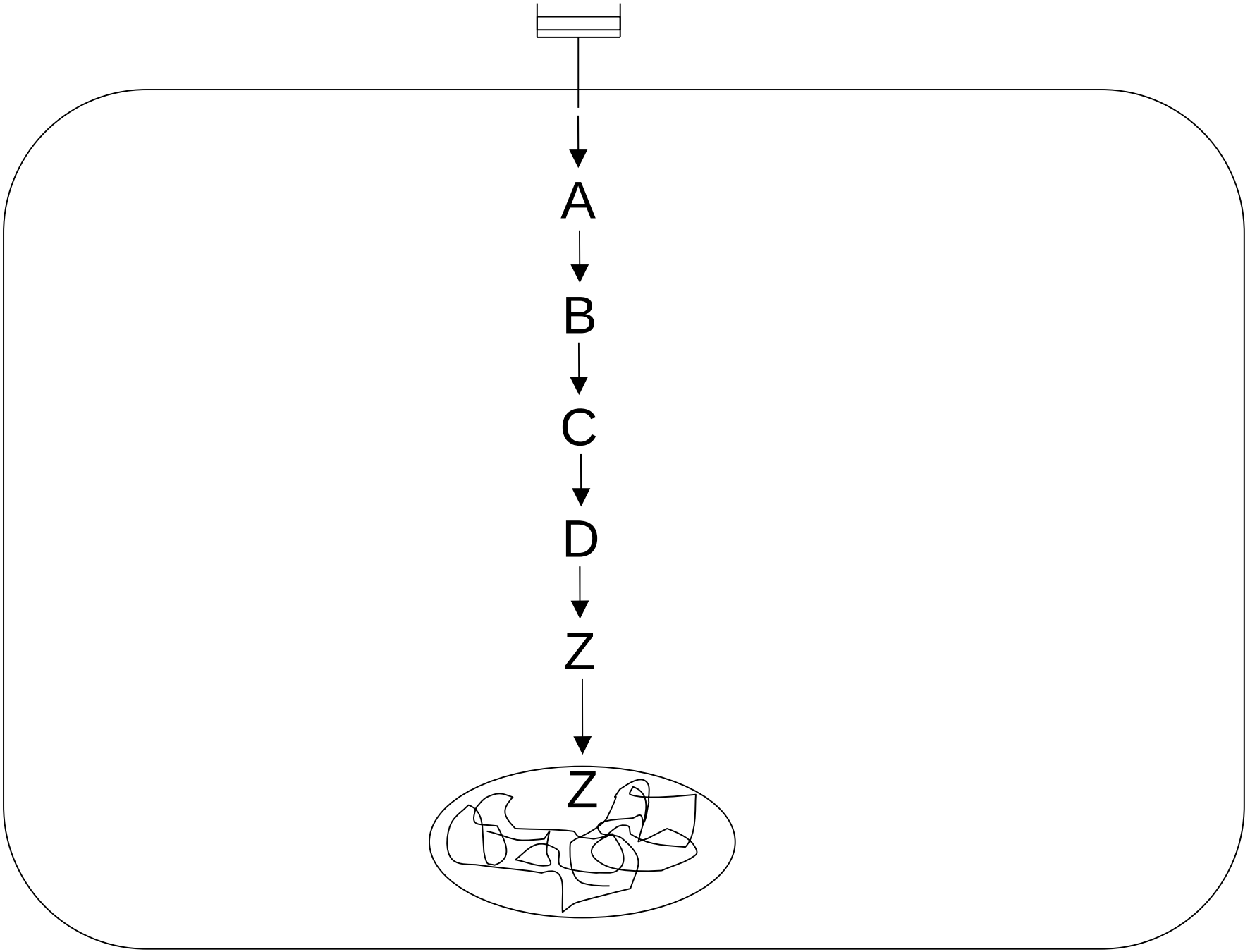
ChemChains sandbox

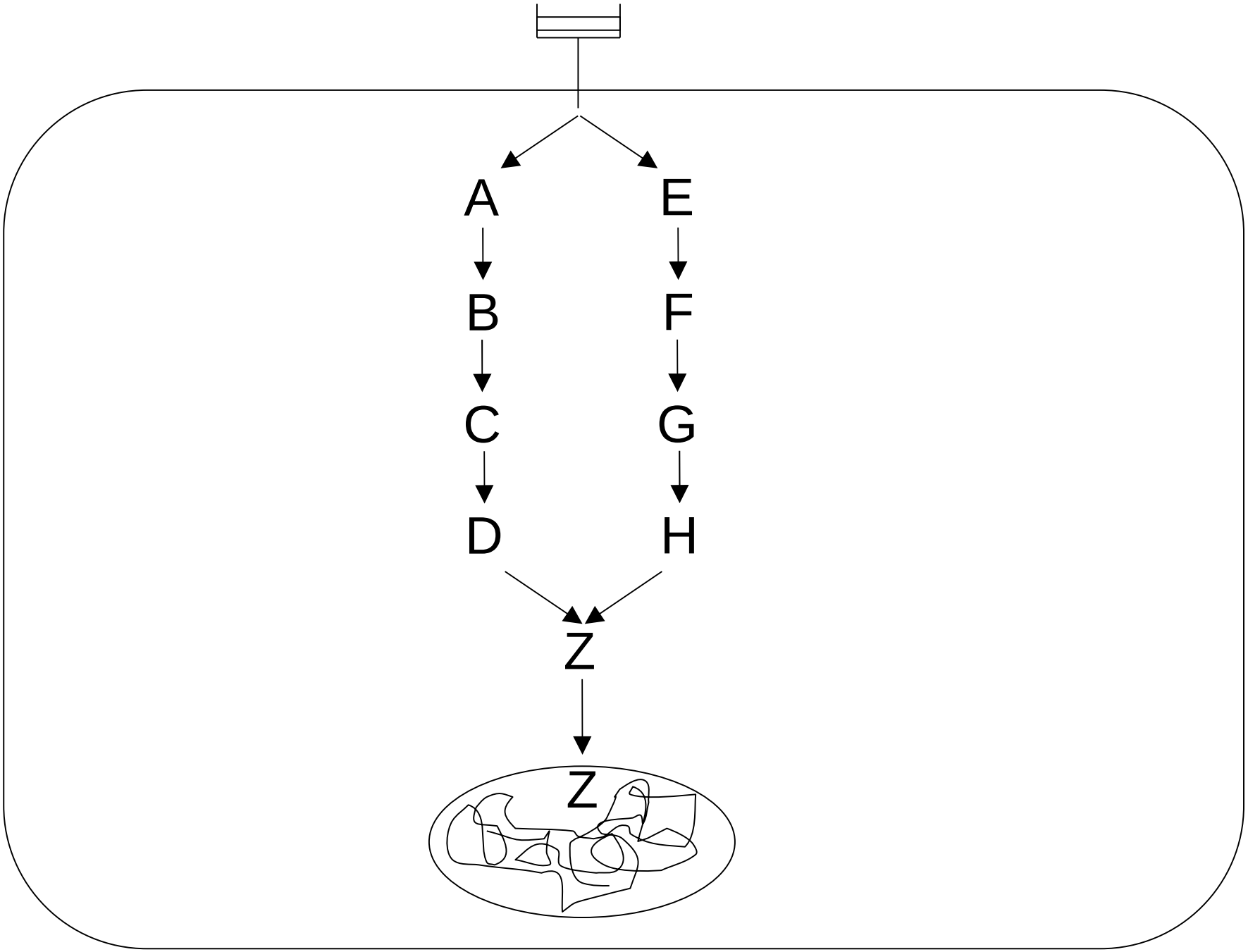
http://jays.net/wiki/ChemChains_sandbox

Modeling cell biology in a boolean network.

