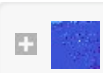
```
In[ ]:= SetDirectory[
          "C:/Users/serha/OneDrive/Masaüstü/MyRepo/master_thesis_MMT003/210421_OR_model_and
            _other_lines_sliding"];
```

FBA Model Network

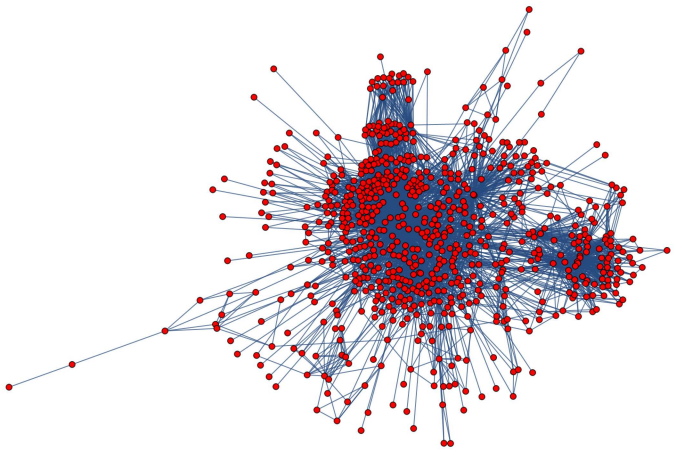
```
In[ ]:= stoichioforhomosapiens =
          Drop[Import["../210324_disc_time_windows_and_OR_model/iAT_PLT_636_stoichiomat.csv",
            HeaderLines → 1], None, {1}];
        SparseArray@stoichioforhomosapiens
```

```
Out[ ]= SparseArray[  Specified elements: 4006
                     Dimensions: {738, 1008} ]
```

```
In[ ]:= stochmatrix = stoichioforhomosapiens;
        AdjmatR = Transpose[stochmatrix].stochmatrix;
        NormAdjmatR = AdjmatR /. x_ /; x ≠ 0 → 1;
        NormAdjmatR = NormAdjmatR /. 0. → 0;
        NormAdjmatR = UpperTriangularize[NormAdjmatR, 1] + LowerTriangularize[NormAdjmatR, -1];
        AdjmatM = stochmatrix.Transpose[stochmatrix];
        NormAdjmatM = AdjmatM /. x_ /; x ≠ 0 → 1;
        NormAdjmatM = NormAdjmatM /. 0. → 0;
        NormAdjmatM = UpperTriangularize[NormAdjmatM, 1] + LowerTriangularize[NormAdjmatM, -1];
```

```
In[ ]:= (*AdjacencyGraph[NormAdjmatR,{DirectedEdges→False,VertexSize→6,VertexStyle→Red(*,
          VertexLabels→{1->"v1",2->"v2",3->"v3",4->"v4",5->"b1",6->"b2",7->"b3"}*)}]*)
        AdjacencyGraph[NormAdjmatM, {DirectedEdges → False, VertexSize → 6,
          VertexStyle → Red(*,VertexLabels→{1->"A",2->"B",3->"C"}*)}]
```

Out[ ]=



```
        stoichiometricmatrix = stoichioforhomosapiens;
        metabolites = 738;
        fluxexchanges = 1008;
        steadystatevector = ConstantArray[{0, 0}, metabolites];
        boundaries = ConstantArray[{0, 500}, fluxexchanges];
        first[a_] := First /@ GatherBy[Ordering@a, a[[#]] &] // Sort;
```

```
In[ ]:= syntheticseqgenerator[stoichiometricmatrix_,
          steadystatevector_, boundaries_, fluxexchanges_, sequencesize_] := Module[
          {subsetsizechoice, subsetpositions, coefficients, objectivefunctions, solutionvectors},
          subsetsizechoice = RandomInteger[{1, fluxexchanges}];
          subsetpositions = RandomSample[Range@fluxexchanges, subsetsizechoice];
          coefficients = Table[RandomReal[{-2, 2}, subsetsizechoice], sequencesize];
          objectivefunctions = Table[ReplacePart[ConstantArray[0., fluxexchanges],
             MapThread[#1 → #2 &, {subsetpositions, coefficients[[i]]}]], {i, sequencesize}];
          solutionvectors = Table[LinearProgramming[-objectivefunctions[[i]],
             stoichiometricmatrix, steadystatevector,
             boundaries], {i, Length@objectivefunctions}]]

        SeedRandom@5;
        AbsoluteTiming[
         sequences = Table[syntheticseqgenerator[stoichiometricmatrix, steadystatevector,
             boundaries, fluxexchanges, 300], 200];]
        sequenceschopped = Chop[sequences, 10^-5];

        Table[Length@((sequenceschopped[[i]])[[first@sequenceschopped[[i]], All]]), {i, 200}]
        Length@(Flatten[sequenceschopped, 1])[[first@Flatten[sequenceschopped, 1], All]]
        Dimensions@(Flatten[sequenceschopped, 1])[[All, first[(Flatten[sequenceschopped, 1])^T]]]
```

