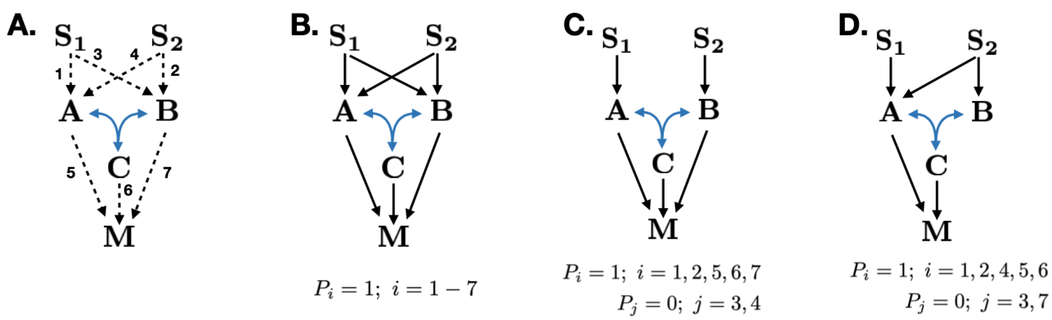
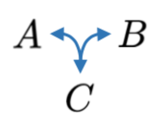
Minimal binding network for slope antagonism

Here we analyze possible binding networks given in the following picture-



$$P_i = \{0, 1\} \equiv \{\textbf{edge absent, edge present}\}$$

We first perform calculation for the general network A using-



$$\dot{c} = k_1 ab - k_2 c$$

The dynamical equations are-

In[ ]:=
```
dadt = k_a0 + P_1 * k_1 * s_1 + P_4 * k_4 * s_2 - k_da * a - γ * a * b
dbdt = k_b0 + P_3 * k_3 * s_1 + P_2 * k_2 * s_2 - k_db * b - γ * a * b
Solve[{dadt == 0, dbdt == 0}, {a, b}]
```

Out[ ]= $-a\,b\,\gamma + k_{a0} - a\,k_{da} + k_1 P_1 s_1 + k_4 P_4 s_2$

Out[ ]= $-a\,b\,\gamma + k_{b0} - b\,k_{db} + k_3 P_3 s_1 + k_2 P_2 s_2$

Out[ ]=
$$\Big\{\Big\{a \to \frac{1}{2\gamma k_{da}}\Big(\gamma k_{a0} - \gamma k_{b0} - k_{da} k_{db} + \gamma k_1 P_1 s_1 - \gamma k_3 P_3 s_1 - \gamma k_2 P_2 s_2 + \gamma k_4 P_4 s_2 - \sqrt{\big((-\gamma k_{a0} + \gamma k_{b0} + k_{da} k_{db} - \gamma k_1 P_1 s_1 + \gamma k_3 P_3 s_1 + \gamma k_2 P_2 s_2 - \gamma k_4 P_4 s_2)^2 - 4\gamma k_{da}(-k_{a0} k_{db} - k_1 k_{db} P_1 s_1 - k_4 k_{db} P_4 s_2)\big)}\Big),$$
$$b \to \frac{1}{k_{db}}\Big(-\frac{k_{a0}}{2} + \frac{k_{b0}}{2} - \frac{k_{da} k_{db}}{2\gamma} - \frac{1}{2} k_1 P_1 s_1 + \frac{1}{2} k_3 P_3 s_1 + \frac{1}{2} k_2 P_2 s_2 - \frac{1}{2} k_4 P_4 s_2 - \frac{1}{2\gamma}\Big(\sqrt{\big((-\gamma k_{a0} + \gamma k_{b0} + k_{da} k_{db} - \gamma k_1 P_1 s_1 + \gamma k_3 P_3 s_1 + \gamma k_2 P_2 s_2 - \gamma k_4 P_4 s_2)^2 - 4\gamma k_{da}(-k_{a0} k_{db} - k_1 k_{db} P_1 s_1 - k_4 k_{db} P_4 s_2)\big)}\Big)\Big)\Big\},$$
$$\Big\{a \to \frac{1}{2\gamma k_{da}}\Big(\gamma k_{a0} - \gamma k_{b0} - k_{da} k_{db} + \gamma k_1 P_1 s_1 - \gamma k_3 P_3 s_1 - \gamma k_2 P_2 s_2 + \gamma k_4 P_4 s_2 + \sqrt{\big((-\gamma k_{a0} + \gamma k_{b0} + k_{da} k_{db} - \gamma k_1 P_1 s_1 + \gamma k_3 P_3 s_1 + \gamma k_2 P_2 s_2 - \gamma k_4 P_4 s_2)^2 - 4\gamma k_{da}(-k_{a0} k_{db} - k_1 k_{db} P_1 s_1 - k_4 k_{db} P_4 s_2)\big)}\Big),$$
$$b \to \frac{1}{k_{db}}\Big(-\frac{k_{a0}}{2} + \frac{k_{b0}}{2} - \frac{k_{da} k_{db}}{2\gamma} - \frac{1}{2} k_1 P_1 s_1 + \frac{1}{2} k_3 P_3 s_1 + \frac{1}{2} k_2 P_2 s_2 - \frac{1}{2} k_4 P_4 s_2 + \frac{1}{2\gamma}\Big(\sqrt{\big((-\gamma k_{a0} + \gamma k_{b0} + k_{da} k_{db} - \gamma k_1 P_1 s_1 + \gamma k_3 P_3 s_1 + \gamma k_2 P_2 s_2 - \gamma k_4 P_4 s_2)^2 - 4\gamma k_{da}(-k_{a0} k_{db} - k_1 k_{db} P_1 s_1 - k_4 k_{db} P_4 s_2)\big)}\Big)\Big)\Big\}\Big\}$$

Accounting for the positivity of a and b we can write the steady state expressions for a and b as,

In[ ]:=
$$\textbf{aSS = FullSimplify}\Big[\frac{1}{2\gamma k_{da}}\Big(\gamma k_{a0} - \gamma k_{b0} - k_{da} k_{db} + \gamma k_1 P_1 s_1 - \gamma k_3 P_3 s_1 - \gamma k_2 P_2 s_2 + \gamma k_4 P_4 s_2 + \sqrt{\big((-\gamma k_{a0} + \gamma k_{b0} + k_{da} k_{db} - \gamma k_1 P_1 s_1 + \gamma k_3 P_3 s_1 + \gamma k_2 P_2 s_2 - \gamma k_4 P_4 s_2)^2 - 4\gamma k_{da}(-k_{a0} k_{db} - k_1 k_{db} P_1 s_1 - k_4 k_{db} P_4 s_2)\big)}\Big)\Big]$$

Out[ ]=
$$\frac{1}{2\gamma k_{da}}\Big(-k_{da} k_{db} + \gamma(k_{a0} - k_{b0} + (k_1 P_1 - k_3 P_3) s_1 + (-k_2 P_2 + k_4 P_4) s_2) + \sqrt{\big(4\gamma k_{da} k_{db}(k_{a0} + k_1 P_1 s_1 + k_4 P_4 s_2) + (k_{da} k_{db} + \gamma(-k_{a0} + k_{b0} + (-k_1 P_1 + k_3 P_3) s_1 + (k_2 P_2 - k_4 P_4) s_2))^2\big)}\Big)$$

