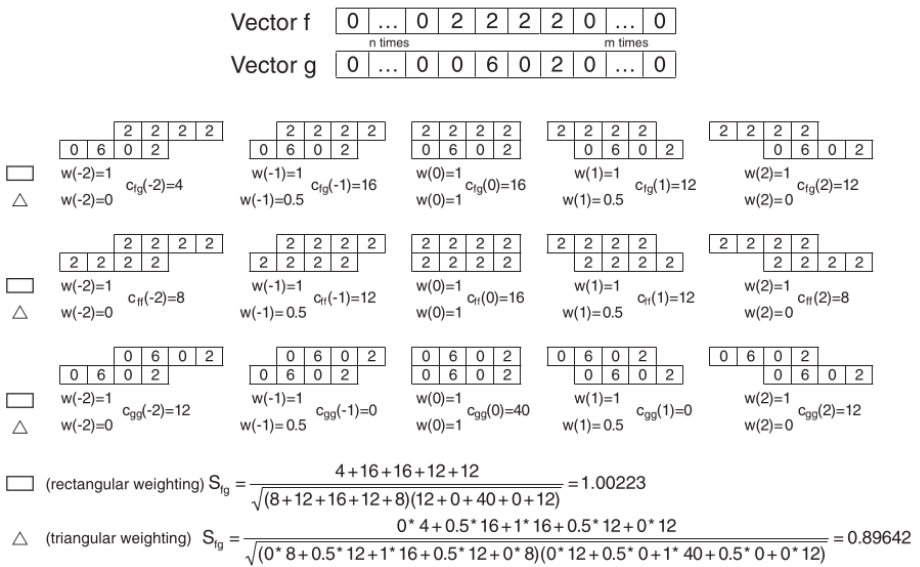
Graph Rewriting and NMR Spectroscopy in Chemical Reaction Network Modelling

by Kilian Seng

Thesis Goal

- Analyze NMR Spectra
- Use characteristics to determine Reactions

NMR comparison



- ^{13}C-NMR: 25 – 180 ppm
- Bin sizes: 0.1 to 1.0, 0.1 steps
- Interval:
  - floor(min) – b
  - ceiling(max) + b
- Triangle overlap
- Multiplication

ILP: Variables

- b_e: Is edge used?
- x_e: How often used?
- $n_{m,e}$: Which edges contribute?
- b_v: Is vertice produced?
- $n_{m,v}$: Which Vertices contribute?

ILP: Constants

- $p_{m,e}$: How likely is the edge?
- $p_{m,v}$: How likely is the vertice?

ILP: Constraints

- $x_e \geq b_e$
- $b_e \geq n_{m,e}$
- $b_v \geq n_{m,v}$
- inflow(v) = outflow(v)
- No circular edges
- $\sum_e n_{m,e} \leq 1$ $\sum_m n_{m,e} \leq 1$ $\sum_v n_{m,v} \leq 1$