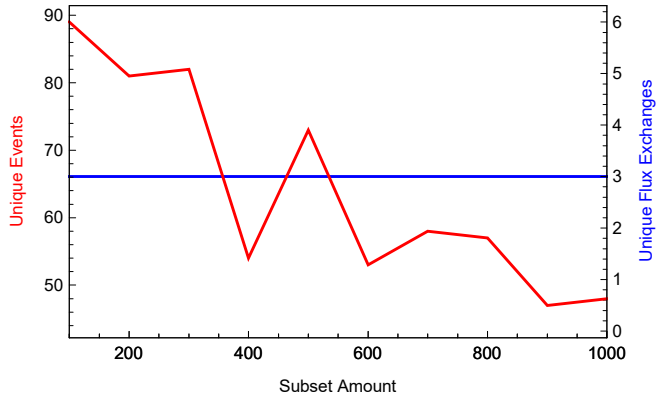
Varying Amount of Selected Subsets

```
In[ ]:= syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix_, steadystatevector_,
          boundaries_, fluxexchanges_, sequencesize_, subsetnumber_] := Module[
          {subsetsizechoice, subsetpositions, coefficients, objectivefunctions, solutionvectors},
          subsetsizechoice = subsetnumber;
          subsetpositions = RandomSample[Range@fluxexchanges, subsetsizechoice];
          coefficients = Table[RandomReal[{-2, 2}, subsetsizechoice], sequencesize];
          objectivefunctions = Table[ReplacePart[ConstantArray[0., fluxexchanges],
             MapThread[#1 → #2 &, {subsetpositions, coefficients[[i]]}]], {i, sequencesize}];
          solutionvectors = Table[LinearProgramming[-objectivefunctions[[i]],
             stoichiometricmatrix, steadystatevector,
             boundaries], {i, Length@objectivefunctions}]]

In[ ]:= subsetamounts = Range[100, 1000, 100];
        SeedRandom@5;
        AbsoluteTiming[sequencesfixedsubsetsize =
           Table[Table[syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix,
              steadystatevector, boundaries, fluxexchanges, 10, i], 10], {i, subsetamounts}];]
        sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
        uniquefluxexchanges = Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}];
        uniqueevents =
          Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}];
Out[ ]= {30.5997, Null}

In[ ]:= Thread[{subsetamounts, uniqueevents}]
```

Out[•]= {{100, 89}, {200, 81}, {300, 82}, {400, 54},
{500, 73}, {600, 53}, {700, 58}, {800, 57}, {900, 47}, {1000, 48}}

In[•]:=
```
plot1 = Overlay[{ListLinePlot[Thread[{subsetamounts, uniquefluxexchanges}], Frame → True,
    ImagePadding → 35, FrameTicks → {{None, All}, {All, None}}, FrameLabel →
     {{None, Style["Unique Flux Exchanges", Blue]}, {None, None}}, PlotStyle → Blue,
    ImageSize → 350, PlotRange → {{First@subsetamounts, Last@subsetamounts}, All}],
   ListLinePlot[Thread[{subsetamounts, uniqueevents}], Frame → True,
    ImagePadding → 35, FrameTicks → {{All, None}, {All, None}},
    FrameLabel → {"Subset Amount", Style["Unique Events", Red]}, PlotStyle → Red,
    ImageSize → 350, PlotRange → {{First@subsetamounts, Last@subsetamounts}, All}]}]
```

Out[•]=



Varying Range of Objective Function Coefficients

In[•]:=
```
boundaries = ConstantArray[{0, 500}, fluxexchanges];
coefboundaries = {{0, 1}, {-1, 0}, {0, 2}, {-2, 0},
   {-1, 1}, {-2, 2}, {-3, 3}, {0, 5}, {0, -5}, {1, 1}, {-5, 5}, {-4, 4}};
```

