5	mkk4	1	p38
6	mkk7	1	jnk
7	map3k7	1	mkk4
8	map3k7	1	nik
9	jnk	1	cjun
10	tnfr	1	pi3k
11	tnfr	1	traf2
12	traf2	1	map3k7
13	egfr	1	sos
14	egfr	1	pi3k
15	pi3k	1	rac
16	pi3k	1	akt
17	ph	-1	sos
18	ex	1	ikb
19	ikb	-1	nfkb
20	mek	1	p90rsk
21	mek	1	erk
22	erk	1	ph
23	ras	1	map3k1
24	ras	1	raf1
25	map3k1	1	mkk4
26	map3k1	1	mkk7
27	raf1	1	mek
28	tnfa	1	tnfr
29	akt	-1	gsk3
30	egf	1	egfr
31	nfkb	1	ex
32	cjun	1	ap1
33	sos	1	ras
34			

Prior Knowledge Network (PKN)

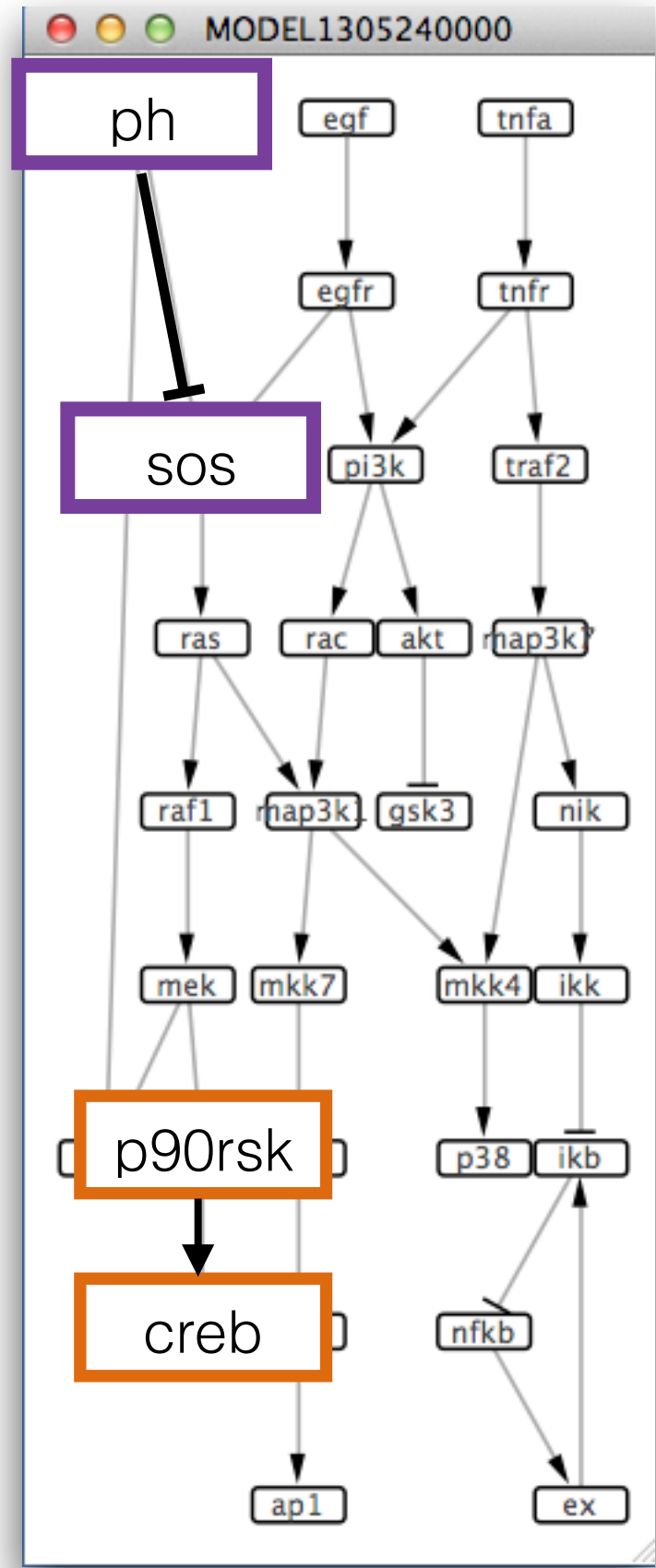
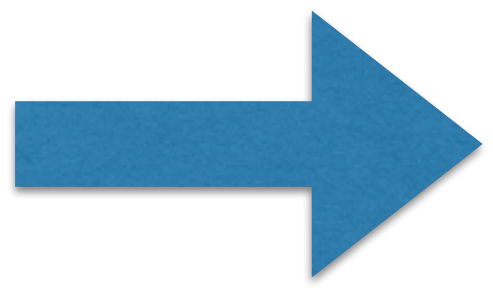
TovModelPB.sif