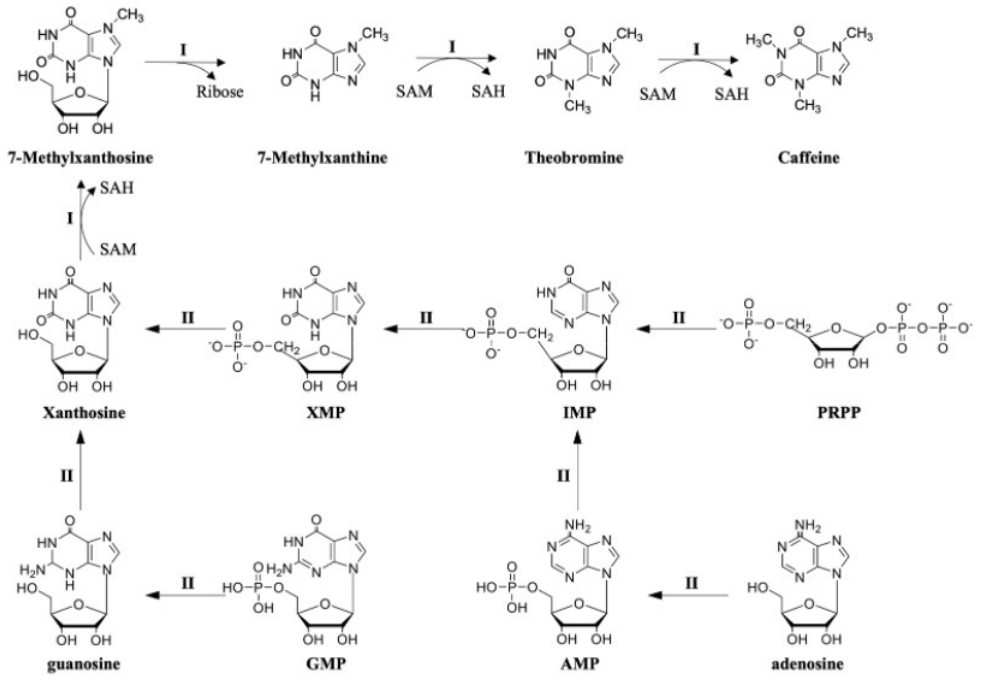
ILP:Objective edges

- max: $$z = \sum_{e} \sum_{m} 1000 \times n_{m,e} \times p_{m,e} - \frac{1}{p_{max,e}} \times x_{e}$$

ILP:Objective vertices

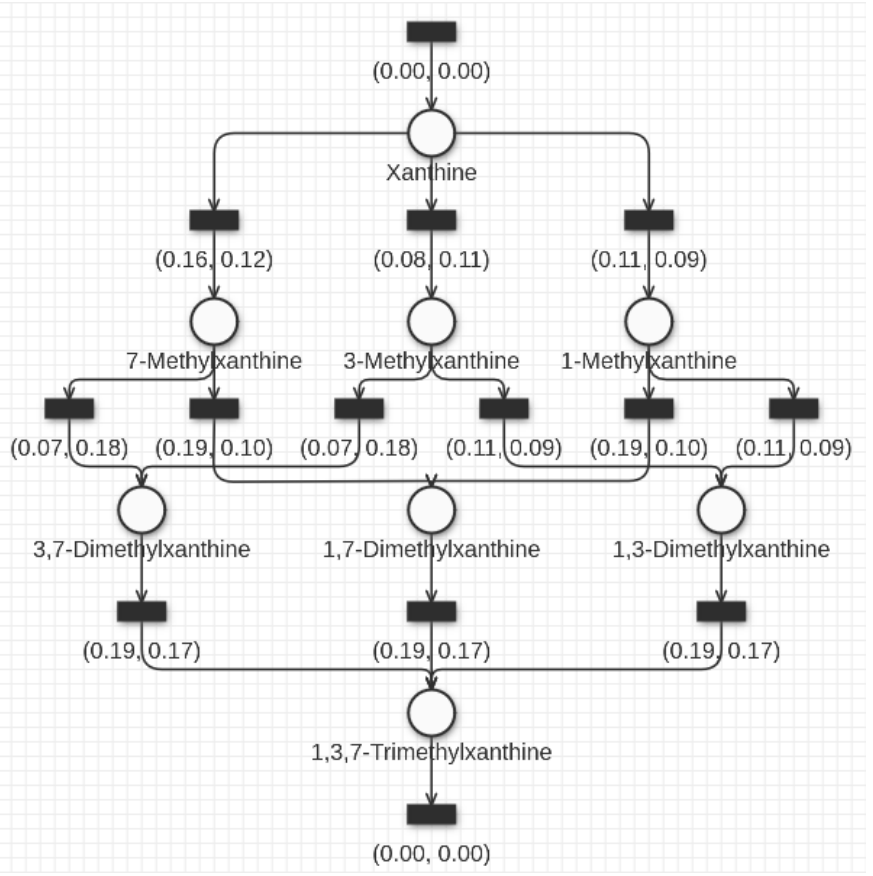
- max: $z_1 = \sum_v \sum_m n_{m,v} \times p_{m,v}$
- min: $z_2 = \sum_e b_e$
- min: $z_3 = \sum_e x_e$