YAPC::NA 2008

Jay Hannah, Omaha.pm


A
B
C
D
Z
Z


A
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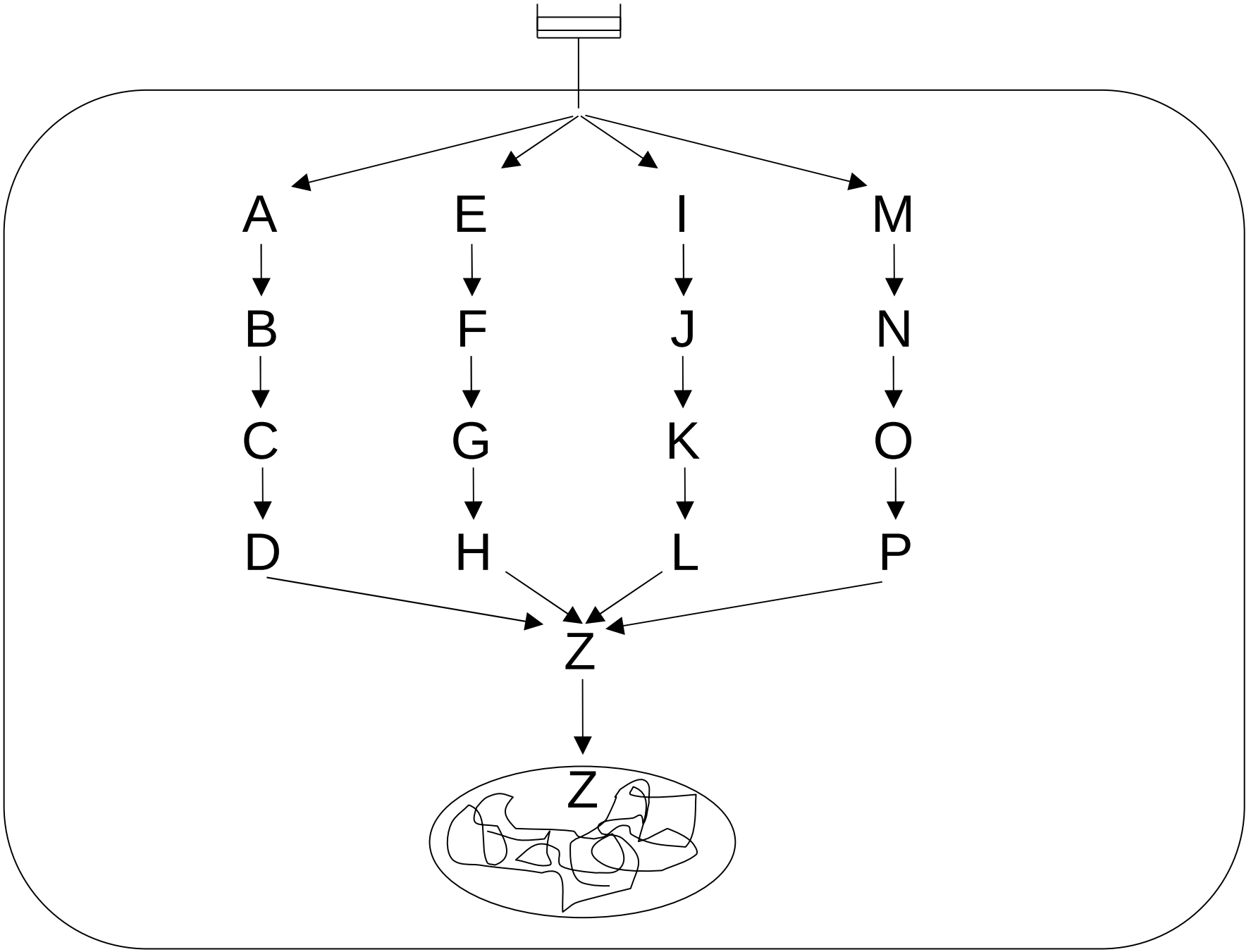
A
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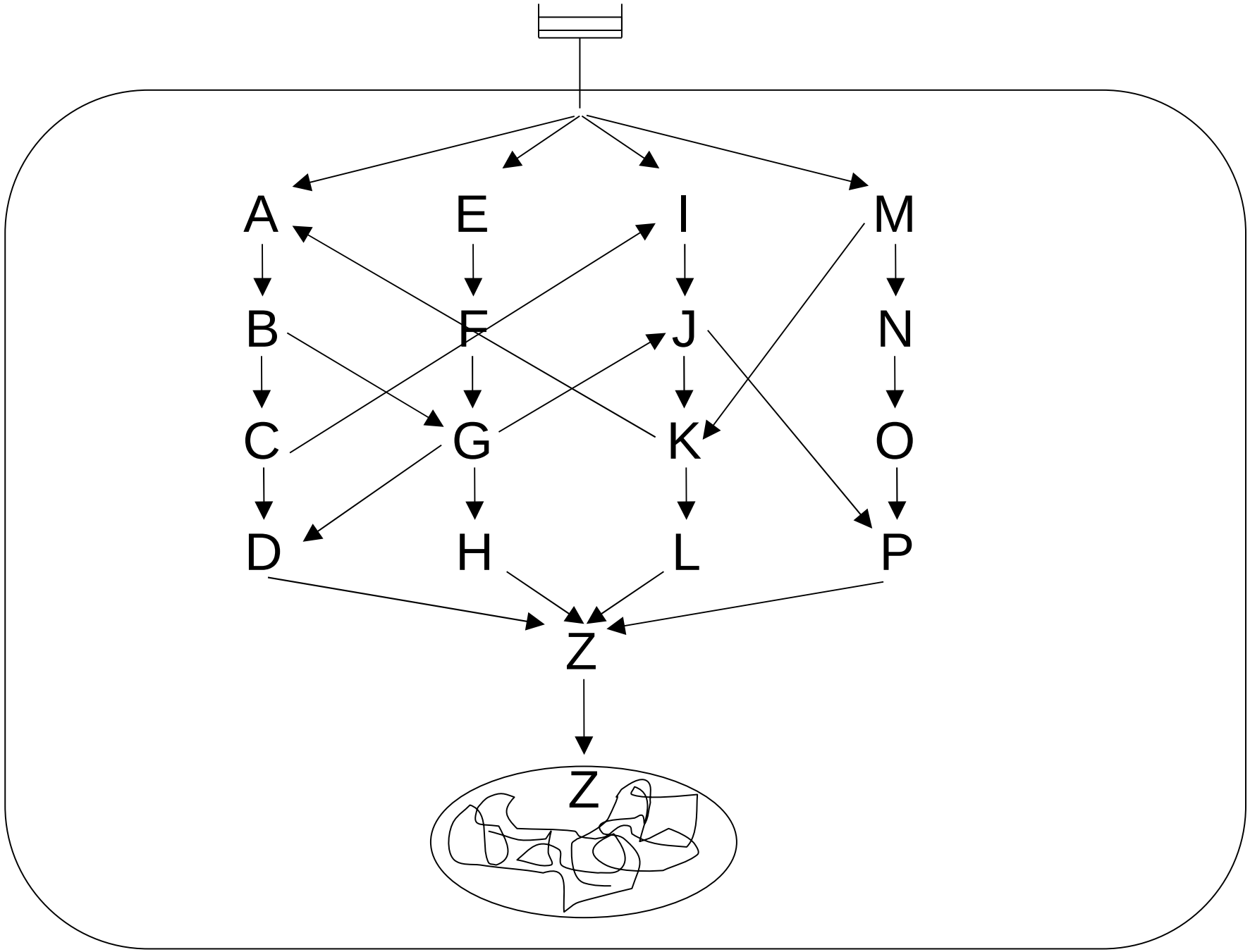
Z