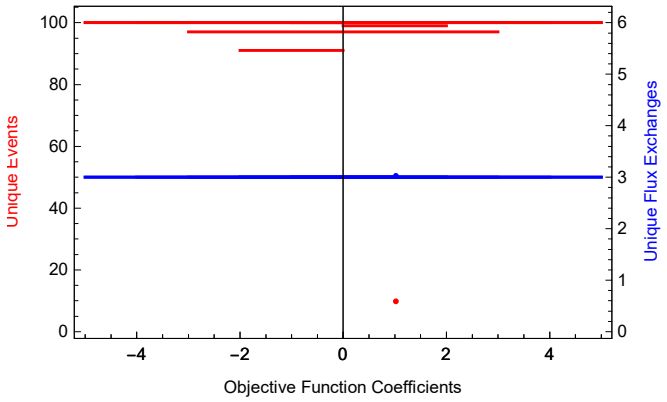
In[•]:=
```
syntheticseqgeneratorfxdsubsetsizevaryingcoeff[stoichiometricmatrix_, steadystatevector_,
  boundaries_, fluxexchanges_, sequencesize_, subsetnumber_, coefboundaries_] := Module[
  {subsetsizechoice, subsetpositions, coefficients, objectivefunctions, solutionvectors},
  subsetsizechoice = subsetnumber;
  subsetpositions = RandomSample[Range@fluxexchanges, subsetsizechoice];
  coefficients = Table[RandomReal[coefboundaries, subsetsizechoice], sequencesize];
  objectivefunctions = Table[ReplacePart[ConstantArray[0., fluxexchanges],
     MapThread[#1 → #2 &, {subsetpositions, coefficients[[i]]}]], {i, sequencesize}];
  solutionvectors = Table[LinearProgramming[-objectivefunctions[[i]],
     stoichiometricmatrix, steadystatevector,
     boundaries], {i, Length@objectivefunctions}]]
```

```
In[ ]:= SeedRandom@5;
AbsoluteTiming[sequencesfixedsubsetsize =
   Table[Table[syntheticseqgeneratorfxdsubsetsizevaryingcoeff[stoichiometricmatrix,
      steadystatevector, boundaries, fluxexchanges, 10, 20, i], 10], {i, coefboundaries}];]
sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
uniquefluxexchanges = Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}];
uniqueevents =
  Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}];
```

```
Out[ ]= {32.9353, Null}
```

```
In[ ]:= plot2 = Overlay[{ListLinePlot[
    MapThread[{{#1[[1]], #2}, {#1[[2]], #2}} &, {coefboundaries, uniquefluxexchanges}],
    Frame → True, ImagePadding → 35, FrameTicks → {{None, All}, {All, None}},
    FrameLabel → {{None, Style["Unique Fluxes Exchanges", Blue]}, {None, None}},
    PlotStyle → Blue, ImageSize → 350, PlotRange → All], ListLinePlot[
    MapThread[{{#1[[1]], #2}, {#1[[2]], #2}} &, {coefboundaries, uniqueevents}],
    Frame -> True, ImagePadding → 35, FrameTicks → {{All, None}, {All, None}},
    FrameLabel → {"Objective Function Coefficients", Style["Unique Events", Red]},
    PlotStyle → Red, ImageSize → 350, PlotRange → All]}]
```

Out[ ]=



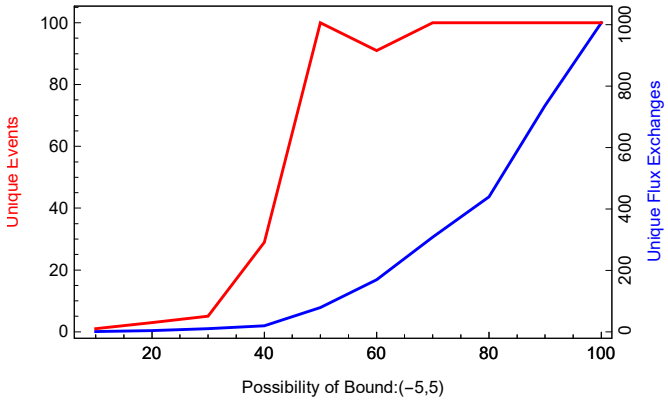
Varying Vector of Boundaries

```
In[ ]:= xaxis = Reverse@Range[10, 100, 10];
SeedRandom@5;
boundaries = Table[RandomChoice[i → {{-5, 5}, {0, 0}}, fluxexchanges],
   {i, Drop[MapThread[{#1, #2} &, {Reverse@Range[0, 1, 0.1], Range[0, 1, 0.1]}], -1]}];
SeedRandom@5;
AbsoluteTiming[sequencesfixedsubsetsize =
   Table[Table[syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix,
      steadystatevector, i, fluxexchanges, 10, 20], 10], {i, boundaries}];]
sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
uniquefluxexchanges = Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}];
uniqueevents =
  Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}];
```