p90rsk1creb

4	ikk	-1	ikb
5	mkk4	1	p38
6	mkk7	1	jnk
7	map3k7	1	mkk4
8	map3k7	1	nik
9	tnfr	1	pi3k
10	tnfr	1	traf2
11	traf2	1	map3k7
12	egfr	1	sos
13	egfr	1	pi3k

ph-1sos

19	ikk	-1	nfkb
20	mek	1	p90rsk
21	mek	1	erk
22	erk	1	ph
23	ras	1	map3k1
24	ras	1	raf1
25	map3k1	1	mkk4
26	map3k1	1	mkk7
27	raf1	1	mek
28	tnfa	1	tnfr
29	akt	-1	gsk3
30	egf	1	egfr
31	nfkb	1	ex
32	cjun	1	ap1
33	sos	1	ras
34			



Experimental data

- Data is stored in MIDAS files
- MIDAS: **M**inimum **I**nformation for **D**ata **A**nalysis in **S**ystems Biology
- csv file with specified structure

```
ToyModelPB.csv
TR:Cell:CellLine, TR:egf, TR:tnfa, TR:pi3ki, TR:raf1i, DA:raf1, DA:erk, DA:ap1, DA:gsk3, DA:p38, DA:nfkb, DV:raf1, DV:erk, DV:ap1, DV:gsk3, DV:p38, DV:nfkb
1,0,0,0,0,0,0,0,0,0,0,0,0.113273458,0.157629482,0.165686548,0.900470819,0.107672569,0.135582705
1,1,0,0,0,0,0,0,0,0,0,0.161252619,0.136127386,0.132165733,0.973463471,0.126018911,0.137593912
1,0,1,0,0,0,0,0,0,0,0,0.18118642,0.171172805,0.069216889,0.833938898,0.143094829,0.111949527
1,1,1,0,0,0,0,0,0,0,0,0.204532136,0.075609551,0.16402037,0.83166228,0.145759195,0.187964898
1,1,0,1,0,0,0,0,0,0,0,0.16324977,0.147945527,0.157562806,0.934339135,0.086896169,0.153629572
1,0,1,1,0,0,0,0,0,0,0,0.158026707,0.136434731,0.180032868,0.848411795,0.226635572,0.15556591
1,1,1,1,0,0,0,0,0,0,0,0.135451913,0.153500205,0.135521064,0.89481319,0.05830718,0.133181325
1,1,0,0,1,0,0,0,0,0,0,0.082807004,0.115530747,0.147297449,0.962855757,0.144970489,0.188848398|
1,0,1,0,1,0,0,0,0,0,0,0.133160344,0.153239082,0.098038148,0.852769287,0.171006652,0.125711512
1,1,1,0,1,0,0,0,0,0,0,0.114319825,0.09963248,0.155512388,0.968806568,0.105584024,0.083550813
1,0,0,0,0,2,2,2,2,2,2,0.198299667,0.140645582,0.175126149,0.904183049,0.094413478,0.214599563
1,1,0,0,0,2,2,2,2,2,2,0.602498653,0.763488384,0.305469399,0.641274819,0.152680489,0.182447362
1,0,1,0,0,2,2,2,2,2,2,0.155188125,0.147881622,0.380404874,0.940715143,0.184757911,0.740173257
1,1,1,0,0,2,2,2,2,2,2,0.657885557,0.720306337,0.364615678,0.622286802,0.187638999,0.705852669
1,1,0,1,0,2,2,2,2,2,2,0.692530243,0.801365631,0.280240963,0.887692802,0.112033162,0.198296597
1,0,1,1,0,2,2,2,2,2,2,0.143369979,0.131457095,0.392918862,0.880872231,0.19777232,0.745405859
1,1,1,1,0,2,2,2,2,2,2,0.669624661,0.837450417,0.326696968,0.901872707,0.04859938,0.624857712
1,1,0,0,1,2,2,2,2,2,2,0.175648722,0.129299364,0.36266489,0.627175393,0.131089441,0.19785061
1,0,1,0,1,2,2,2,2,2,2,0.119595368,0.163255646,0.34708573,0.903120838,0.088607025,0.691261127
1,1,1,0,1,2,2,2,2,2,2,0.164973809,0.170214992,0.242168331,0.555841739,0.166428234,0.702749483
1,0,0,0,0,4,4,4,4,4,4,0.092998769,0.066336993,0.108561619,0.937502167,0.144800969,0.182535084
1,1,0,0,0,4,4,4,4,4,4,0.857535183,0.833476326,0.612769544,0.464345142,0.165753249,0.140449005
1,0,1,0,0,4,4,4,4,4,4,0.073259441,0.152377506,0.51660454,0.849942037,0.093956969,0.431710911
1,1,1,0,0,4,4,4,4,4,4,0.872738158,0.799038863,0.583169724,0.412469896,0.192409925,0.479626065
are biological perturbations to a system (such as the addition or extracellular ligands)
```

