IO17 | Large Scale Bioinformatics for Immuno-Oncology

Signaling pathways with Omnipath

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Part of the slides are curtesy of Attila Gabor

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INSTITUTO GULBENKIAN DE CIÊNCIA

Prior Knowledge Network (PKN)

ToyModelPB.sif

```
p90rsk  1   creb
rac 1   map3k1
nik 1   ikk
ikk -1  ikb
mkk4    1   p38
mkk7    1   jnk
map3k7  1   mkk4
map3k7  1   nik
jnk 1   cjun
tnfr    1   pi3k
tnfr    1   traf2
traf2   1   map3k7
egfr    1   sos
egfr    1   pi3k
pi3k    1   rac
pi3k    1   akt
ph  -1  sos
ex  1   ikb
ikb -1  nfkb
mek 1   p90rsk
mek 1   erk
erk 1   ph
ras 1   map3k1
ras 1   raf1
map3k1  1   mkk4
map3k1  1   mkk7
raf1    1   mek
tnfa    1   tnfr
akt -1  gsk3
egf 1   egfr
nfkb    1   ex
cjun    1   ap1
sos 1   ras
```

Prior Knowledge Network (PKN)

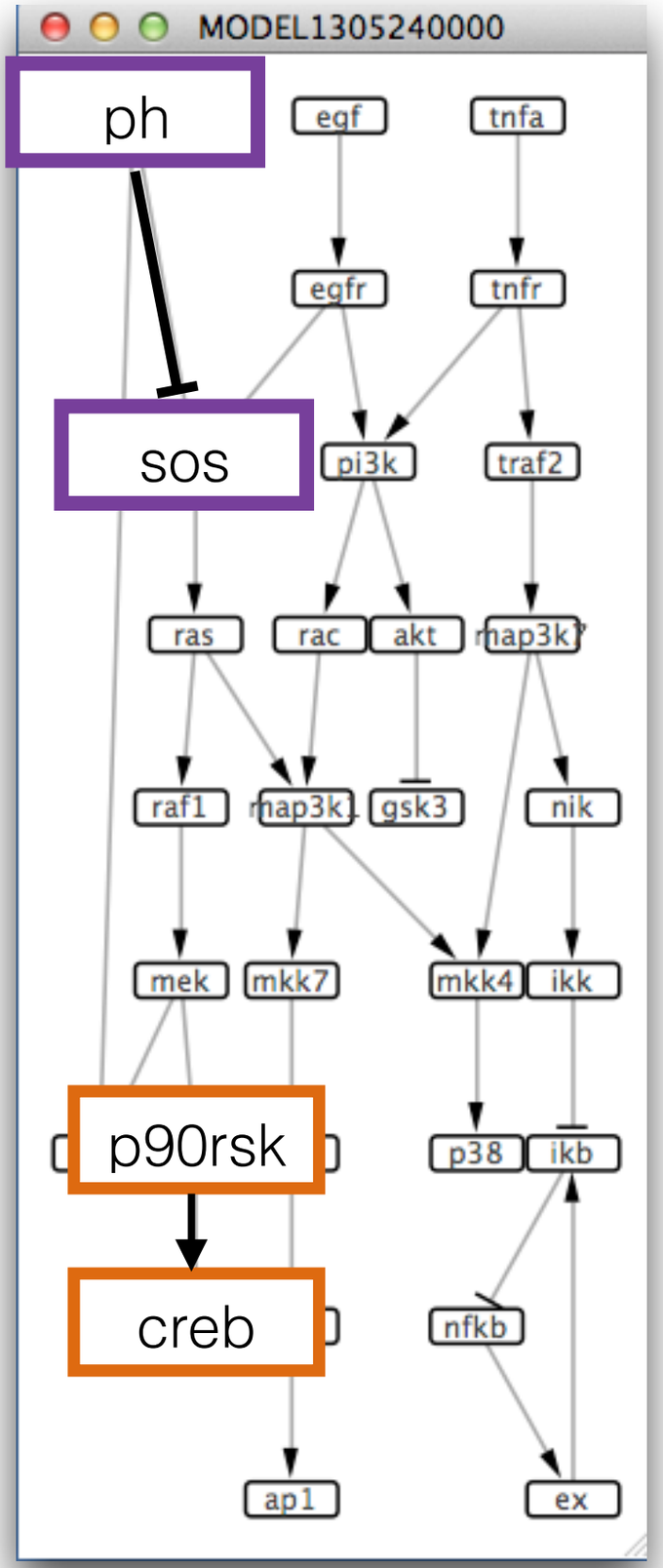
ToyModelPB.sif

p90rsk 1 creb

```
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
```

ph -1 sos

```
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
```



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
1,0,0,0,0,0,0,0,0,0,0,0.113273458,0.157629482,0.165686548,0.900470819,0.107672569,0.135582705
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 of extracellular ligands)

Experimental data

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

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

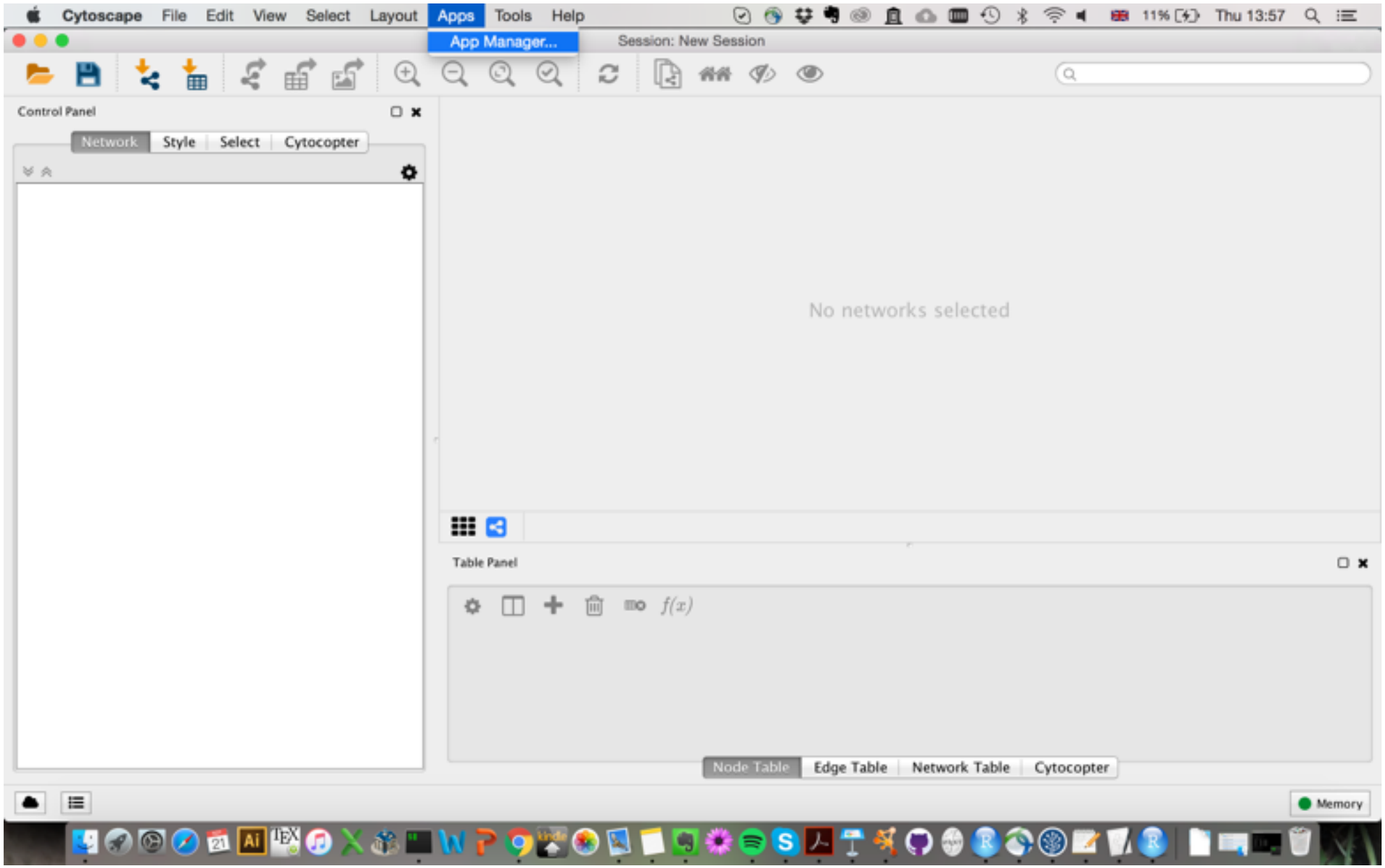
1. To install Cytoscape from the terminal type:

```
sh Cytoscape_3_4_0_unix.sh
```