In[∘]:= **bSS =**

$$\text{FullSimplify}\Big[\frac{1}{k_{db}}\Big(-\frac{k_{a0}}{2}+\frac{k_{b0}}{2}-\frac{k_{da}\,k_{db}}{2\,\gamma}-\frac{1}{2}\,k_1\,P_1\,s_1+\frac{1}{2}\,k_3\,P_3\,s_1+\frac{1}{2}\,k_2\,P_2\,s_2-\frac{1}{2}\,k_4\,P_4\,s_2+\frac{1}{2\,\gamma}\Big(\sqrt{\big((-\gamma\,k_{a0}+\gamma\,k_{b0}+k_{da}\,k_{db}-\gamma\,k_1\,P_1\,s_1+\gamma\,k_3\,P_3\,s_1+\gamma\,k_2\,P_2\,s_2-\gamma\,k_4\,P_4\,s_2)^2-4\,\gamma\,k_{da}\,(-k_{a0}\,k_{db}-k_1\,k_{db}\,P_1\,s_1-k_4\,k_{db}\,P_4\,s_2)\big)}\Big)\Big)\Big]$$

Out[∘]=

$$\frac{1}{2\,\gamma\,k_{db}}\Big(-k_{da}\,k_{db}+\gamma\,(-k_{a0}+k_{b0}+(-k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2-k_4\,P_4)\,s_2)+\sqrt{\big(4\,\gamma\,k_{da}\,k_{db}\,(k_{a0}+k_1\,P_1\,s_1+k_4\,P_4\,s_2)+(k_{da}\,k_{db}+\gamma\,(-k_{a0}+k_{b0}+(-k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2-k_4\,P_4)\,s_2))^2\big)}\Big)$$

The expression for c in steady state is,

In[∘]:= **cSS = FullSimplify[γ * aSS * bSS / k_{dc}]**

Out[∘]=

$$\frac{1}{2\,\gamma\,k_{dc}}\Big(k_{da}\,k_{db}+\gamma\,(k_{a0}+k_{b0}+(k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2+k_4\,P_4)\,s_2)-\sqrt{\big(4\,\gamma\,k_{da}\,k_{db}\,(k_{a0}+k_1\,P_1\,s_1+k_4\,P_4\,s_2)+(k_{da}\,k_{db}+\gamma\,(-k_{a0}+k_{b0}+(-k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2-k_4\,P_4)\,s_2))^2\big)}\Big)$$

And finally the steady state expressions for m is-

In[∘]:= **mSS = FullSimplify[(k_{m0} + P_5 * k_5 * aSS + P_6 * k_6 * cSS + P_7 * k_7 * bSS) / k_{dm}]**

Out[∘]=

$$\frac{1}{2\,k_{dm}}\Big(2\,k_{m0}+\frac{1}{\gamma\,k_{dc}}\,k_6\,P_6\,\Big(k_{da}\,k_{db}+\gamma\,(k_{a0}+k_{b0}+(k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2+k_4\,P_4)\,s_2)-\sqrt{\big(4\,\gamma\,k_{da}\,k_{db}\,(k_{a0}+k_1\,P_1\,s_1+k_4\,P_4\,s_2)+(k_{da}\,k_{db}+\gamma\,(-k_{a0}+k_{b0}+(-k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2-k_4\,P_4)\,s_2))^2\big)}\Big)+\frac{1}{\gamma\,k_{db}}\,k_7\,P_7\,\Big(-k_{da}\,k_{db}+\gamma\,(-k_{a0}+k_{b0}+(-k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2-k_4\,P_4)\,s_2)+\sqrt{\big(4\,\gamma\,k_{da}\,k_{db}\,(k_{a0}+k_1\,P_1\,s_1+k_4\,P_4\,s_2)+(k_{da}\,k_{db}+\gamma\,(-k_{a0}+k_{b0}+(-k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2-k_4\,P_4)\,s_2))^2\big)}\Big)+\frac{1}{\gamma\,k_{da}}\,k_5\,P_5\,\Big(-k_{da}\,k_{db}+\gamma\,(k_{a0}-k_{b0}+(k_1\,P_1-k_3\,P_3)\,s_1+(-k_2\,P_2+k_4\,P_4)\,s_2)+\sqrt{\big(4\,\gamma\,k_{da}\,k_{db}\,(k_{a0}+k_1\,P_1\,s_1+k_4\,P_4\,s_2)+(k_{da}\,k_{db}+\gamma\,(-k_{a0}+k_{b0}+(-k_1\,P_1+k_3\,P_3)\,s_1+(k_2\,P_2-k_4\,P_4)\,s_2))^2\big)}\Big)\Big)$$

Now we set all reaction rates to 1 and determine the expressions for a,b,c and m in steady state for further analysis-

In[∘]:=
```
dadt = 1 + P1 * 1 * s1 + P4 * 1 * s2 - 1 * a - 1 * a * b
dbdt = 1 + P3 * 1 * s1 + P2 * 1 * s2 - 1 * b - 1 * a * b
Solve[{dadt == 0, dbdt == 0}, {a, b}]
```

Out[∘]= $1 - a - a\,b + P_1\,s_1 + P_4\,s_2$

Out[∘]= $1 - b - a\,b + P_3\,s_1 + P_2\,s_2$

Out[∘]=
$$\Big\{\Big\{a \to \frac{1}{2} \times \Big(-1 + P_1\,s_1 - P_3\,s_1 - P_2\,s_2 + P_4\,s_2 - \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big),\ b \to \frac{1}{2} \times \Big(-1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2 - \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big)\Big\},$$
$$\Big\{a \to \frac{1}{2} \times \Big(-1 + P_1\,s_1 - P_3\,s_1 - P_2\,s_2 + P_4\,s_2 + \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big),\ b \to \frac{1}{2} \times \Big(-1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2 + \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big)\Big\}\Big\}$$

Out[∘]=
$$\boldsymbol{\Big\{\Big\{a \to \frac{1}{2} \times \Big(-1 + P_1\,s_1 - P_3\,s_1 - P_2\,s_2 + P_4\,s_2 - \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big),\ b \to \frac{1}{2} \times \Big(-1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2 - \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big)\Big\},}$$
$$\boldsymbol{\Big\{a \to \frac{1}{2} \times \Big(-1 + P_1\,s_1 - P_3\,s_1 - P_2\,s_2 + P_4\,s_2 + \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big),\ b \to \frac{1}{2} \times \Big(-1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2 + \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big)\Big\}\Big\}}$$

The steady state expressions are,

In[∘]:=
$$\boldsymbol{aP = \mathrm{FullSimplify}\Big[\frac{1}{2} \times \Big(-1 + P_1\,s_1 - P_3\,s_1 - P_2\,s_2 + P_4\,s_2 + \sqrt{-4 \times (-1 - P_1\,s_1 - P_4\,s_2) + (1 - P_1\,s_1 + P_3\,s_1 + P_2\,s_2 - P_4\,s_2)^2}\Big)\Big]}$$