Import to R:

	TR.Cell.CellLine	TR.egf	TR.tnfa	TR.pi3ki	TR.raf1i	DA.raf1	DA.erk	DA.ap1	DA.gsk3	DA.p38	DA.nfkb	DV.raf1	DV.erk	DV.ap1	DV.gsk3	DV.p38	DV.nfkb
1	1	0	0	0	0	0	0	0	0	0	0	0.1132735	0.15762948	0.16568655	0.9004708	0.10767257	0.1355827
2	1	1	0	0	0	0	0	0	0	0	0	0.1612526	0.13612739	0.13216573	0.9734635	0.12601891	0.1375939
3	1	0	1	0	0	0	0	0	0	0	0	0.1811864	0.17117281	0.06921689	0.8339389	0.14309483	0.1119495
4	1	1	1	0	0	0	0	0	0	0	0	0.2045321	0.07560955	0.16402037	0.8316623	0.14575920	0.1879649
5	1	1	0	1	0	0	0	0	0	0	0	0.1632498	0.14794553	0.15756281	0.9343391	0.08689617	0.1536296
6	1	0	1	1	0	0	0	0	0	0	0	0.1580267	0.13643473	0.18003287	0.8484118	0.22663557	0.1555659

Header

TR	treatment
DA	data acquisition
DV	data value

Experimental data

Treatments
Stimulated: egf, tnfa
Inhibited: pi3k, raf1

TR.Cell.CellLine		TR.egf	TR.tnfa	TR.pi3ki	TR.raf1i	DA.raf1	DA.erk	DA.ap1	DA.gsk3	DA.p38	DA.nfkb	DV.raf1	DV.erk
1	1	0	0	0	0	0	0	0	0	0	0	0.1132735	0.15762948
2	1	1	0	0	0	0	0	0	0	0	0	0.1612526	0.13612739
3	1	0	1	0	0	0	0	0	0	0	0	0.1811864	0.17117281
4	1	1	1	0	0	0	0	0	0	0	0	0.2045321	0.07560955
5	1	1	0	1	0	0	0	0	0	0	0	0.1632498	0.14794553
6	1	0	1	1	0	0	0	0	0	0	0	0.1580267	0.13643473

Header

TR	treatment
DA	data acquisition
DV	data value

Experimental Data

raf1, erk, ap1, gsk3, p38, nfkb

TR.raf1i	DA.raf1	DA.erk	DA.ap1	DA.gsk3	DA.p38	DA.nfkb	DV.raf1	DV.erk	DV.ap1	DV.gsk3	DV.p38	DV.nfkb
0	0	0	0	0	0	0	0.1132735	0.15762948	0.16568655	0.9004708	0.10767257	0.1355827
0	0	0	0	0	0	0	0.1612526	0.13612739	0.13216573	0.9734635	0.12601891	0.1375939
0	0	0	0	0	0	0	0.1811864	0.17117281	0.06921689	0.8339389	0.14309483	0.1119495
0	0	0	0	0	0	0	0.2045321	0.07560955	0.16402037	0.8316623	0.14575920	0.1879649
0	0	0	0	0	0	0	0.1632498	0.14794553	0.15756281	0.9343391	0.08689617	0.1536296
0	0	0	0	0	0	0	0.1580267	0.13643473	0.18003287	0.8484118	0.22663557	0.1555659