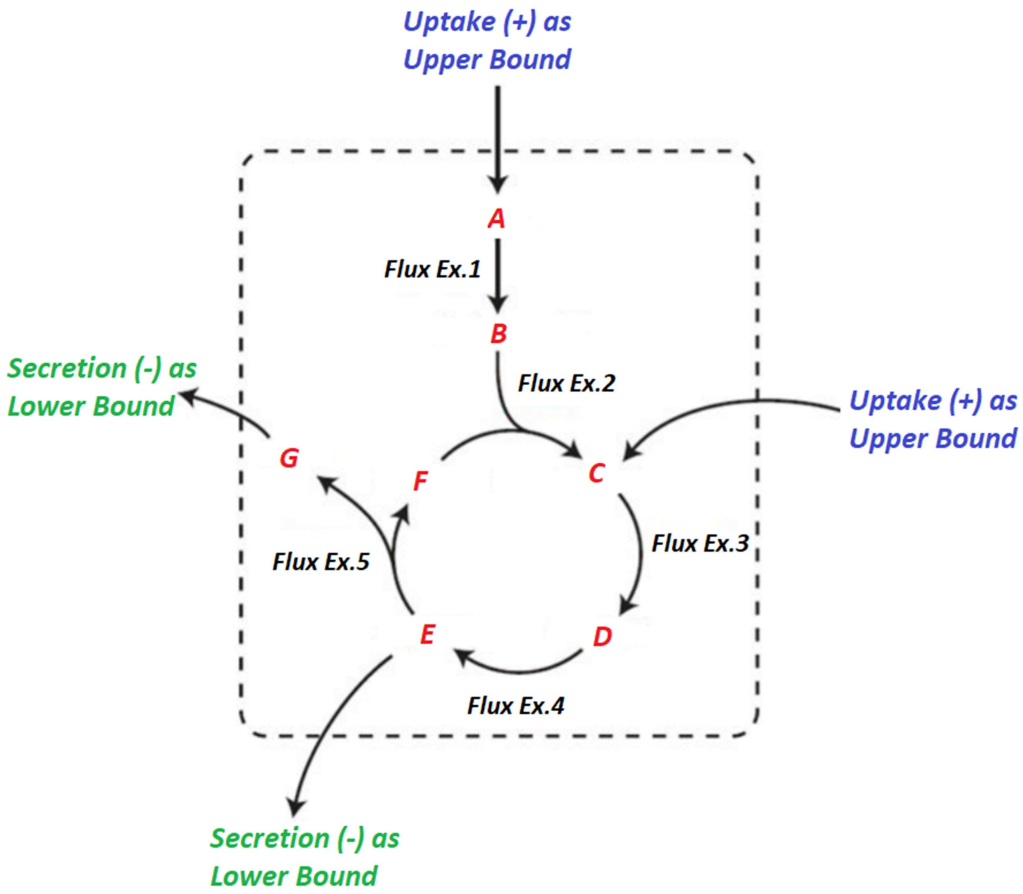
Out[ ]= {16.1978, Null}

In[ ]:=
```
tickvalues = {{0, 0}, {200, 200}, {400, 400}, {600, 600}, {800, 800}, {1000, 1000}};
ticks = MapAt[Rotate[#, Pi / 2] &, tickvalues, {All, -1}];
plot3 = Overlay[{ListLinePlot[Thread[{xaxis, uniquefluxexchanges}],
     Frame → True, ImagePadding → 35, FrameTicks → {{None, ticks}, {All, None}},
     FrameLabel → {{None, Style["Unique Flux Exchanges", Blue]}, {None, None}},
     PlotStyle → Blue, ImageSize → 350, PlotRange → All, ImagePadding → 20],
    ListLinePlot[Thread[{xaxis, uniqueevents}], Frame → True, ImagePadding → 35,
     FrameTicks → {{All, None}, {All, None}}, FrameLabel →
      {"Possibility of Bound:(-5,5)", Style["Unique Events", Red]}, PlotStyle → Red,
     ImageSize → 350, PlotRange → All, ImagePadding → 20]}, ImageSize → Large]
```