Out[∘]=
$$\frac{1}{2} \times \Big(-1 + P_1\,s_1 - P_3\,s_1 - P_2\,s_2 + P_4\,s_2 + \sqrt{(1 + (-P_1 + P_3)\,s_1 + (P_2 - P_4)\,s_2)^2 + 4 \times (1 + P_1\,s_1 + P_4\,s_2)}\Big)$$

In[∘]:= **bP = FullSimplify[$\frac{1}{2}\times\left(-1 - P_1 s_1 + P_3 s_1 + P_2 s_2 - P_4 s_2 + \sqrt{-4\times(-1 - P_1 s_1 - P_4 s_2) + (1 - P_1 s_1 + P_3 s_1 + P_2 s_2 - P_4 s_2)^2}\right)$]**

Out[∘]= $\frac{1}{2}\times\left(-1 - P_1 s_1 + P_3 s_1 + P_2 s_2 - P_4 s_2 + \sqrt{(1 + (-P_1 + P_3)\ s_1 + (P_2 - P_4)\ s_2)^2 + 4\times(1 + P_1 s_1 + P_4 s_2)}\right)$

The steady state expressions for c is,

In[∘]:= **cP = FullSimplify[aP * bP]**

Out[∘]= $\frac{1}{2}\times\left(3 + P_1 s_1 + P_3 s_1 + P_2 s_2 + P_4 s_2 - \sqrt{(1 + (-P_1 + P_3)\ s_1 + (P_2 - P_4)\ s_2)^2 + 4\times(1 + P_1 s_1 + P_4 s_2)}\right)$

And, finally the expression for the output m-

In[∘]:= **mP = FullSimplify[1 + P_5 * 1 * aP + P_6 * 1 * cP + P_7 * 1 * bP]**

Out[∘]= $\frac{1}{2}\times\Big(2 + P_6 \left(3 + P_1 s_1 + P_3 s_1 + P_2 s_2 + P_4 s_2 - \sqrt{(1 + (-P_1 + P_3)\ s_1 + (P_2 - P_4)\ s_2)^2 + 4\times(1 + P_1 s_1 + P_4 s_2)}\right) + P_7 \left(-1 - P_1 s_1 + P_3 s_1 + P_2 s_2 - P_4 s_2 + \sqrt{(1 + (-P_1 + P_3)\ s_1 + (P_2 - P_4)\ s_2)^2 + 4\times(1 + P_1 s_1 + P_4 s_2)}\right) + P_5 \left(-1 + P_1 s_1 - P_3 s_1 - P_2 s_2 + P_4 s_2 + \sqrt{(1 + (-P_1 + P_3)\ s_1 + (P_2 - P_4)\ s_2)^2 + 4\times(1 + P_1 s_1 + P_4 s_2)}\right)\Big)$

Expression for m only when one input is present,

In[∘]:= **mP1 = FullSimplify[mP /. $s_2 \to 0$]**

Out[∘]= $\frac{1}{2}\times\Big(2 + P_6 \left(3 + P_1 s_1 + P_3 s_1 - \sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3)\ s_1)^2}\right) + P_5 \left(-1 + P_1 s_1 - P_3 s_1 + \sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3)\ s_1)^2}\right) + P_7 \left(-1 - P_1 s_1 + P_3 s_1 + \sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3)\ s_1)^2}\right)\Big)$

In[∘]:= **mP2 = FullSimplify[mP /. $s_1 \to 0$]**

Out[∘]= $\frac{1}{2}\times\Big(2 + 3 P_6 - P_7 + P_2 (P_6 + P_7)\ s_2 - (P_6 - P_7) \left(-P_4 s_2 + \sqrt{5 + 2 (P_2 + P_4)\ s_2 + (P_2 - P_4)^2 s_2^2}\right) + P_5 \left(-1 + (-P_2 + P_4)\ s_2 + \sqrt{5 + 2 (P_2 + P_4)\ s_2 + (P_2 - P_4)^2 s_2^2}\right)\Big)$

Derivatives

In[∘]:= **m₁ = FullSimplify[D[mP1, s₁]]**

Out[∘]=
$$\frac{1}{2}\left(P_6\left(P_1+P_3+\frac{-P_1-P_3-(P_1-P_3)^2\,s_1}{\sqrt{4+4\,P_1\,s_1+(1+(-P_1+P_3)\,s_1)^2}}\right)+P_5\left(P_1-P_3+\frac{P_1+P_3+(P_1-P_3)^2\,s_1}{\sqrt{4+4\,P_1\,s_1+(1+(-P_1+P_3)\,s_1)^2}}\right)+P_7\left(-P_1+P_3+\frac{P_1+P_3+(P_1-P_3)^2\,s_1}{\sqrt{4+4\,P_1\,s_1+(1+(-P_1+P_3)\,s_1)^2}}\right)\right)$$

In[∘]:= **m₂ = FullSimplify[D[mP2, s₂]]**

Out[∘]=
$$\frac{1}{2}\left(P_2\,(P_6+P_7)-(P_6-P_7)\left(-P_4+\frac{P_2+P_4+(P_2-P_4)^2\,s_2}{\sqrt{5+2\,(P_2+P_4)\,s_2+(P_2-P_4)^2\,s_2^2}}\right)+P_5\left(-P_2+P_4+\frac{P_2+P_4+(P_2-P_4)^2\,s_2}{\sqrt{5+2\,(P_2+P_4)\,s_2+(P_2-P_4)^2\,s_2^2}}\right)\right)$$

In[∘]:= **m₁₂ = FullSimplify[D[mP, s₁] + D[mP, s₂]]**

Out[∘]=
$$\frac{1}{2}\left(P_6\left(P_1+P_3-\frac{4\,P_1+2\,(-P_1+P_3)\,(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)}{2\,\sqrt{(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)^2+4\times(1+P_1\,s_1+P_4\,s_2)}}\right)+P_5\left(P_1-P_3+\frac{4\,P_1+2\,(-P_1+P_3)\,(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)}{2\,\sqrt{(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)^2+4\times(1+P_1\,s_1+P_4\,s_2)}}\right)+P_7\left(-P_1+P_3+\frac{4\,P_1+2\,(-P_1+P_3)\,(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)}{2\,\sqrt{(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)^2+4\times(1+P_1\,s_1+P_4\,s_2)}}\right)+P_6\left(P_2+P_4-\frac{4\,P_4+2\,(P_2-P_4)\,(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)}{2\,\sqrt{(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)^2+4\times(1+P_1\,s_1+P_4\,s_2)}}\right)+P_7\left(P_2-P_4+\frac{4\,P_4+2\,(P_2-P_4)\,(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)}{2\,\sqrt{(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)^2+4\times(1+P_1\,s_1+P_4\,s_2)}}\right)+P_5\left(-P_2+P_4+\frac{4\,P_4+2\,(P_2-P_4)\,(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)}{2\,\sqrt{(1+(-P_1+P_3)\,s_1+(P_2-P_4)\,s_2)^2+4\times(1+P_1\,s_1+P_4\,s_2)}}\right)\right)$$