Header

TR	treatment
DA	data acquisition
DV	data value

Install Cytoscape

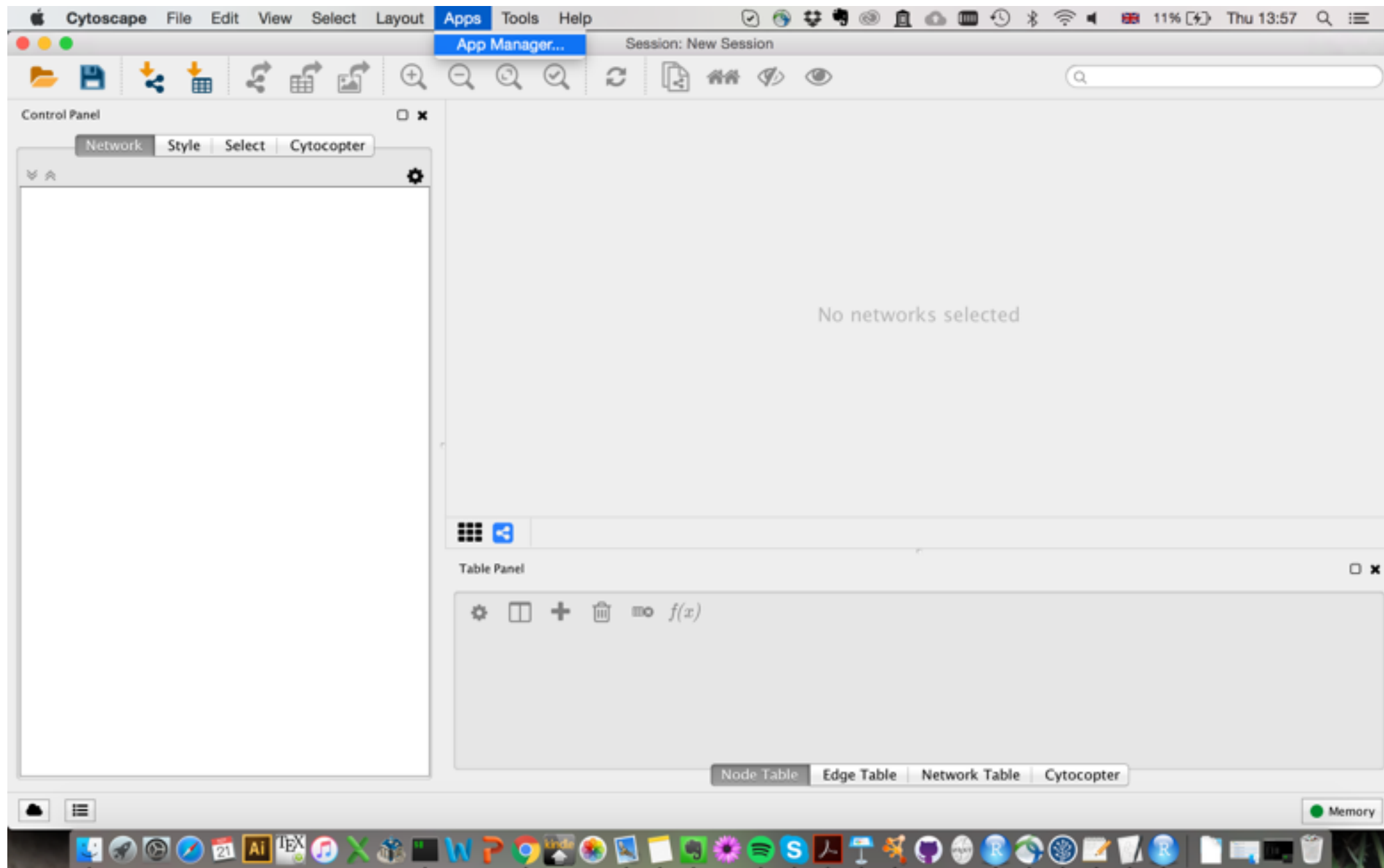
1. To install Cytoscape from the terminal type:

```
sh Cytoscape_3_4_0_unix.sh
```