A
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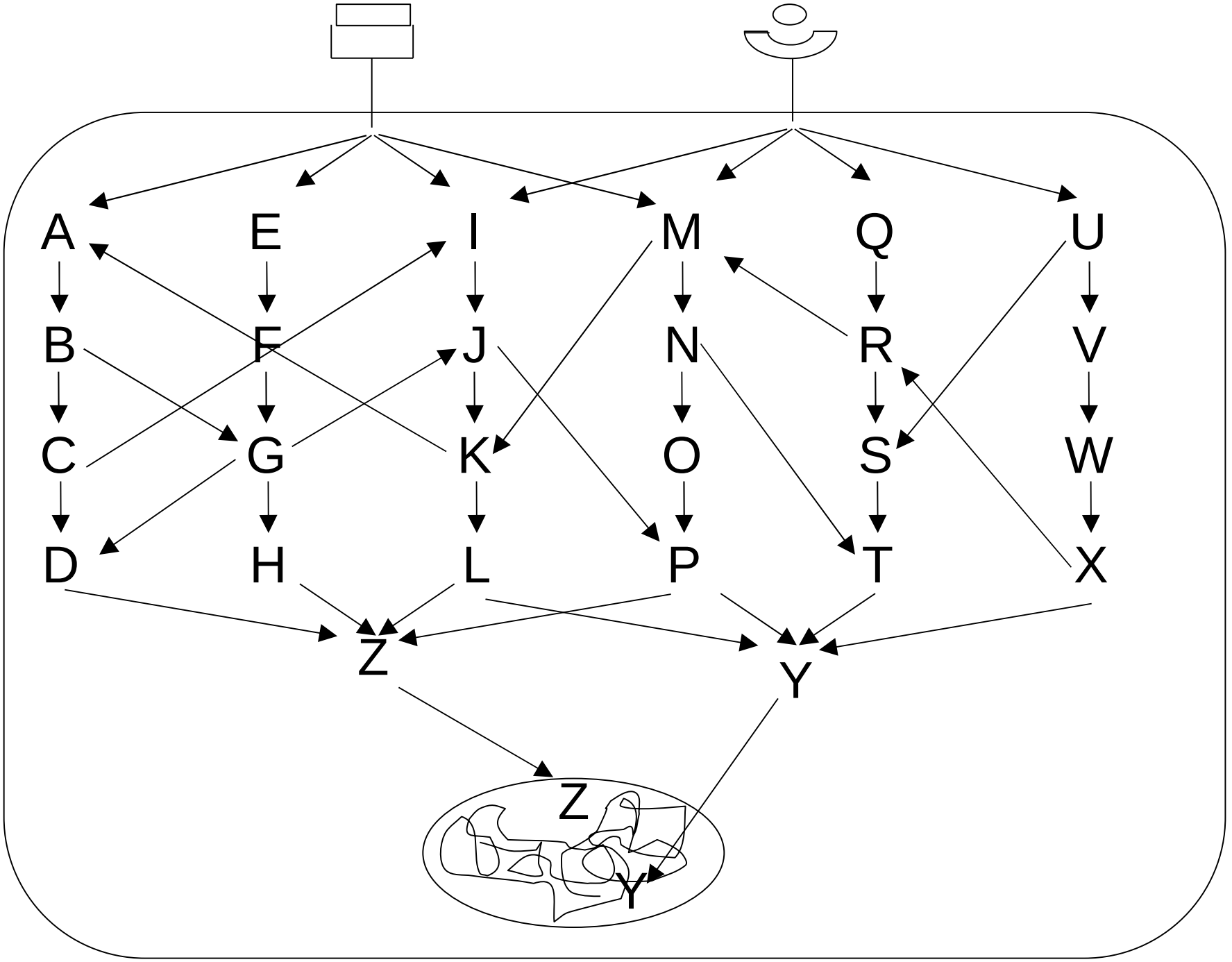
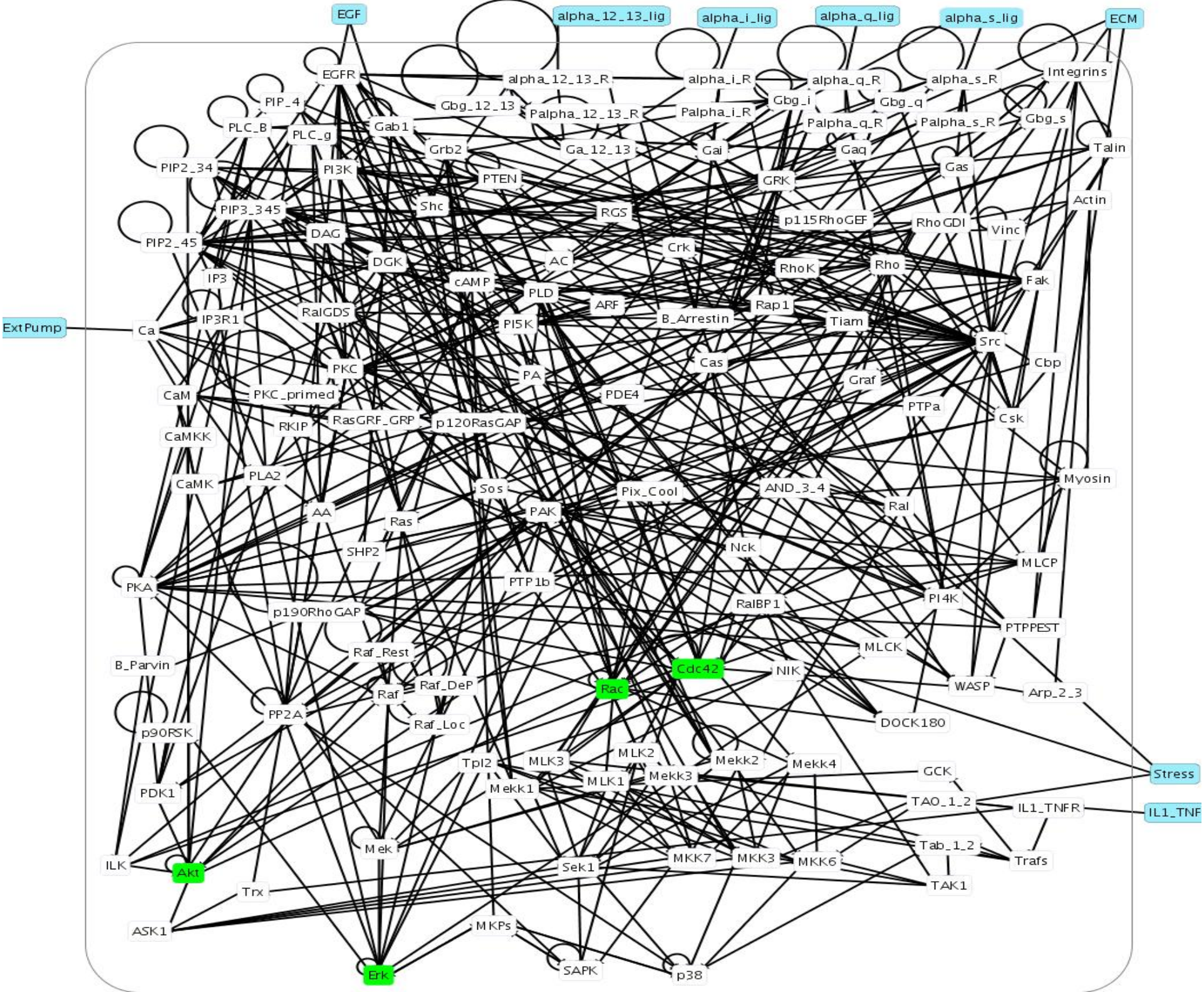
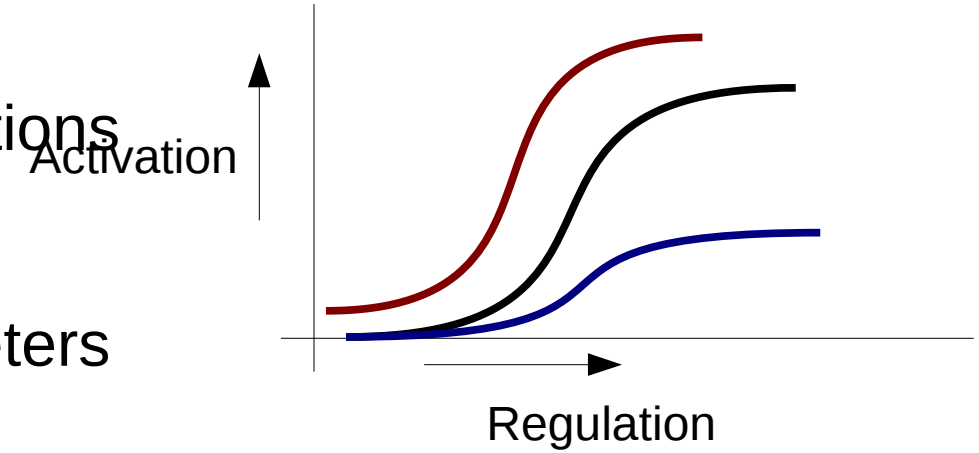
Z