Out[ ]=



Model Cartoon



Other Trials

```
In[ ]:= SeedRandom@5;
boundaries = Table[RandomChoice[i → {{0, 500}, {0, 0}}, fluxexchanges],
   {i, Drop[MapThread[{#1, #2} &, {Reverse@Range[0, 1, 0.1], Range[0, 1, 0.1]}], -1]}];
```

```
In[ ]:= Drop[MapThread[{#1, #2} &, {Reverse@Range[0, 1, 0.1], Range[0, 1, 0.1]}], -1]
Dimensions@boundaries
```

```
Out[ ]= {{1., 0.}, {0.9, 0.1}, {0.8, 0.2}, {0.7, 0.3}, {0.6, 0.4},
  {0.5, 0.5}, {0.4, 0.6}, {0.3, 0.7}, {0.2, 0.8}, {0.1, 0.9}}
```

```
Out[ ]= {10, 1008, 2}
```

```
In[ ]:= SeedRandom@5;
AbsoluteTiming[sequencesfixedsubsetsize =
   Table[Table[syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix,
      steadystatevector, i, fluxexchanges, 300, 500], 10], {i, boundaries}];]
sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
Table[Length@first[(Flatten[i, 1])ᵀ], {i, sequenceschopped}]
Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}]
```

```
Out[ ]= {774.792, Null}
```

```
Out[ ]= {3, 1, 3, 3, 1, 2, 1, 3, 1, 1}
```

Out[•]= {1803, 1, 1617, 1748, 1, 1638, 1, 1642, 1, 1}

In[•]:=
```
SeedRandom@5;
AbsoluteTiming[sequencesfixedsubsetsize =
   Table[Table[syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix,
      steadystatevector, i, fluxexchanges, 300, 200], 10], {i, boundaries}];]
sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}]
Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}]
```

Out[•]= {711.616, Null}

Out[•]= {3, 1, 3, 3, 1, 3, 1, 3, 1, 1}

Out[•]= {2410, 1, 2521, 2527, 1, 2370, 1, 1932, 1, 1}

In[•]:=
```
SeedRandom@5;
AbsoluteTiming[sequencesfixedsubsetsize =
   Table[Table[syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix,
      steadystatevector, i, fluxexchanges, 300, 20], 10], {i, boundaries}];]
sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}]
Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}]
```

Out[•]= {686.88, Null}

Out[•]= {3, 1, 3, 3, 1, 3, 1, 2, 1, 1}

Out[•]= {3000, 1, 3000, 3000, 1, 2404, 1, 7, 1, 1}

In[•]:=
```
SeedRandom@5;
boundaries = Table[RandomChoice[i → {{0, 5}, {0, 0}}, fluxexchanges],
   {i, Drop[MapThread[{#1, #2} &, {Reverse@Range[0, 1, 0.1], Range[0, 1, 0.1]}], -1]}];
```

In[•]:=
```
SeedRandom@5;
AbsoluteTiming[sequencesfixedsubsetsize =
   Table[Table[syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix,
      steadystatevector, i, fluxexchanges, 300, 20], 10], {i, boundaries}];]
sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}]
Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}]
```