Natural Caffeine Synthesis



NMR-Similarity

	7-Methylxanthine	3,7-Dimethylxanthine
Xanthine	0.08	0.14
1-Methylxanthine	0.11	0.09
3-Methylxanthine	0.08	0.11
7-Methylxanthine	0.16	0.12
1,3-Dimethylxanthine	0.11	0.09
1,7-Dimethylxanthine	0.19	0.10
3,7-Dimethylxanthine	0.07	0.18
1,3,7-Trimethylxanthine	0.19	0.17



ILP: Caffeine

- m = 2
  - 1: 7-Methylxanthine
  - 2: 3,7-Dimethylxanthine
- 1: → Xanthine, $x_1 = 1$
- 14: 1,3,7-Trimethylxanthine → , $x_{14} = 1$

Solution: Caffeine

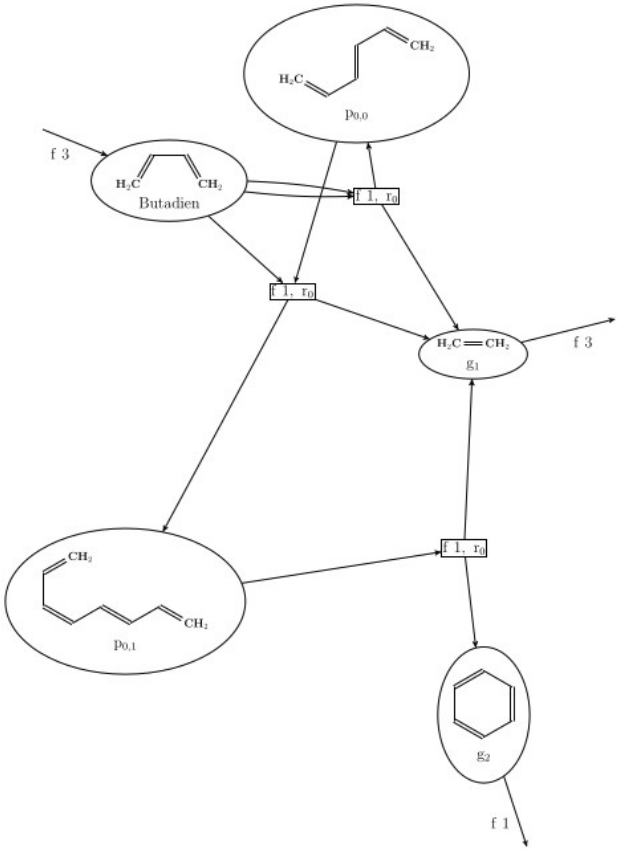
- 1: → Xanthine, $x_1 = 1$
- 4: Xanthine → 7-Methyxanthine, $x_4 = 1$
- 10: 7-Methlyxanthine → 3,7-Dimeythlxanthine, $x_{10} = 1$
- 13: 3,7-Dimeythlxanthine → 1,3,7-Trimethylxanthine, $x_{13} = 1$
- 14: 1,3,7-Trimethylxanthine → , $x_{14} = 1$
- $z = 1000\ (0.16 + 0.18) – (1/0.16 + 1/0.18 + 1/0.19) = 349.9$

Goal:

- Butadien+Butadien → Ethylen+Hexatrien
- Butadien+Butadien → g_1+$p_{0,0}$

- Butadien+Hexatrien → Ethylen+Octatetraen
- Butadien+$p_{0,0}$ → g_1+$p_{0,1}$

- Octatetraen → Ethylen+Benzene
- $p_{0,1}$ → g_1+g_2



ILP: Butadien

- m = 3
  - 1: Ethylene + Hexatriene
  - 2: Ethylene + Octatetraene
  - 3: Ethylene + Benzene
- 213: → Butadiene, $x_{213} = 3$