Surface maps for networks B,C,D

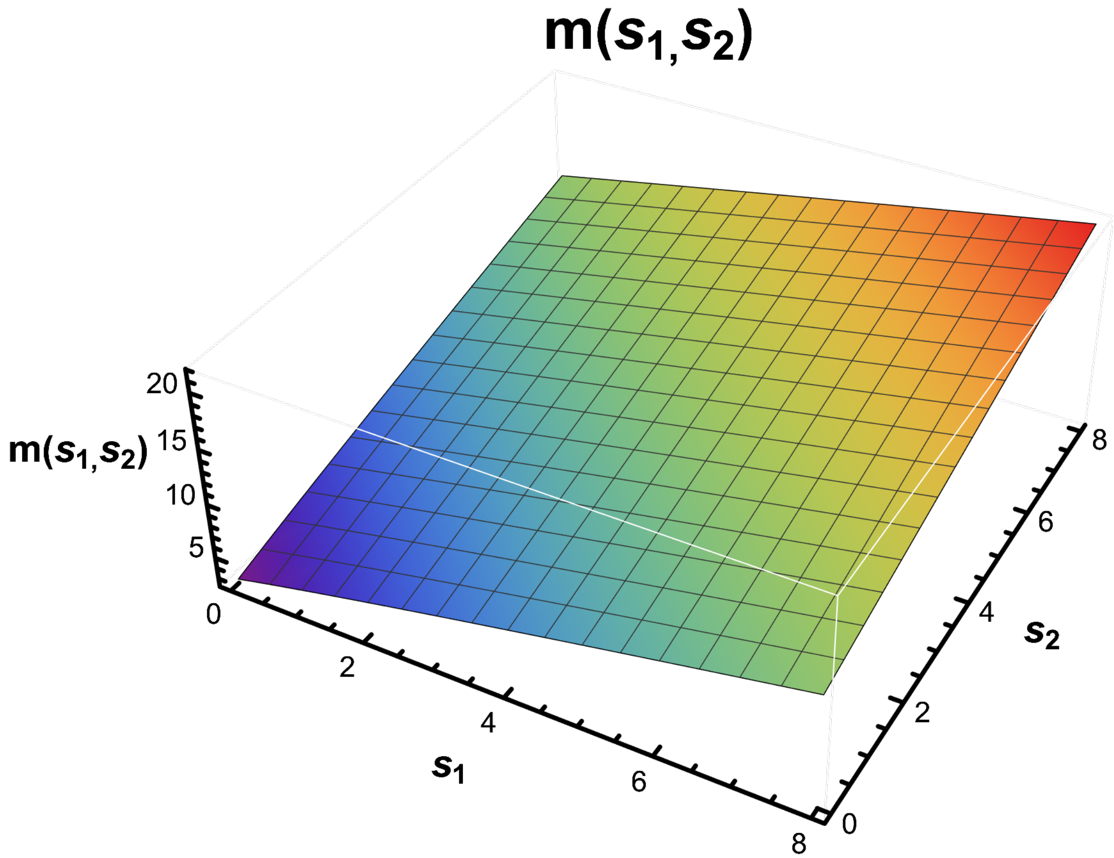
Network B

In[∘]:=
$$P_1 = 1;$$
$$P_2 = 1;$$
$$P_3 = 1;$$
$$P_4 = 1;$$
$$P_5 = 1;$$
$$P_6 = 1;$$
$$P_7 = 1;$$
$$mPB = \frac{1}{2} \times \left(2 + P_6 \left(3 + P_1\, s_1 + P_3\, s_1 + P_2\, s_2 + P_4\, s_2 - \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\right) + P_7 \left(-1 - P_1\, s_1 + P_3\, s_1 + P_2\, s_2 - P_4\, s_2 + \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\right) + P_5 \left(-1 + P_1\, s_1 - P_3\, s_1 - P_2\, s_2 + P_4\, s_2 + \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\right)\right)$$

Out[∘]=
$$\frac{1}{2} \times \left(3 + 2\, s_1 + 2\, s_2 + \sqrt{1 + 4 \times (1 + s_1 + s_2)}\right)$$

In[ ]:=
```
Plot3D[mPB, {s1, 0, 8}, {s2, 0, 8}, AxesLabel →
  {Style["s1", Bold, 20, FontColor → Black], Style["s2", Bold, 20, FontColor → Black],
   Style["m(s1,s2)", Bold, 20, FontColor → Black]},
 PlotLabel → Style["m(s1,s2)", Bold, 30, FontColor → Black],
 ColorFunction → "Rainbow", AxesStyle → Thickness[0.005], BoxStyle → GrayLevel[2],
 TicksStyle → Directive[Black, 15], ImageSize → Large, PlotRange → Full]
```

Out[ ]=



Network C

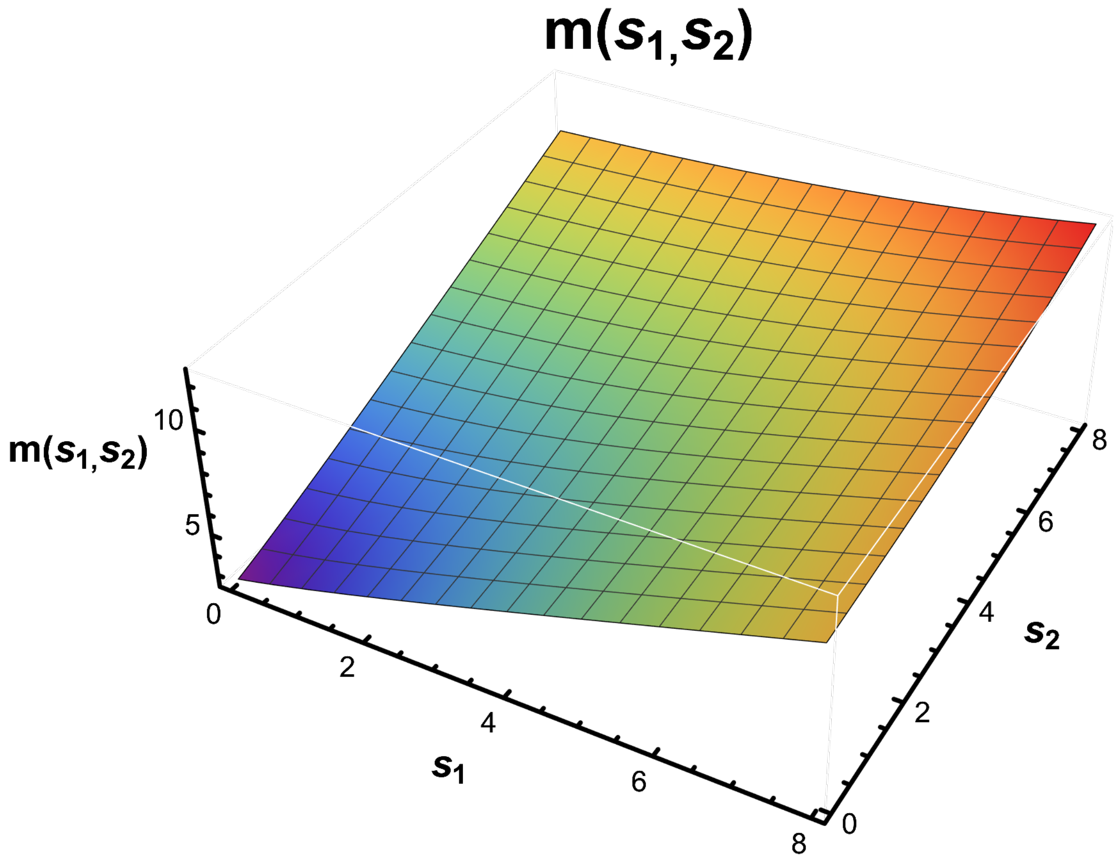
In[∘]:=
$P_1 = 1;$
$P_2 = 1;$
$P_3 = 0;$
$P_4 = 0;$
$P_5 = 1;$
$P_6 = 1;$
$P_7 = 1;$