A
E
I
M
Q
U
B
F
J
N
R
V
C
G
K
O
S
W
D
H
L
P
T
X
Z
Y
Z
Y


EGF
alpha_12_13_lig
alpha_i_lig
alpha_q_lig
alpha_s_lig
ECM
EGFR
alpha_12_13_R
alpha_i_R
alpha_q_R
alpha_s_R
Integrins
PIP_4
Gbg_12_13
Palpha_12_13_R
Palpha_i_R
Gbg_i
Gbg_q
Palpha_q_R
Palpha_s_R
Gbg_s
PLC_B
PLC_g
Gab1
Grb2
Ga_12_13
Gai
Gaq
Talin
PIP2_34
PI3K
PTEN
GRK
Gas
Actin
PIP3_345
Shc
RGS
p115RhoGEF
RhoGDI
Vinc
DAG
PIP2_45
Crk
DGK
AC
RhoK
Rho
Fak
IP3
cAMP
PLD
ARF
Rap1
RalGDS
ExtPump
Ca
IP3R1
PI5K
B_Arrestin
Tiam
Src
Cas
Cbp
PKC
PA
Graf
CaM
PKC_primed
PDE4
PTPa
Csk
RasGRF_GRP
p120RasGAP
RKIP
CaMKK
CaMK
PLA2
Sos
Pix_Cool
AND_3_4
Myosin
AA
Ras
PAK
Ral
SHP2
Nck
MLCP
PKA
PTP1b
RalBP1
PI4K
p190RhoGAP
PTPPEST
Raf_Rest
MLCK
B_Parvin
Cdc42
NIK
Rac
Raf
Raf_DeP
WASP
Arp_2_3
PP2A
DOCK180
Raf_Loc
p90RSK
Tpl2
MLK3
MLK2
Mekk2
Mekk4
GCK
Stress
PDK1
MLK1
Mekk3
Mekk1
TAO_1_2
IL1_TNFR
IL1_TNF
Mek
Tab_1_2
ILK
Akt
MKK7
MKK3
MKK6
Trafs
Sek1
TAK1
Trx
ASK1
MKPs
Erk
SAPK
p38