2. open Cytoscape

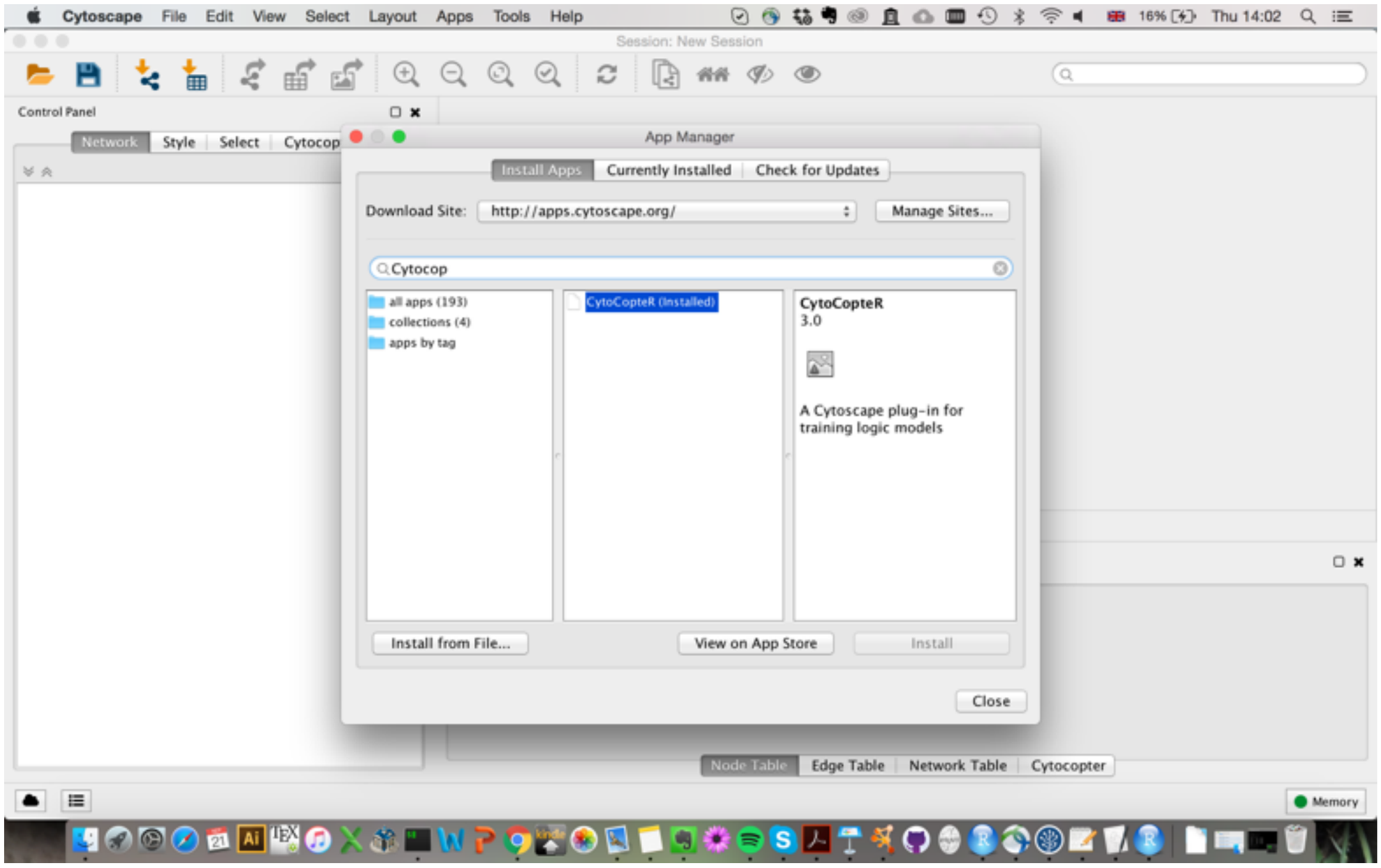
Install CytocoptR app (1)