$$mPC = \frac{1}{2} \times \left(2 + P_6 \left(3 + P_1\, s_1 + P_3\, s_1 + P_2\, s_2 + P_4\, s_2 - \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\right) + P_7 \left(-1 - P_1\, s_1 + P_3\, s_1 + P_2\, s_2 - P_4\, s_2 + \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\right) + P_5 \left(-1 + P_1\, s_1 - P_3\, s_1 - P_2\, s_2 + P_4\, s_2 + \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\right)\right)$$

Out[∘]=
$$\frac{1}{2} \times \left(3 + s_1 + s_2 + \sqrt{4 \times (1 + s_1) + (1 - s_1 + s_2)^2}\right)$$

In[∘]:=
```
Plot3D[mPC, {s1, 0, 8}, {s2, 0, 8}, AxesLabel →
  {Style["s1", Bold, 20, FontColor → Black], Style["s2", Bold, 20, FontColor → Black],
   Style["m(s1,s2)", Bold, 20, FontColor → Black]},
 PlotLabel → Style["m(s1,s2)", Bold, 30, FontColor → Black],
 ColorFunction → "Rainbow", AxesStyle → Thickness[0.005], BoxStyle → GrayLevel[2],
 TicksStyle → Directive[Black, 15], ImageSize → Large, PlotRange → Full]
```

Out[∘]=



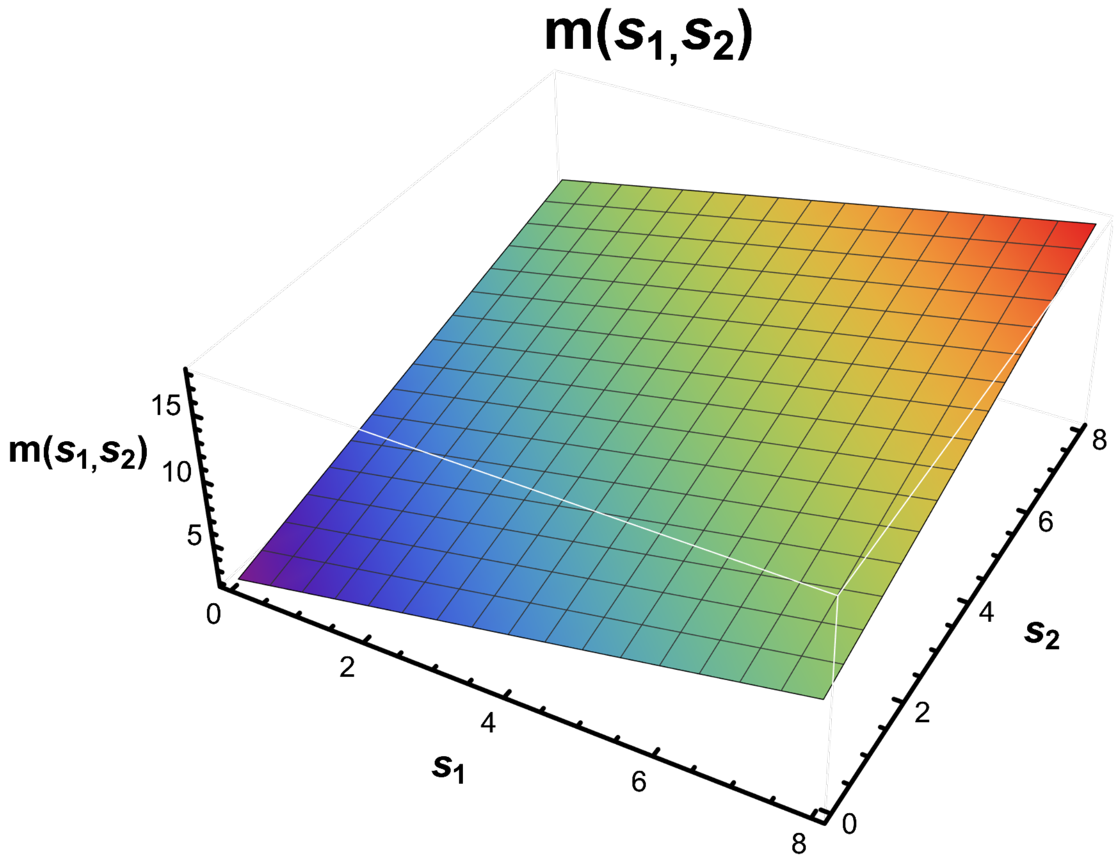
Network D

In[∘]:=
$$P_1 = 1;$$
$$P_2 = 1;$$
$$P_3 = 0;$$
$$P_4 = 1;$$
$$P_5 = 1;$$
$$P_6 = 1;$$
$$P_7 = 0;$$
$$\text{mPD} = \frac{1}{2} \times \Big(2 + P_6 \Big(3 + P_1\, s_1 + P_3\, s_1 + P_2\, s_2 + P_4\, s_2 - \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\Big) + P_7 \Big(-1 - P_1\, s_1 + P_3\, s_1 + P_2\, s_2 - P_4\, s_2 + \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\Big) + P_5 \Big(-1 + P_1\, s_1 - P_3\, s_1 - P_2\, s_2 + P_4\, s_2 + \sqrt{(1 + (-P_1 + P_3)\, s_1 + (P_2 - P_4)\, s_2)^2 + 4 \times (1 + P_1\, s_1 + P_4\, s_2)}\Big)\Big)$$

Out[∘]=
$$\frac{1}{2} \times (4 + 2\, s_1 + 2\, s_2)$$

In[ ]:=
```
Plot3D[mPD, {s1, 0, 8}, {s2, 0, 8}, AxesLabel →
  {Style["s1", Bold, 20, FontColor → Black], Style["s2", Bold, 20, FontColor → Black],
   Style["m(s1,s2)", Bold, 20, FontColor → Black]},
 PlotLabel → Style["m(s1,s2)", Bold, 30, FontColor → Black],
 ColorFunction → "Rainbow", AxesStyle → Thickness[0.005], BoxStyle → GrayLevel[2],
 TicksStyle → Directive[Black, 15], ImageSize → Large, PlotRange → Full]
```