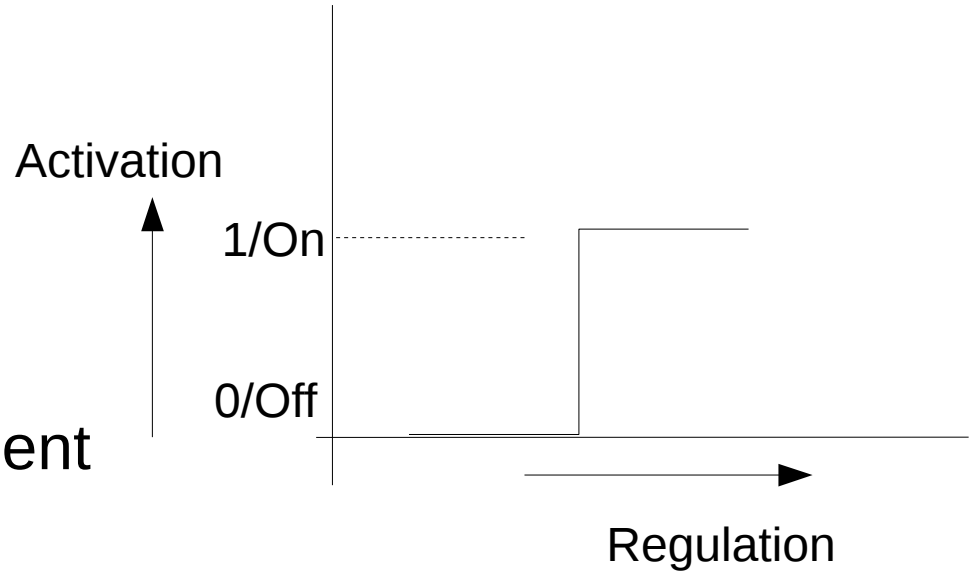
Modeling Methods

- Continuous
  - Uses differential equations
  - Dependent on parameters

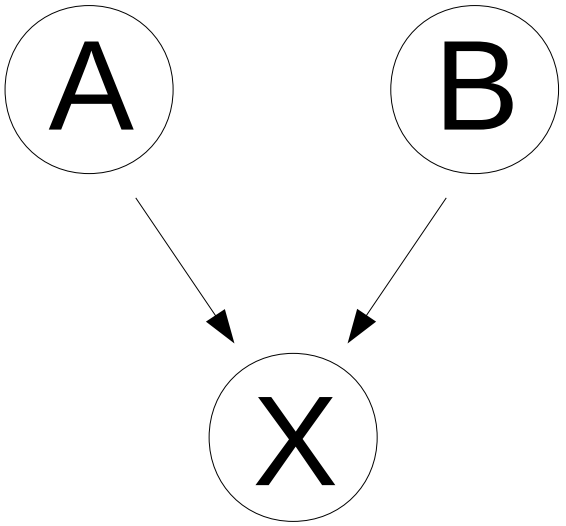


Modeling Methods

- Discrete - Boolean
  - *On* or *Off*
  - Parameter independent



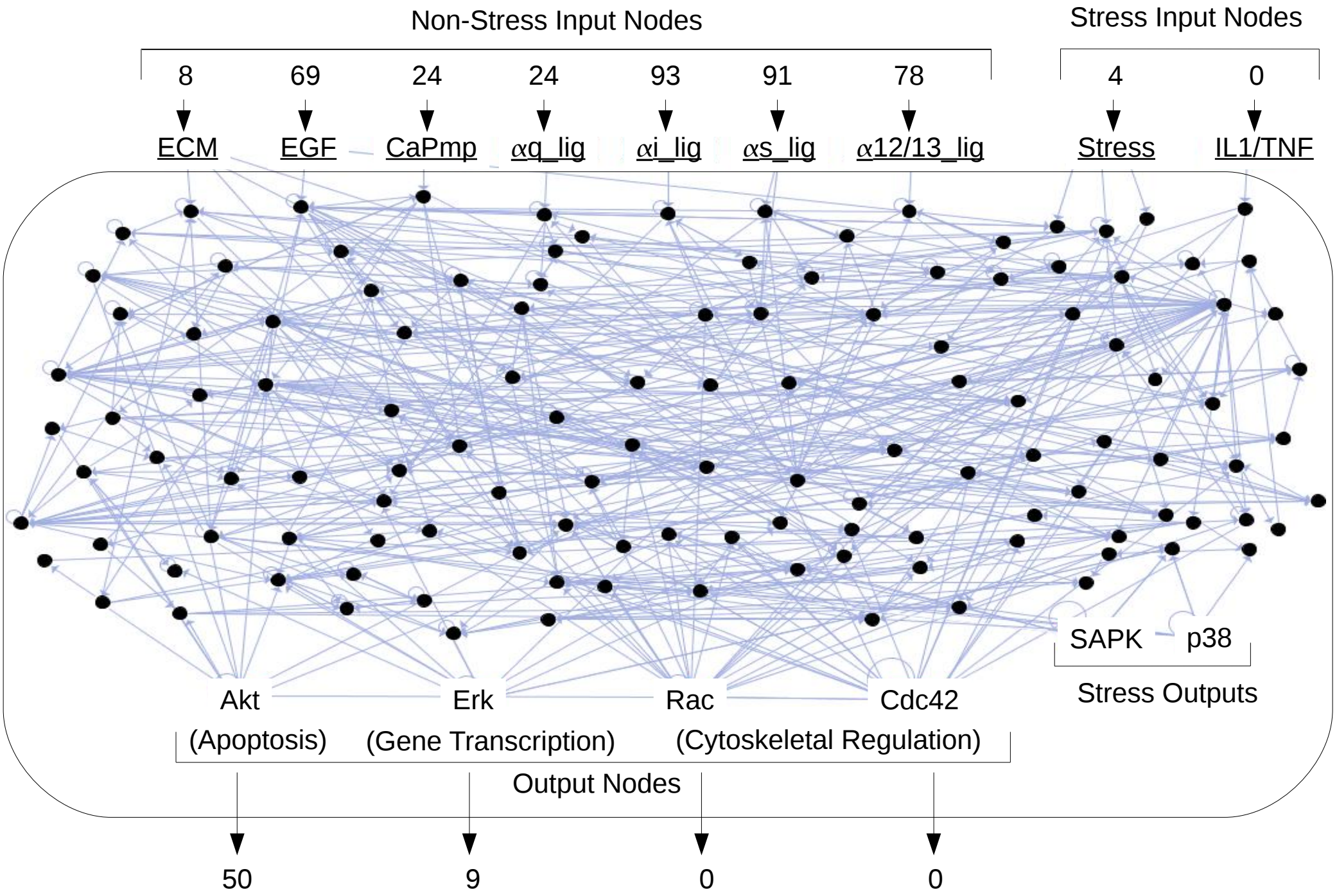
- Qualitative logic, i.e. “Protein *A* activates protein *B”*
- - straight forward to retrieve from biochemical literature