2. open Cytoscape

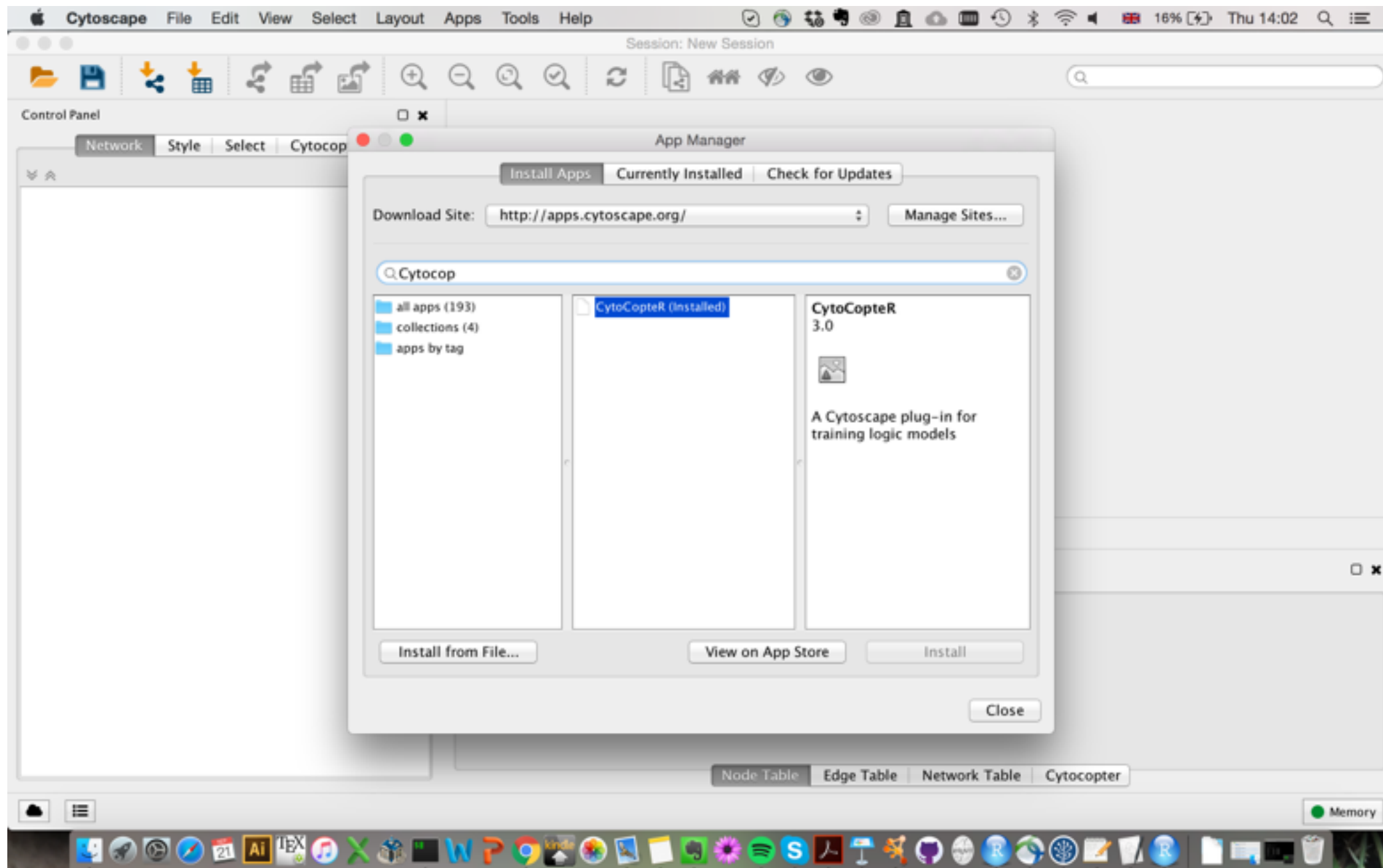
Install CytoceptR app (1)

3. To install CytoceptR app:



Install CytoCoptR app (1)