Out[ ]=



Successful network value antagonism

This is the code to test the successful network for value antagonism -

```
npts = 10 000; (*number of random {s_1,s_2} pairs
 over which the antagonism condition is verified*)
smax = 100; (*maximum value of s_1 and s_2*)
nedges = 7; (*maximum number of edges*)
Print["Successful binding networks for value antagonism-\n"]
For[i = 0, i < 2^nedges, i++, P_1 = PadLeft[IntegerDigits[i, 2], nedges][[1]];
 P_2 = PadLeft[IntegerDigits[i, 2], nedges][[2]];
 P_3 = PadLeft[IntegerDigits[i, 2], nedges][[3]];
 P_4 = PadLeft[IntegerDigits[i, 2], nedges][[4]];
 P_5 = PadLeft[IntegerDigits[i, 2], nedges][[5]];
 P_6 = PadLeft[IntegerDigits[i, 2], nedges][[6]];
 P_7 = PadLeft[IntegerDigits[i, 2], nedges][[7]];
 For[j = 0, j < npts, j++, s_1 = smax * RandomReal[];
  s_2 = smax * RandomReal[];
```

$$mP = \frac{1}{2} \times \left(2 + P_6 \left(3 + P_1 s_1 + P_3 s_1 + P_2 s_2 + P_4 s_2 - \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4 \times (1 + P_1 s_1 + P_4 s_2)}\right) + P_7 \left(-1 - P_1 s_1 + P_3 s_1 + P_2 s_2 - P_4 s_2 + \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4 \times (1 + P_1 s_1 + P_4 s_2)}\right) + P_5 \left(-1 + P_1 s_1 - P_3 s_1 - P_2 s_2 + P_4 s_2 + \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4 \times (1 + P_1 s_1 + P_4 s_2)}\right)\right);$$

$$m00 = \frac{1}{2} \times \left(2 + \left(-1 + \sqrt{5}\right) P_5 - \left(-3 + \sqrt{5}\right) P_6 + \left(-1 + \sqrt{5}\right) P_7\right);$$

$$mP1 = \frac{1}{2} \times \left(2 + P_6 \left(3 + P_1 s_1 + P_3 s_1 - \sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3) s_1)^2}\right) + P_5 \left(-1 + P_1 s_1 - P_3 s_1 + \sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3) s_1)^2}\right) + P_7 \left(-1 - P_1 s_1 + P_3 s_1 + \sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3) s_1)^2}\right)\right);$$

$$mP2 = \frac{1}{2} \times \left(2 + 3 P_6 - P_7 + P_2 (P_6 + P_7) s_2 - (P_6 - P_7) \left(-P_4 s_2 + \sqrt{5 + 2 (P_2 + P_4) s_2 + (P_2 - P_4)^2 s_2^2}\right) + P_5 \left(-1 + (-P_2 + P_4) s_2 + \sqrt{5 + 2 (P_2 + P_4) s_2 + (P_2 - P_4)^2 s_2^2}\right)\right);$$

```
  If[mP1 > m00 && mP2 > m00 && mP < Min[mP1, mP2],
   Print["P_1=", P_1, ", P_2=", P_2, ", P_3=", P_3, ", P_4=", P_4, ", P_5=", P_5, ", P_6=", P_6,
    ", P_7=", P_7, ", Total edges=", Total[IntegerDigits[i, 2]]] && Break[], 0]]]
```

```
Successful binding networks for value antagonism-

P_1=0, P_2=0, P_3=1, P_4=1, P_5=1, P_6=0, P_7=1, Total edges=4
P_1=1, P_2=1, P_3=0, P_4=0, P_5=1, P_6=0, P_7=1, Total edges=4
```

This is the surface map for the successful network-

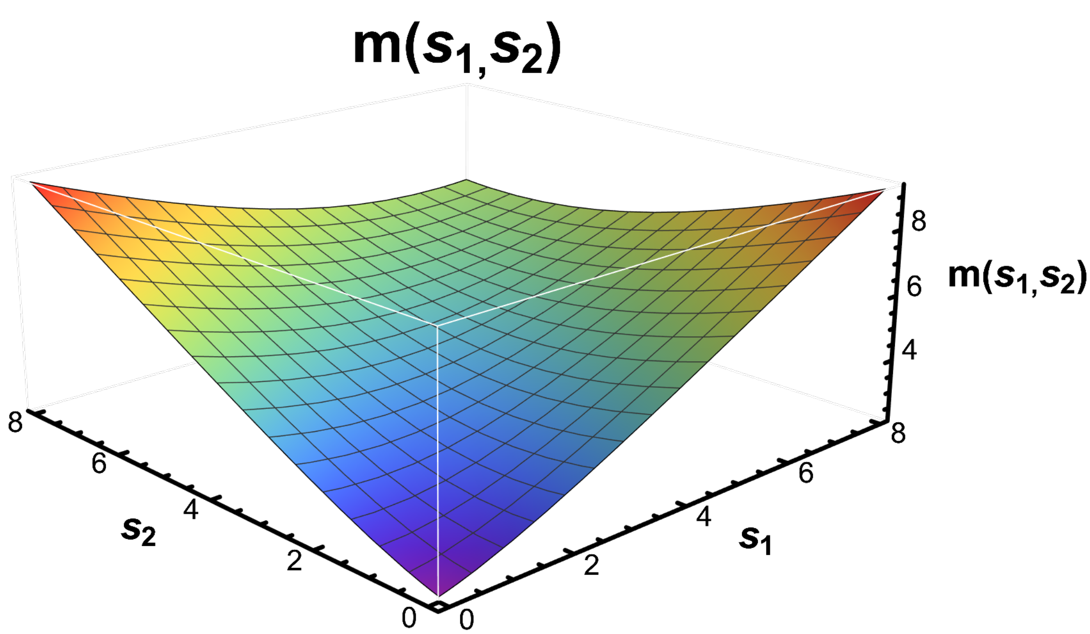
```
P1 = 1;
P2 = 1;
P3 = 0;
P4 = 0;
P5 = 1;
P6 = 0;
P7 = 1;
```

$$mPSV = \frac{1}{2} \times \Big(2 + P_6 \Big(3 + P_1 s_1 + P_3 s_1 + P_2 s_2 + P_4 s_2 - \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4 \times (1 + P_1 s_1 + P_4 s_2)}\Big) + P_7 \Big(-1 - P_1 s_1 + P_3 s_1 + P_2 s_2 - P_4 s_2 + \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4 \times (1 + P_1 s_1 + P_4 s_2)}\Big) + P_5 \Big(-1 + P_1 s_1 - P_3 s_1 - P_2 s_2 + P_4 s_2 + \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4 \times (1 + P_1 s_1 + P_4 s_2)}\Big)\Big)$$

Out[ ]= $\sqrt{4 \times (1 + s_1) + (1 - s_1 + s_2)^2}$

```
Plot3D[mPSV, {s1, 0, 8}, {s2, 0, 8}, AxesLabel →
  {Style["s1", Bold, 20, FontColor → Black], Style["s2", Bold, 20, FontColor → Black],
   Style["m(s1,s2)", Bold, 20, FontColor → Black]},
 PlotLabel → Style["m(s1,s2)", Bold, 30, FontColor → Black],
 ColorFunction → "Rainbow", AxesStyle → Thickness[0.005], BoxStyle → GrayLevel[2],
 TicksStyle → Directive[Black, 15], ImageSize → Large, PlotRange → Full]
```