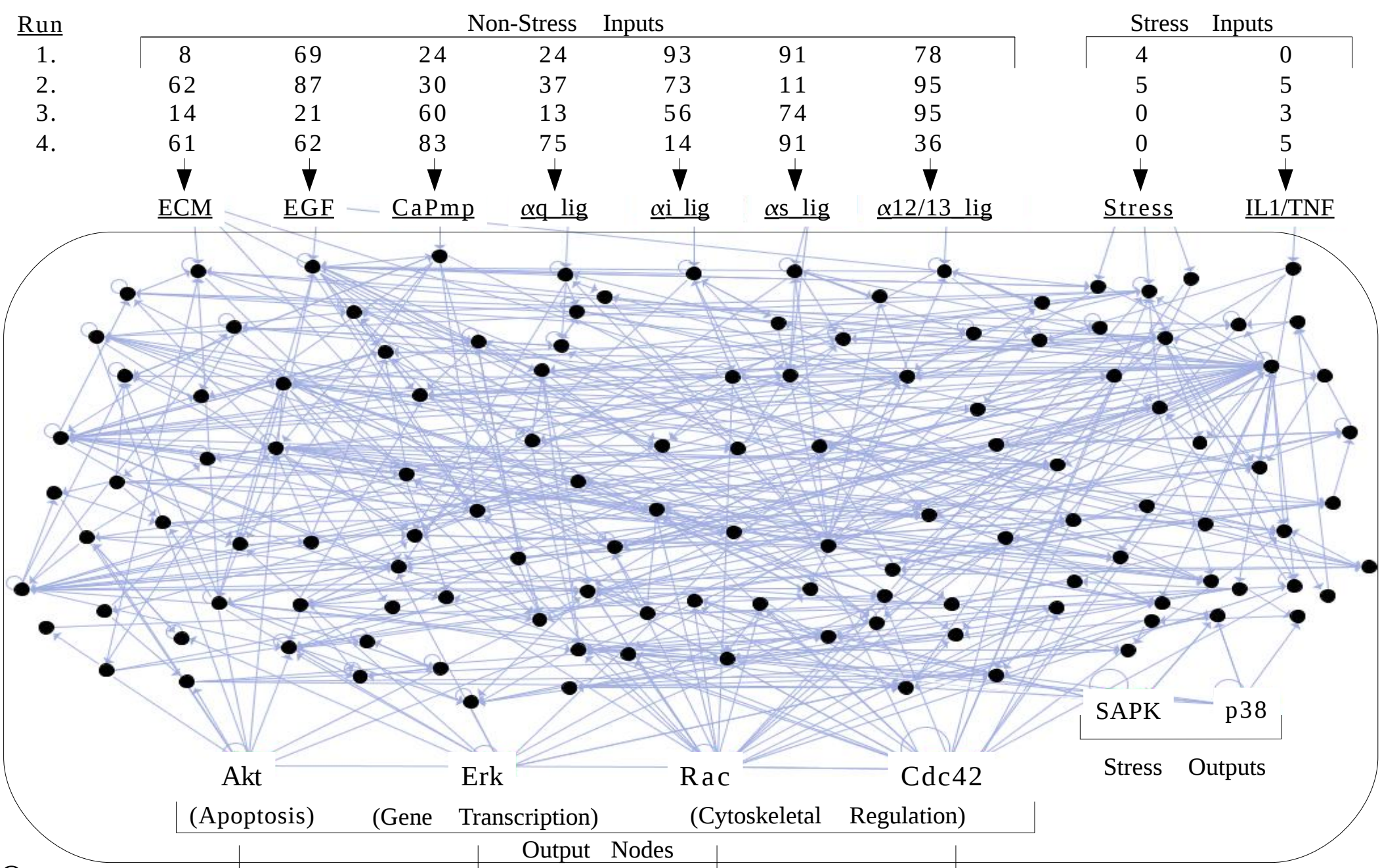


A	B	X
0	0	0
0	1	0
1	0	0
1	1	1

AND

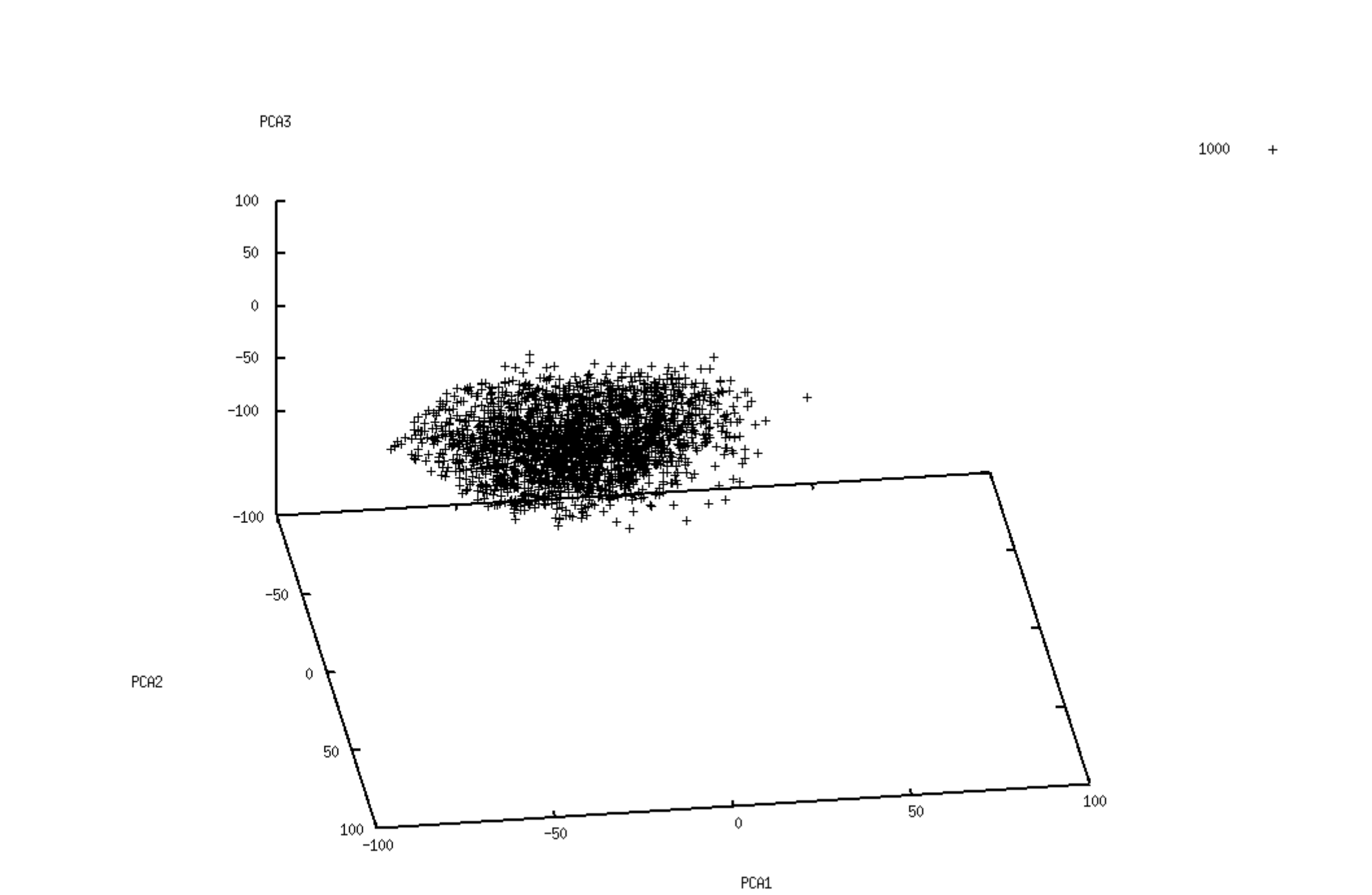
$$\frac{\partial^2}{\partial t^2} X(A,B) = c^2 \left| \frac{\partial^2}{\partial x^2} X(A,B) \right| - \gamma \left| \frac{\partial}{\partial t} X(A,B) \right| + h(A,B)$$

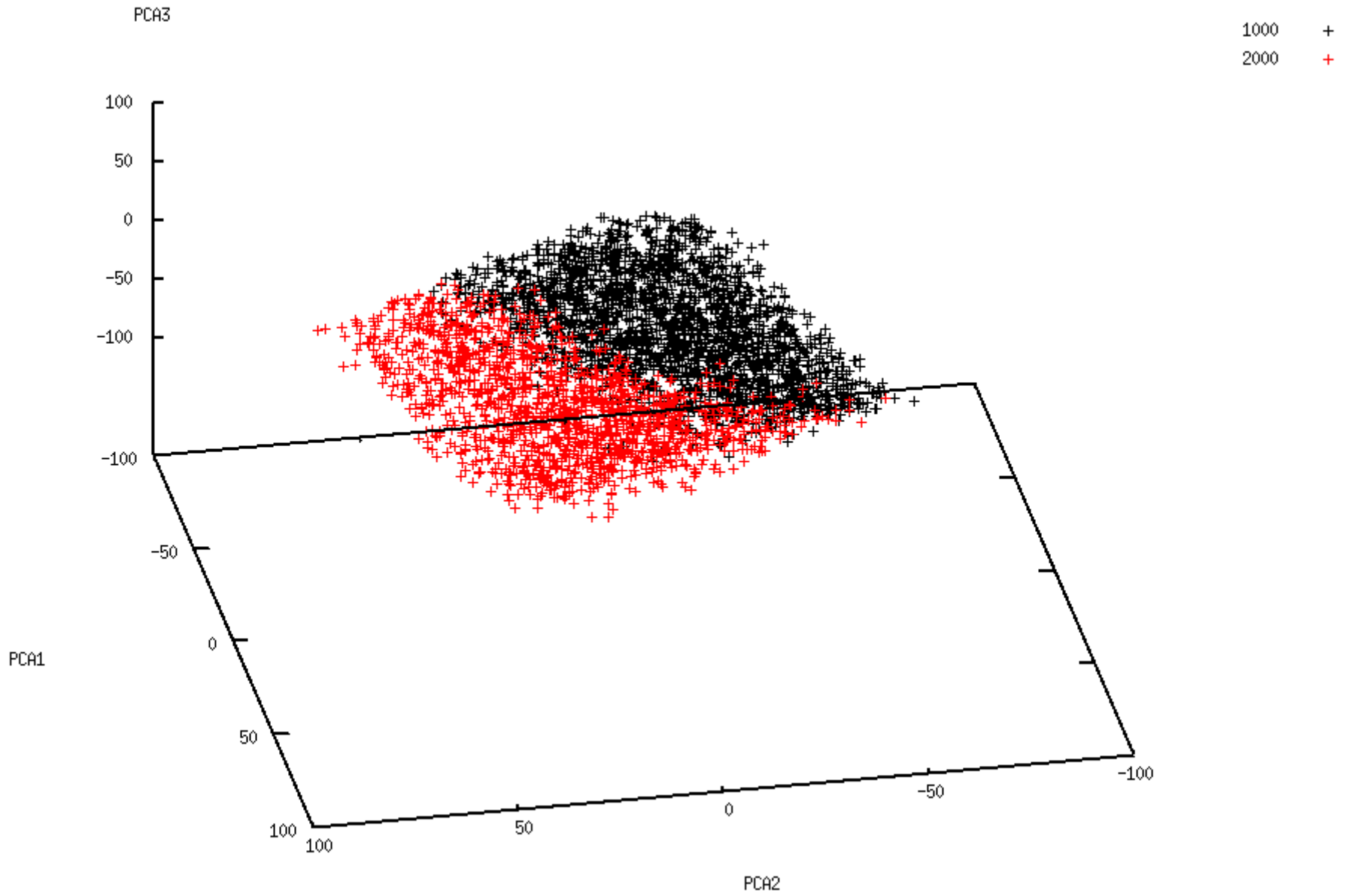

Non-Stress Input Nodes
Stress Input Nodes
8
69
24
24
93
91
78
4
0
ECM
EGF
CaPmp
αq_lig
αi_lig
αs_lig
α12/13_lig
Stress
IL1/TNF
SAPK
p38
Stress Outputs
Akt
Erk
Rac
Cdc42
(Apoptosis)
(Gene Transcription)
(Cytoskeletal Regulation)
Output Nodes
50
9
0
0