3. To install CytocoptR app:



Install CytocoptR app (1)

3. To install CytocoptR app:

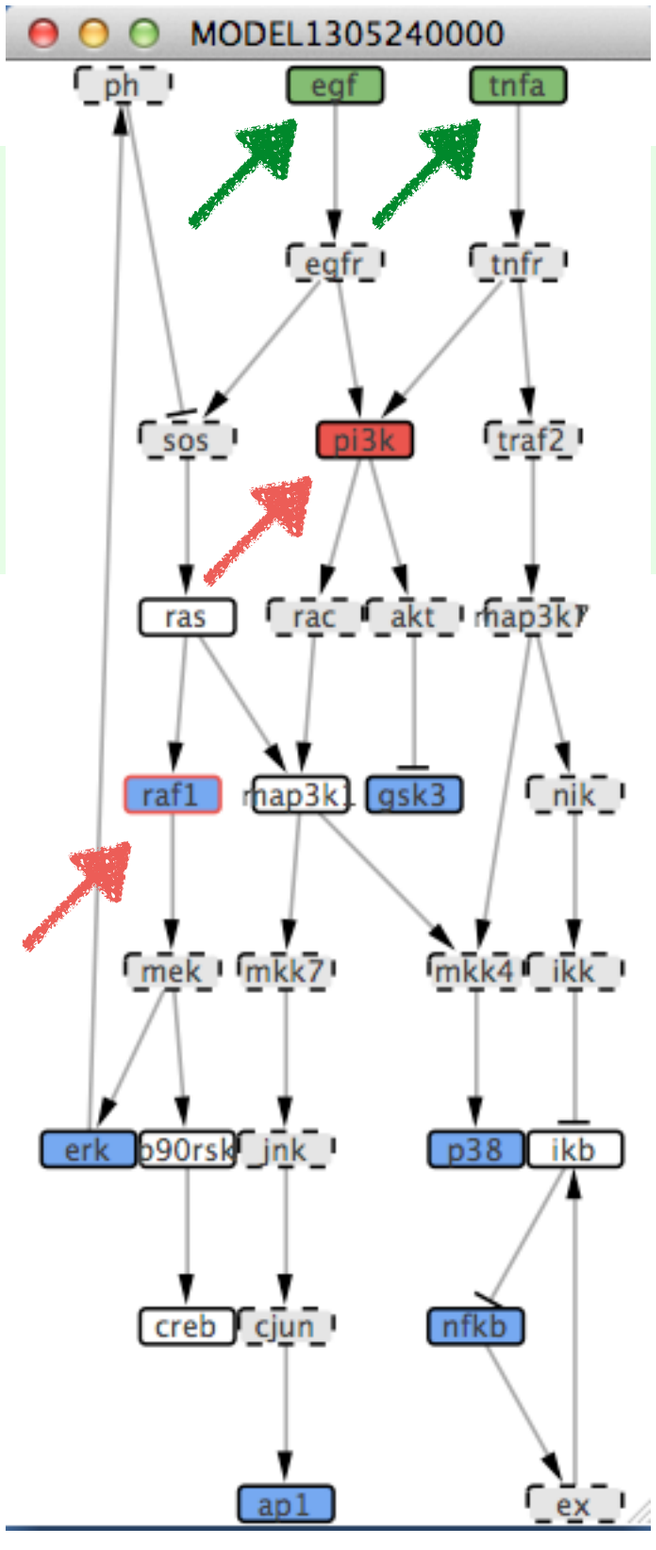


Network + experimental conditions

```
> data = read.csv(file="/Users/admin/Documents/SaezGrp/20160202_Heide
> head(data)
  TR.Cell.CellLine TR.egf TR.tnfa TR.pi3ki TR.raf1i DA.raf1 DA.erk DA.
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 = ID
    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