Out[ ]=



Successful network slope antagonism

This is the code to test the successful network for slope antagonism-

```
npts = 10 000; (*number of random {s₁,s₂} pairs
 over which the antagonism condition is verified*)
smax = 100; (*maximum value of s₁ and s₂*)
nedges = 7; (*maximum number of edges*)
Print["Successful binding networks for slope antagonism-\n"]
For[i = 0, i < 2^nedges, i++, P₁ = PadLeft[IntegerDigits[i, 2], nedges][[1]];
 P₂ = PadLeft[IntegerDigits[i, 2], nedges][[2]];
 P₃ = PadLeft[IntegerDigits[i, 2], nedges][[3]];
 P₄ = PadLeft[IntegerDigits[i, 2], nedges][[4]];
 P₅ = PadLeft[IntegerDigits[i, 2], nedges][[5]];
 P₆ = PadLeft[IntegerDigits[i, 2], nedges][[6]];
 P₇ = PadLeft[IntegerDigits[i, 2], nedges][[7]];
 For[j = 0, j < npts, j++, s₁ = smax * RandomReal[];
  s₂ = smax * RandomReal[];
```

$$m_{12} = \frac{1}{2}\left(P_6\left(P_1+P_3-\frac{4P_1+2(-P_1+P_3)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1 s_1+P_4 s_2)}}\right)+\right.$$
$$P_5\left(P_1-P_3+\frac{4P_1+2(-P_1+P_3)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1 s_1+P_4 s_2)}}\right)+$$
$$P_7\left(-P_1+P_3+\frac{4P_1+2(-P_1+P_3)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1 s_1+P_4 s_2)}}\right)+$$
$$P_6\left(P_2+P_4-\frac{4P_4+2(P_2-P_4)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1 s_1+P_4 s_2)}}\right)+$$
$$P_7\left(P_2-P_4+\frac{4P_4+2(P_2-P_4)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1 s_1+P_4 s_2)}}\right)+$$
$$\left.P_5\left(-P_2+P_4+\frac{4P_4+2(P_2-P_4)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1 s_1+P_4 s_2)}}\right)\right);$$

$$m_{00} = 0;$$

$$m_1 = \frac{1}{2}\left(P_6\left(P_1+P_3+\frac{-P_1-P_3-(P_1-P_3)^2 s_1}{\sqrt{4+4P_1 s_1+(1+(-P_1+P_3)s_1)^2}}\right)+\right.$$

$$P_5\left(P_1 - P_3 + \frac{P_1 + P_3 + (P_1 - P_3)^2 s_1}{\sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3) s_1)^2}}\right) +$$

$$P_7\left(-P_1 + P_3 + \frac{P_1 + P_3 + (P_1 - P_3)^2 s_1}{\sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3) s_1)^2}}\right)\Bigg);$$

$$m_2 = \frac{1}{2}\left(P_2 (P_6 + P_7) - (P_6 - P_7)\left(-P_4 + \frac{P_2 + P_4 + (P_2 - P_4)^2 s_2}{\sqrt{5 + 2 (P_2 + P_4) s_2 + (P_2 - P_4)^2 s_2^2}}\right) +\right.$$

$$\left.P_5\left(-P_2 + P_4 + \frac{P_2 + P_4 + (P_2 - P_4)^2 s_2}{\sqrt{5 + 2 (P_2 + P_4) s_2 + (P_2 - P_4)^2 s_2^2}}\right)\right);$$

```
If[m1 > m00 && m2 > m00 && m12 < Min[m1, m2], Print["P1=", P1, ", P2=", P2,
   ", P3=", P3, ", P4=", P4, ", P5=", P5, ", P6=", P6, ", P7=", P7,
   ", Total edges=", Total[IntegerDigits[i, 2]]] && Break[], 0]]]
```

Successful binding networks for slope antagonism-

P_1=0, P_2=0, P_3=1, P_4=1, P_5=1, P_6=0, P_7=1, Total edges=4

P_1=0, P_2=1, P_3=1, P_4=0, P_5=0, P_6=1, P_7=0, Total edges=3

P_1=1, P_2=0, P_3=0, P_4=1, P_5=0, P_6=1, P_7=0, Total edges=3

P_1=1, P_2=1, P_3=0, P_4=0, P_5=1, P_6=0, P_7=1, Total edges=4

In[∘]:=

$P_1 = 0;$
$P_2 = 1;$
$P_3 = 1;$
$P_4 = 0;$
$P_5 = 0;$
$P_6 = 1;$
$P_7 = 0;$

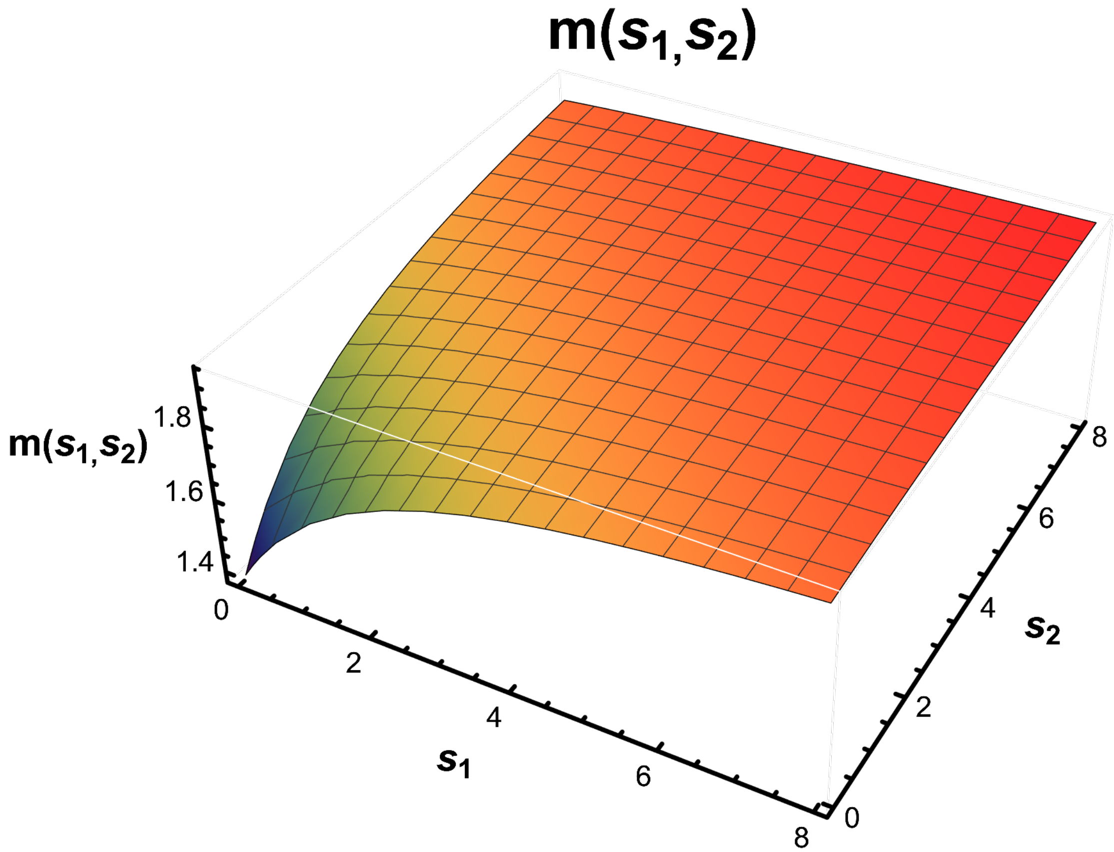
$$\text{mPSS} = \text{FullSimplify}\Big[\frac{1}{2}\times\Big(2 + P_6\Big(3 + P_1 s_1 + P_3 s_1 + P_2 s_2 + P_4 s_2 - \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4\times(1 + P_1 s_1 + P_4 s_2)}\Big) + P_7\Big(-1 - P_1 s_1 + P_3 s_1 + P_2 s_2 - P_4 s_2 + \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4\times(1 + P_1 s_1 + P_4 s_2)}\Big) + P_5\Big(-1 + P_1 s_1 - P_3 s_1 - P_2 s_2 + P_4 s_2 + \sqrt{(1 + (-P_1 + P_3) s_1 + (P_2 - P_4) s_2)^2 + 4\times(1 + P_1 s_1 + P_4 s_2)}\Big)\Big)\Big]$$