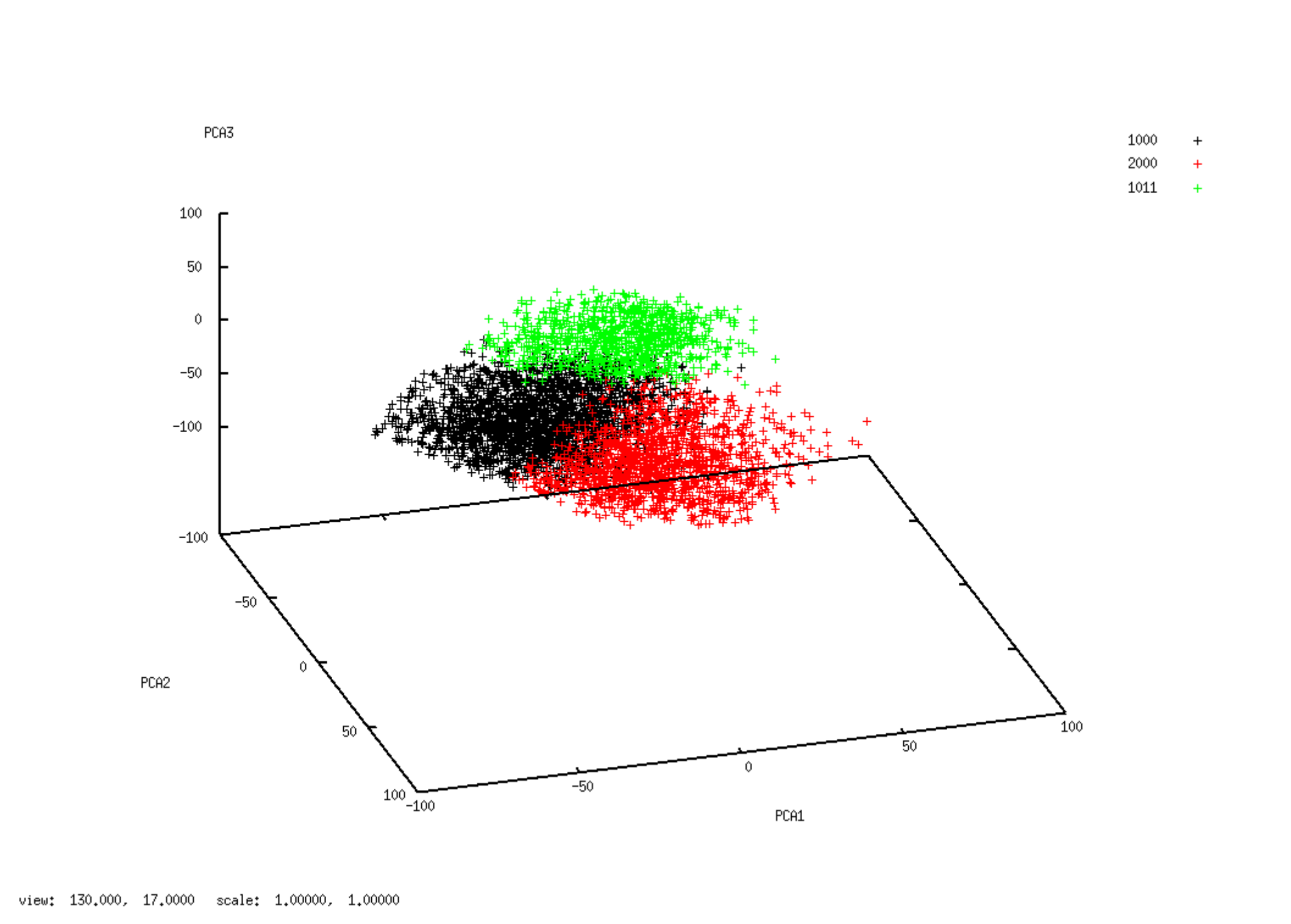
Output

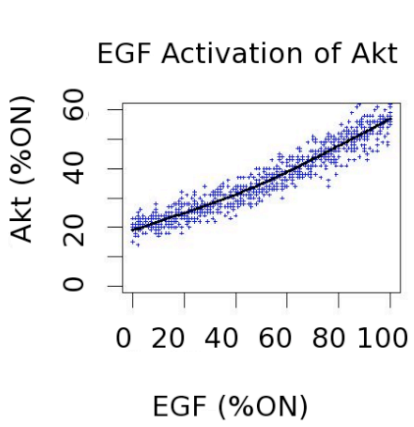
1.	50	9	0	0
2.	46	25	15	6
3.	15	0	0	1
4.	25	2	19	10

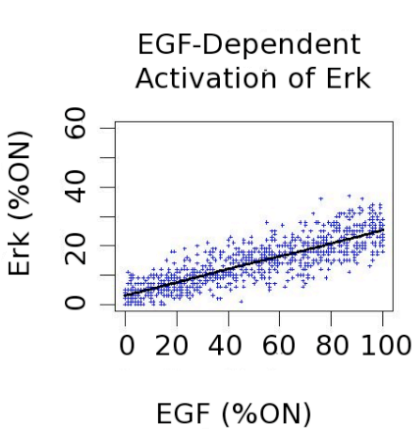

PCA3
1000
100
50
0
-50
-100
-100
-50
0
50
100
PCA2
100
-100
-50
0
50
100
PCA1
view: 135.000, 8.00000 scale: 1.00000, 1.00000

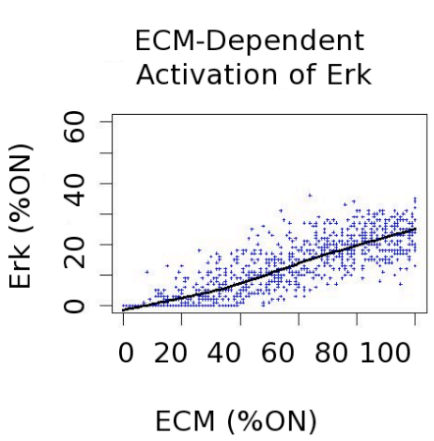


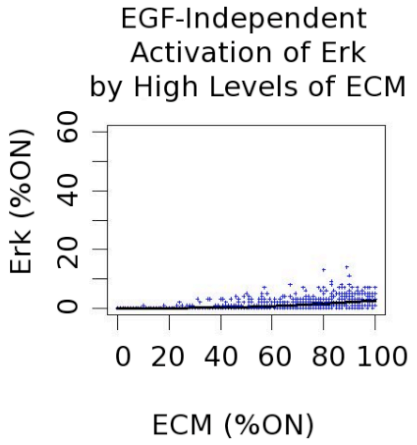
view: 137.000, 281.000 scale: 1.00000, 1.00000

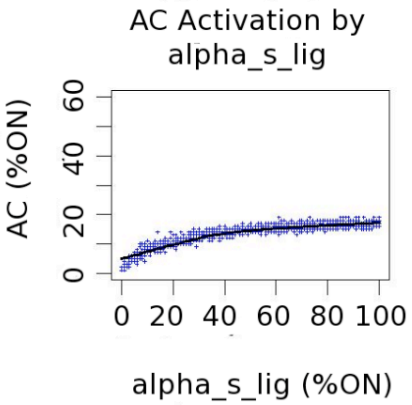

PCA3
1000
2000
1011
100
50
0
-50
-100
-100
-50
0
50
100
PCA2
-100
-50
0
50
100
PCA1
view: 130.000, 17.0000 scale: 1.00000, 1.00000

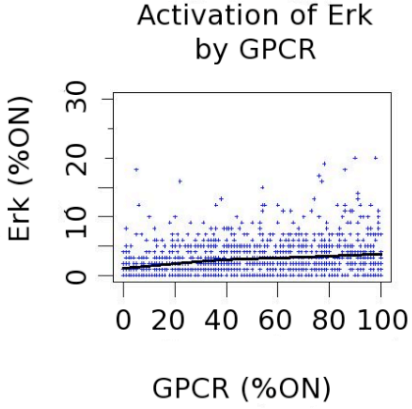

EGF Activation of Akt
Akt (%ON)
0 20 40 60
0 20 40 60 80 100
EGF (%ON)

