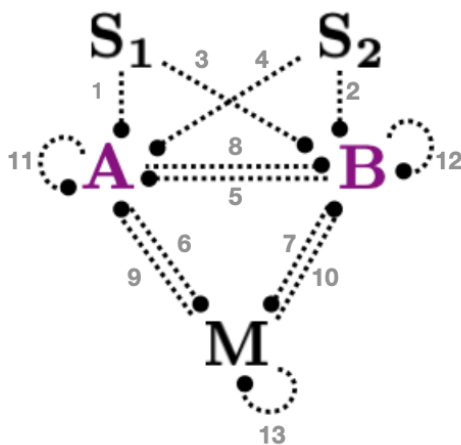


Minimal regulation network for value antagonism

In this code we extract minimal networks with nedges that shows value antagonism using regulation. The most general network looks like -



Now each network is perfectly characterized by two lists of P_i 's and A_i 's ($i=1$ to 13 for 13 possible edges). $P_i=1(0)$ represents i^{th} edge being present(absent) and $A_i=1(0)$ represents i^{th} edge being activation(repression) given $P_i=1$. The code below selects successful five node nedge(possible number of edges) network in terms of P_i 's and A_i 's that can satisfy value antagonism.

```
(*Extract all possible networks with nedges*)
nedges = 6; (*numbr of edges present*)
HA = 1; (*Power of auto activation da/dt=a^HA,
in our calculations we use linear auto-activation*)
maxedges = 13;
npts = 100;
smax = 100;
AAR = 1; (*Auto-activation rate/degradation rate, default is 1*)
nedgenetwork = {};
For[i = 0, i < 2^maxedges, i++,
  ls = PadLeft[IntegerDigits[i, 2], maxedges]; (*Getting list of P's*)
```

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(*Getting possible lists*)
T = Total[ls]; (*Total number of edges present*)
If[T == nedges, AppendTo[nedgenetwork, ls], 0]]
(*Only choosing network with nedges present*)

(*Extract list of Ais, if Ai is 1(0) and edge i is present Pi=
1 the interaction is activation(repression)*)
L = Length[nedgenetwork]; (*Length of three edge network*)
listofA = {}; (*possible values of 3 Ai's present*)
For[i = 0, i < 2^nedges, i++, ls = PadLeft[IntegerDigits[i, 2], nedges];
  (*Getting possible list of A's*)
  AppendTo[listofA, ls]
  (*Append possible lists*)]
Print[listofA]
LA = Length[listofA]; (*Length of list of subsets in our case it is 8*)
listofallA = {}; (*All possible list of A's*)
For[i = 1, i ≤ L, i++, ls = nedgenetwork[[i];
  (*ith list in 3 edge network*)
  lP = Position[ls, 1]; (*List of position of 1's present*)
  lA = {};
  (*Initialising list of networks
  with A for a given network with 3 edges present*)
  For[j = 1, j ≤ LA, j++, ls = ConstantArray[0, maxedges];
    For[k = 1, k ≤ nedges, k++, pos = lP[[k]][[1];
      (*position in A list which needs to be updated*)
      elem = listofA[[j]][[k];
      (*corresponding elements in list of A's microlist*)
      ls[[pos]] += elem];
    AppendTo[lA, ls](*Append microlist to lA*)];
  AppendTo[listofallA, lA](*Append list lA to superlist*)]

NP = Length[nedgenetwork]; (*number of 3 edge networks with unique Pi*)
NA = 2^nedges; (*number of 3 edge networks with unique Ai per NP network*)
For[i = NP, i ≥ 1, i--,
  Print[i];
  Plist = nedgenetwork[[i]; (*Extracting three edge network*)
  (*extracting individual Pi values*)
  P1 = Plist[[1];
  P2 = Plist[[2];
  P3 = Plist[[3];
  P4 = Plist[[4];
  P5 = Plist[[5];
  P6 = Plist[[6];
  P7 = Plist[[7];

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P8 = Plist[[8]];
P9 = Plist[[9]];
P10 = Plist[[10]];
P11 = Plist[[11]];
P12 = Plist[[12]];
P13 = Plist[[13]];
For[k = 1, k ≤ NA, k++,
  Alist = listofallA[[i]][[k]]; (*Corresponding list of A's*)
  (*extracting individual Ai values*)
  A1 = Alist[[1]];
  A2 = Alist[[2]];
  A3 = Alist[[3]];
  A4 = Alist[[4]];
  A5 = Alist[[5]];
  A6 = Alist[[6]];
  A7 = Alist[[7]];
  A8 = Alist[[8]];
  A9 = Alist[[9]];
  A10 = Alist[[10]];
  A11 = Alist[[11]];
  A12 = Alist[[12]];
  A13 = Alist[[13]];