Out[∘]=

$$\frac{1}{2}\times\left(5 + s_1 + s_2 - \sqrt{4 + (1 + s_1 + s_2)^2}\right)$$

In[∘]:=
```
Plot3D[mPSS, {s1, 0, 8}, {s2, 0, 8}, AxesLabel →
  {Style["s1", Bold, 20, FontColor → Black], Style["s2", Bold, 20, FontColor → Black],
   Style["m(s1,s2)", Bold, 20, FontColor → Black]},
 PlotLabel → Style["m(s1,s2)", Bold, 30, FontColor → Black],
 ColorFunction → "Rainbow", AxesStyle → Thickness[0.005], BoxStyle → GrayLevel[2],
 TicksStyle → Directive[Black, 15], ImageSize → Large, PlotRange → Full]
```

Out[∘]=



Calculating m_1, m_2 and m_{12} for succesful slope antagonism

In[∘]:=
$P_1 = 0;$
$P_2 = 1;$
$P_3 = 1;$
$P_4 = 0;$
$P_5 = 0;$
$P_6 = 1;$
$P_7 = 0;$

$$m_{S1} = \text{FullSimplify}\left[\frac{1}{2}\left(P_6\left(P_1 + P_3 + \frac{-P_1 - P_3 - (P_1 - P_3)^2 s_1}{\sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3) s_1)^2}}\right) + P_5\left(P_1 - P_3 + \frac{P_1 + P_3 + (P_1 - P_3)^2 s_1}{\sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3) s_1)^2}}\right) + P_7\left(-P_1 + P_3 + \frac{P_1 + P_3 + (P_1 - P_3)^2 s_1}{\sqrt{4 + 4 P_1 s_1 + (1 + (-P_1 + P_3) s_1)^2}}\right)\right)\right]$$

Out[∘]=
$$\frac{1}{2} \times \left(1 + \frac{-1 - s_1}{\sqrt{4 + (1 + s_1)^2}}\right)$$

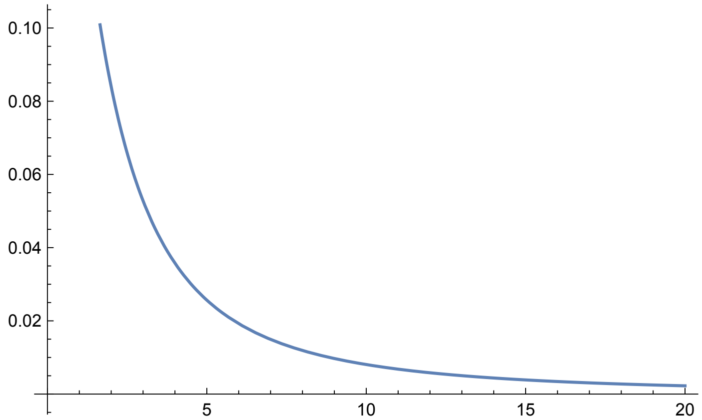
In[∘]:=
$P_1 = 0;$
$P_2 = 1;$
$P_3 = 1;$
$P_4 = 0;$
$P_5 = 0;$
$P_6 = 1;$
$P_7 = 0;$

$$m_{S2} = \text{FullSimplify}\left[\frac{1}{2}\left(P_2 (P_6 + P_7) - (P_6 - P_7)\left(-P_4 + \frac{P_2 + P_4 + (P_2 - P_4)^2 s_2}{\sqrt{5 + 2 (P_2 + P_4) s_2 + (P_2 - P_4)^2 s_2^2}}\right) + P_5\left(-P_2 + P_4 + \frac{P_2 + P_4 + (P_2 - P_4)^2 s_2}{\sqrt{5 + 2 (P_2 + P_4) s_2 + (P_2 - P_4)^2 s_2^2}}\right)\right)\right]$$

Out[∘]=
$$\frac{1}{2} \times \left(1 - \frac{1 + s_2}{\sqrt{5 + s_2 (2 + s_2)}}\right)$$

In[∘]:=
$$\text{Plot}\left[\frac{1}{2}\times\left(1-\frac{1+s_2}{\sqrt{5+s_2\,(2+s_2)}}\right),\ \{s_2,0,20\}\right]$$

Out[∘]=



In[∘]:=
$$P_1 = 0;$$
$$P_2 = 1;$$
$$P_3 = 1;$$
$$P_4 = 0;$$
$$P_5 = 0;$$
$$P_6 = 1;$$
$$P_7 = 0;$$
$$m_{S12} =$$
$$\text{FullSimplify}\Bigg[\frac{1}{2}\Bigg(P_6\left(P_1+P_3-\frac{4P_1+2(-P_1+P_3)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1s_1+P_4s_2)}}\right)+$$
$$P_5\left(P_1-P_3+\frac{4P_1+2(-P_1+P_3)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1s_1+P_4s_2)}}\right)+$$
$$P_7\left(-P_1+P_3+\frac{4P_1+2(-P_1+P_3)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1s_1+P_4s_2)}}\right)+$$
$$P_6\left(P_2+P_4-\frac{4P_4+2(P_2-P_4)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1s_1+P_4s_2)}}\right)+$$
$$P_7\left(P_2-P_4+\frac{4P_4+2(P_2-P_4)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1s_1+P_4s_2)}}\right)+$$
$$P_5\left(-P_2+P_4+\frac{4P_4+2(P_2-P_4)(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)}{2\sqrt{(1+(-P_1+P_3)s_1+(P_2-P_4)s_2)^2+4\times(1+P_1s_1+P_4s_2)}}\right)\Bigg)\Bigg]$$

Out[∘]=
$$1-\frac{1+s_1+s_2}{\sqrt{4+(1+s_1+s_2)^2}}$$