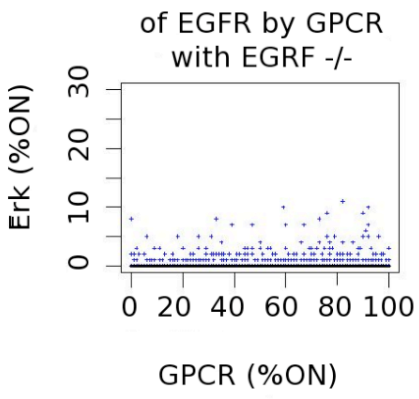

EGF-Dependent
Activation of Erk
Erk (%ON)
0 20 40 60
0 20 40 60 80 100
EGF (%ON)

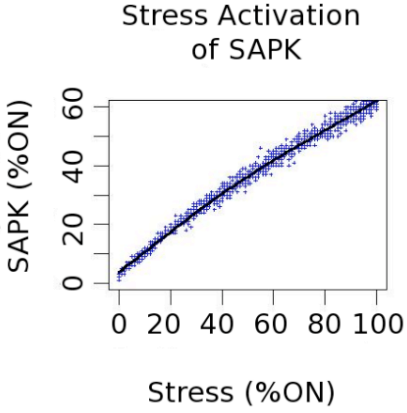

ECM-Dependent
Activation of Erk
Erk (%ON)
0 20 40 60
0 20 40 60 80 100
ECM (%ON)

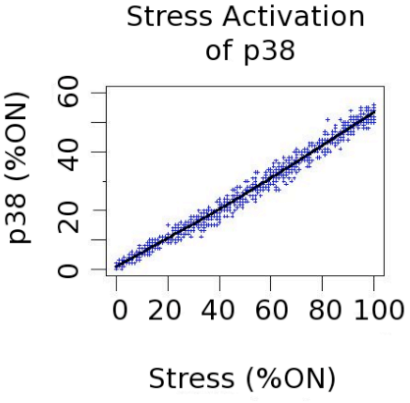

EGF-Independent
Activation of Erk
by High Levels of ECM
Erk (%ON)
0 20 40 60
0 20 40 60 80 100
ECM (%ON)

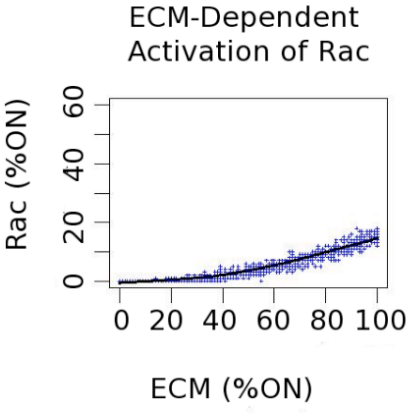

AC Activation by
alpha_s_lig
AC (%ON)
0 20 40 60
0 20 40 60 80 100
alpha_s_lig (%ON)

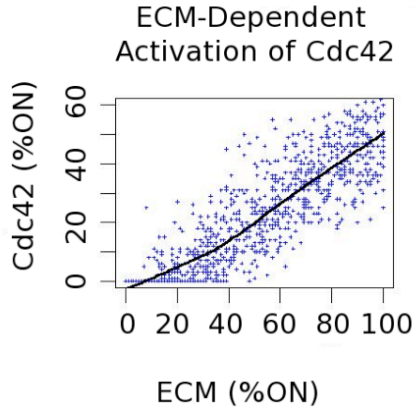

Activation of Erk
by GPCR
Erk (%ON)
0 10 20 30
0 20 40 60 80 100
GPCR (%ON)

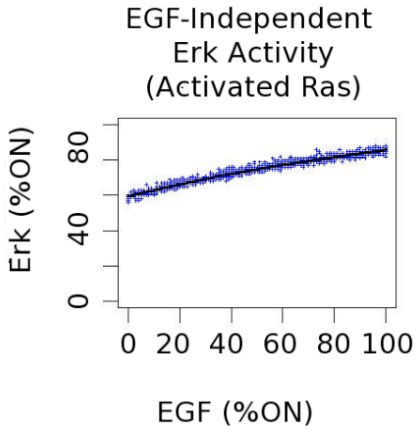

Trans-activation
of EGFR by GPCR
with EGRF -/-
Erk (%ON)
0 10 20 30
0 20 40 60 80 100
GPCR (%ON)


Stress Activation
of SAPK
SAPK (%ON)
0 20 40 60
0 20 40 60 80 100
Stress (%ON)


Stress Activation
of p38
p38 (%ON)
0 20 40 60
0 20 40 60 80 100
Stress (%ON)


ECM-Dependent
Activation of Rac
Rac (%ON)
0 20 40 60
0 20 40 60 80 100
ECM (%ON)


ECM-Dependent
Activation of Cdc42
Cdc42 (%ON)
0 20 40 60
0 20 40 60 80 100
ECM (%ON)


EGF-Independent
Erk Activity
(Activated Ras)
Erk (%ON)
0 40 80
0 20 40 60 80 100
EGF (%ON)

ChemChains sandbox

http://jays.net/wiki/ChemChains_sandbox

It's easy to get started:
(1) Check out the code
(2) Run my simplistic Perl version (**perl/**).
(3) Point and laugh at my source code.
(4) Browse **cpp/** (mature C++ version), the wikis, the mailing lists for more meat

```
$ svn co --username odynug --password odynugmathbio \
  http://mathbio.unomaha.edu/svn/chemchains/trunk/ ChemChains

$ cd ChemChains/perl

$ perl chemchains.pl 10
```

ChemChains sandbox

http://jays.net/wiki/ChemChains_sandbox

perl/ progress so far:

(1) Boolean network in near-zero dependency perl: Reads the real-world research data to configure nodes, edges; iterates the network.

ChemChains sandbox

http://jays.net/wiki/ChemChains_sandbox

```
** Boolean nodes
****************
*Bool:name:initial value:names of input
nodes:input values for which it should be
different from initial value
*-----------------------------------
Bool:AAA:False:BBB,CCC:FF,FF
Bool:BBB:False:AAA,CCC:FF,FF
Bool:CCC:True:AAA,BBB:FF,FF
```

ChemChains sandbox

http://jays.net/wiki/ChemChains_sandbox

```
** Input nodes
*****************
* Input:name:initial/default
value:random(R)/fixed(F):chaotic(C)/fixed/(F):time to
be introduced (changed from initial/default
value):dose (in percentage):duration of the change
from default (0=1 time)
* (Dosages can be in multiple *intervals, separated by
comma)
*---------------------------------------------
Input:ECM:False:R:C:1:0-100:1999
Input:EGF:False:R:C:1:0-100:1999
Input:ExtPump:False:R:C:1:0-100:1999
Input:alpha_q_lig:False:R:C:1:0-100:1999
Input:alpha_i_lig:False:R:C:1:0-100:1999
```

ChemChains sandbox

http://jays.net/wiki/ChemChains_sandbox

Not yet implemented in **perl/**

```
** Mutated nodes
** Delay nodes
** Sustain nodes
** Chaos
** Outputs
```

ChemChains sandbox

http://jays.net/wiki/ChemChains_sandbox

More TODO in **perl/**

- Build test suite for network iteration results: **cpp/** vs. **perl/** vs. whatever other languages the Omaha Dynamic Language Users Group adds.
- Visualizing results: GD::*? Google charts?
- GUIs / simulators for scientific research communities: facilitate lab collaboration.

ChemChains sandbox

http://jays.net/wiki/ChemChains_sandbox

Thank you! Questions?

All graphics courtesy of Dr. Jim Rogers, Ph.D.
Department of Mathematics, University of Nebraska, Omaha