Out[•]= {943.356, Null}

Out[•]= {3, 1, 3, 3, 1, 3, 1, 2, 1, 1}

Out[•]= {246, 1, 2143, 214, 1, 256, 1, 7, 1, 1}

In[•]:=
```
boundaries = Table[RandomChoice[i → {{-Infinity, Infinity}, {0, 0}}, fluxexchanges],
  {i, Drop[MapThread[{#1, #2} &, {Reverse@Range[0, 1, 0.1], Range[0, 1, 0.1]}], -1]}]
```

```
In[ ]:= SeedRandom@56;
AbsoluteTiming[sequencesfixedsubsetsize =
   Quiet@Table[Table[syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix,
       steadystatevector, i, fluxexchanges, 300, 20], 10], {i, boundaries}];]
sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}]
Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}]
```

```
Out[ ]= {3090.45, Null}
```

```
In[ ]:= SeedRandom@5;
boundaries = Table[{0, i}, {i, RandomInteger[{1, 10}, fluxexchanges]}];
boundaries = Table[ReplacePart[boundaries,
    Partition[RandomSample[Range@fluxexchanges, Ceiling[0.1 * fluxexchanges, 1]], 1] →
     {0, 0}], {i, Range[0.1, 1, 0.1]}];
SeedRandom@5;
AbsoluteTiming[sequencesfixedsubsetsize =
   Table[Table[syntheticseqgeneratorfxdsubsetsize[stoichiometricmatrix,
      steadystatevector, i, fluxexchanges, 300, 20], 2], {i, boundaries}];]
sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}]
Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}]
```

```
Out[ ]= {202.306, Null}
```

```
Out[ ]= {1, 3, 3, 3, 3, 3, 3, 1, 3, 3}
```

```
Out[ ]= {1, 600, 600, 600, 600, 600, 600, 1, 600, 600}
```

```
In[ ]:= syntheticseqgenerator2[stoichiometricmatrix_,
  steadystatevector_, boundaries_, fluxexchanges_, sequencesize_] := Module[
  {subsetsizechoice, subsetpositions, coefficients, objectivefunctions, solutionvectors},
  subsetsizechoice = RandomInteger[{1, fluxexchanges}];
  subsetpositions = RandomSample[Range@fluxexchanges, subsetsizechoice];
  coefficients = Table[RandomReal[{0.1, 10}, subsetsizechoice], sequencesize];
  objectivefunctions = Table[ReplacePart[ConstantArray[0., fluxexchanges],
     MapThread[#1 → #2 &, {subsetpositions, coefficients[[i]]}]], {i, sequencesize}];
  solutionvectors = Table[LinearProgramming[-objectivefunctions[[i]],
     stoichiometricmatrix, steadystatevector,
     boundaries], {i, Length@objectivefunctions}]]
```

```
In[ ]:= SeedRandom@5;
boundaries = Table[{0, i}, {i, RandomInteger[{1, 10}, fluxexchanges]}];
boundaries = Table[ReplacePart[boundaries,
    Partition[RandomSample[Range@fluxexchanges, Ceiling[0.1 * fluxexchanges, 1]], 1] →
     {0, 0}], {i, Range[0.1, 1, 0.1]}];
```

```
In[ ]:= AbsoluteTiming[
         sequencesfixedsubsetsize = Table[Table[syntheticseqgenerator2[stoichiometricmatrix,
               steadystatevector, i, fluxexchanges, 300], 2], {i, boundaries}];]
        sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
        Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}]
        Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}]
Out[ ]= {195.126, Null}

Out[ ]= {1, 3, 3, 3, 3, 3, 3, 1, 3, 3}

Out[ ]= {1, 595, 505, 590, 600, 598, 596, 1, 598, 600}
```

Trials with different boundary limits

```
In[ ]:= sequencesize = 300;
        boundaries = Table[{0, i}, {i, RandomInteger[{-200, 200}, fluxexchanges]}];

In[ ]:= subsetsizechoice = 250;
        subsetpositions = RandomSample[Range@fluxexchanges, subsetsizechoice];
        coefficients = Table[RandomReal[{-2, 2}, subsetsizechoice], sequencesize];
        objectivefunctions = Table[ReplacePart[ConstantArray[0., fluxexchanges],
            MapThread[#1 → #2 &, {subsetpositions, coefficients[[i]]}]], {i, sequencesize}];
        solutionvectors = Table[LinearProgramming[-objectivefunctions[[i]], stoichiometricmatrix,
            steadystatevector, boundaries], {i, Length@objectivefunctions}];
        sequenceschopped = Chop[solutionvectors, 10^-5];
        Length@first[(Flatten[sequenceschopped, 1])^T]
        Length@(Flatten[sequenceschopped, 1])[[first@Flatten[sequenceschopped, 1], All]]
Out[ ]= 300

In[ ]:= boundaries = ConstantArray[{-500, 500}, fluxexchanges];
        SeedRandom@5;
        AbsoluteTiming[sequencesfixedsubsetsize =
           Table[Table[syntheticseqgeneratorfxdsubsetsizevaryingcoeff[stoichiometricmatrix,
              steadystatevector, boundaries, fluxexchanges, 10, 20, i], 10], {i, coefboundaries}];]
        sequenceschopped = Table[Chop[i, 10^-5], {i, sequencesfixedsubsetsize}];
        Table[Length@first[(Flatten[i, 1])^T], {i, sequenceschopped}]
        Table[Length@(Flatten[i, 1])[[first@Flatten[i, 1], All]], {i, sequenceschopped}]
Out[ ]= {31.4049, Null}

Out[ ]= {1006, 1007, 1004, 1005, 1004, 1005, 1005, 1006, 1006, 1003}

Out[ ]= {100, 100, 100, 100, 100, 100, 100, 100, 100, 10}
```