3. To install CytoCoptR app:

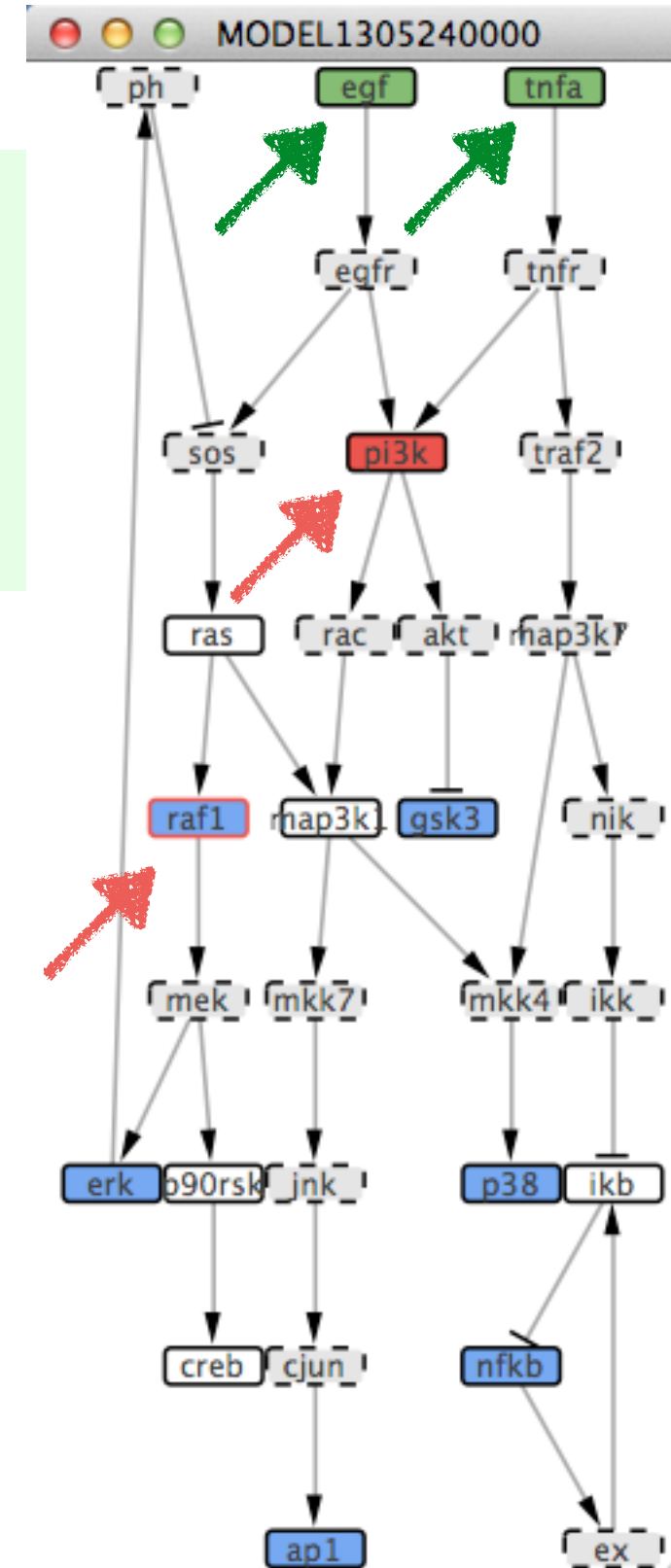


Network + experimental conditions

```
> data = read.csv(file = "/Users/admin/Documents/SaezGrp/20160202_Heide", as.is = TRUE)
> head(data)
  TR.Cell.CellLine TR.egf TR.tnfa TR.pi3ki TR.raf1i DA.raf1 DA.erk DA.c
1                1      0       0         0         0      0      0
2                1      1       0         0         0      0      0
3                1      0       1         0         0      0      0
4                1      1       1         0         0      0      0
5                1      1       0         1         0      0      0
6                1      0       1         1         0      0      0
>
```

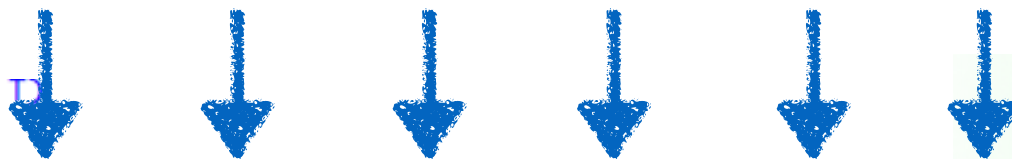
Stimulated

Inhibited



Network + experimental conditions

ader = T



	DV.raf1	DV.erk	DV.ap1	DV.gsk3	DV.p38	DV.nfkb
0	0.1132735	0.15762948	0.16568655	0.9004708	0.10767257	0.1355827
0	0.1612526	0.13612739	0.13216573	0.9734635	0.12601891	0.1375939
0	0.1811864	0.17117281	0.06921689	0.8339389	0.14309483	0.1119495
0	0.2045321	0.07560955	0.16402037	0.8316623	0.14575920	0.1879649
0	0.1632498	0.14794553	0.15756281	0.9343391	0.08689617	0.1536296
0	0.1580267	0.13643473	0.18003287	0.8484118	0.22663557	0.1555659

Stimulated

Inhibited

Measured

Removed

neither measured nor perturbed,
logical consistency not impaired