  (*Both signals present*)
  (*Dynamical equation of A*)
  dadt = 1 - a + P1 * A1 * s1 + P4 * A4 * s2 +
    P5 * A5 * b + P9 * A9 * m + AAR * P11 * A11 * a^HA - a * (P1 * (1 - A1) * s1 +
    P4 * (1 - A4) * s2 + P5 * (1 - A5) * b + P9 * (1 - A9) * m + P11 * (1 - A11) * a);
  (*Dynamical equation of B*)
  dbdt = 1 - b + P2 * A2 * s2 + P3 * A3 * s1 +
    P8 * A8 * a + P10 * A10 * m + AAR * P12 * A12 * b^HA - b * (P2 * (1 - A2) * s2 +
    P3 * (1 - A3) * s1 + P8 * (1 - A8) * a + P10 * (1 - A10) * m + P12 * (1 - A12) * b);
  (*Dynamical equation of M*)
  dmdt = 1 - m + P6 * A6 * a + P7 * A7 * b + AAR * P13 * A13 * m^HA -
    m * (P6 * (1 - A6) * a + P7 * (1 - A7) * b + P13 * (1 - A13) * m);

eqn = Solve[{dadt == 0, dbdt == 0,
  dmdt == 0 && s1 ≥ 0 && s2 ≥ 0 && a ≥ 0 && b ≥ 0 && m ≥ 0}, {a, b, m}];
(*Successful solutions with positivity conditions*)
aS = a /. eqn;
bS = b /. eqn;
mS = m /. eqn;

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(*Write the equations with no signals present*)
dadt00 = dadt /. s1 → 0 /. s2 → 0;
dbdt00 = dbdt /. s1 → 0 /. s2 → 0;
dmdt00 = dmdt /. s1 → 0 /. s2 → 0;

eqn00 = Solve[{dadt00 == 0, dbdt00 == 0,
  dmdt00 == 0 && s1 ≥ 0 && s2 ≥ 0 && a ≥ 0 && b ≥ 0 && m ≥ 0}, {a, b, m}];
(*Successful solutions with positivity conditions*)
aS00 = a /. eqn00;
bS00 = b /. eqn00;
mS00 = m /. eqn00;

(*Write the equations with only signal 1 present*)
dadt1 = dadt /. s2 → 0;
dbdt1 = dbdt /. s2 → 0;
dmdt1 = dmdt /. s2 → 0;

eqn1 = Solve[{dadt1 == 0, dbdt1 == 0,
  dmdt1 == 0 && s1 ≥ 0 && s2 ≥ 0 && a ≥ 0 && b ≥ 0 && m ≥ 0}, {a, b, m}];
(*Successful solutions with positivity conditions*)
aS1 = a /. eqn1;
bS1 = b /. eqn1;
mS1 = m /. eqn1;

(*Write the equations with only signal 2 present*)
dadt2 = dadt /. s1 → 0;
dbdt2 = dbdt /. s1 → 0;
dmdt2 = dmdt /. s1 → 0;

eqn2 = Solve[{dadt2 == 0, dbdt2 == 0,
  dmdt2 == 0 && s1 ≥ 0 && s2 ≥ 0 && a ≥ 0 && b ≥ 0 && m ≥ 0}, {a, b, m}];
(*Successful solutions with positivity conditions*)
aS2 = a /. eqn2;
bS2 = b /. eqn2;
mS2 = m /. eqn2;

If[Length[mS] == 1, (*If a unique solution exist*)
  (*For a given network let us run a loop for *)
  For[j = 0, j < npts, j++,

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(*Let us randomly choose  $s_1, s_2$  values*)
inp1 = smax * RandomReal[]; (* $s_1$ *)
inp2 = smax * RandomReal[]; (* $s_2$ *)

(*Let us evaluate m for fixed value of  $s_1$  and  $s_2$ *)
mP = mS /.  $s_1 \rightarrow$  inp1 /.  $s_2 \rightarrow$  inp2; (*m value for both signal present*)

mP1 = mS1 /.  $s_1 \rightarrow$  inp1 /.  $s_2 \rightarrow$  inp2;
(*m value for only signal 1 signal present*)

mP2 = mS2 /.  $s_1 \rightarrow$  inp1 /.  $s_2 \rightarrow$  inp2; (*m value for only signal 2 present*)

m00 = mS00 /.  $s_1 \rightarrow$  inp1 /.  $s_2 \rightarrow$  inp2;
(*m value for no signals present*)
(*Print and break if value antagonism is present*)
If[mP1[[1]] > m00[[1]] && mP2[[1]] > m00[[1]] && mP[[1]] < 0.99 * Min[mP1[[1]], mP2[[1]]],
  Print["list of Ps=", Plist, ", list of As=", Alist,
    ", Total edges=", Total[Plist]] && Break[], 0], 0]]]

```