Molecules: Vertice likelihood

- [Butadien, Ethylene, Hexatriene, $p_{0,2}$, $p_{0,3}$, Octatetraene, $p_{0,4}$, $p_{0,5}$, $p_{0,6}$, $p_{0,7}$, $p_{0,8}$, $p_{0,9}$, Benzene, $p_{0,10}$, $p_{0,11}$, $p_{0,12}$, $p_{0,13}$, $p_{0,14}$, $p_{0,15}$, $p_{0,16}$]
- Normalized likelihoods:
  - [0.11, 0.18, 0.31, 0.0, 0.04, 0.21, 0.02, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.03, 0.0, 0.0, 0.06, 0.0, 0.03]
  - [0.11, 0.15, 0.2, 0.0, 0.04, 0.31, 0.02, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.03, 0.0, 0.0, 0.07, 0.0, 0.04]
  - [0.0, 0.17, 0.0, 0.0, 0.0, 0.0, 0.03, 0.0, 0.0, 0.01, 0.0, 0.16, 0.51, 0.09, 0.0, 0.0, 0.0, 0.0, 0.0, 0.03]

42: Octatetraene → Benzene + Ethylene

- Benzene: $vl(g_1)=\begin{pmatrix}0.00\\0.00\\0.51\end{pmatrix}$
- Ethylene: $vl(g_0)=\begin{pmatrix}0.18\\0.15\\0.17\end{pmatrix}$
- Average: $el(42)=\frac{1}{2}\left[\begin{pmatrix}0.00\\0.00\\0.51\end{pmatrix}+\begin{pmatrix}0.18\\0.15\\0.17\end{pmatrix}\right]=\begin{pmatrix}0.09\\0.08\\0.34\end{pmatrix}$
- Product: $el(42)=\begin{pmatrix}0.00\\0.00\\0.51\end{pmatrix}\times\begin{pmatrix}0.18\\0.15\\0.17\end{pmatrix}=\begin{pmatrix}0.00\\0.00\\0.09\end{pmatrix}$

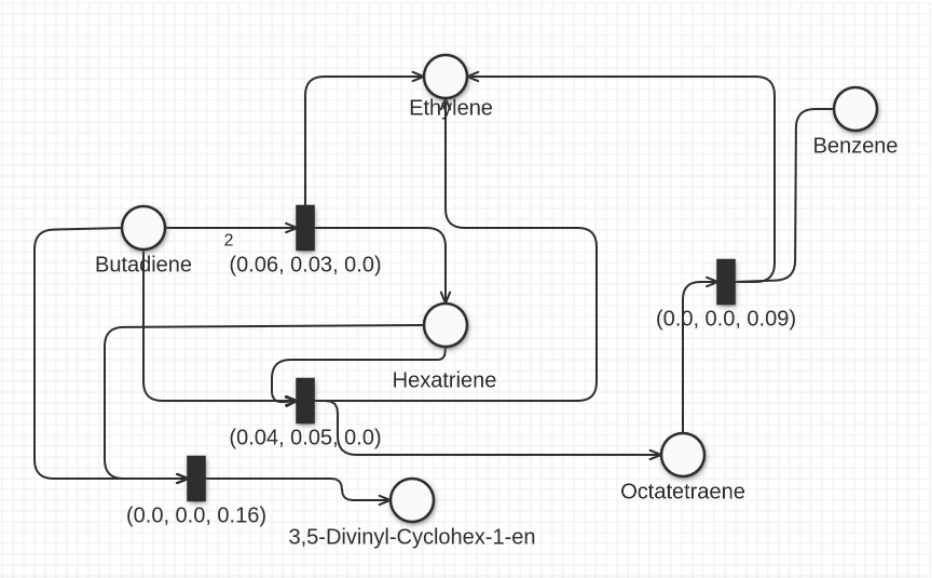
37: Butadien + Hexatriene → 3,5-Divinyl-Cyclohex-1-en

- 3,5-Divinyl-Cyclohex-1-en: $vl(p_{0,9}) = \begin{pmatrix} 0.00 \\ 0.00 \\ 0.16 \end{pmatrix}$
- Average: $el(37) = \frac{1}{1}\left[\begin{pmatrix} 0.00 \\ 0.00 \\ 0.16 \end{pmatrix}\right] = \begin{pmatrix} 0.00 \\ 0.00 \\ 0.16 \end{pmatrix}$
- Product: $el(37) = \begin{pmatrix} 0.00 \\ 0.00 \\ 0.16 \end{pmatrix} = \begin{pmatrix} 0.00 \\ 0.00 \\ 0.16 \end{pmatrix}$

41: Benzene →

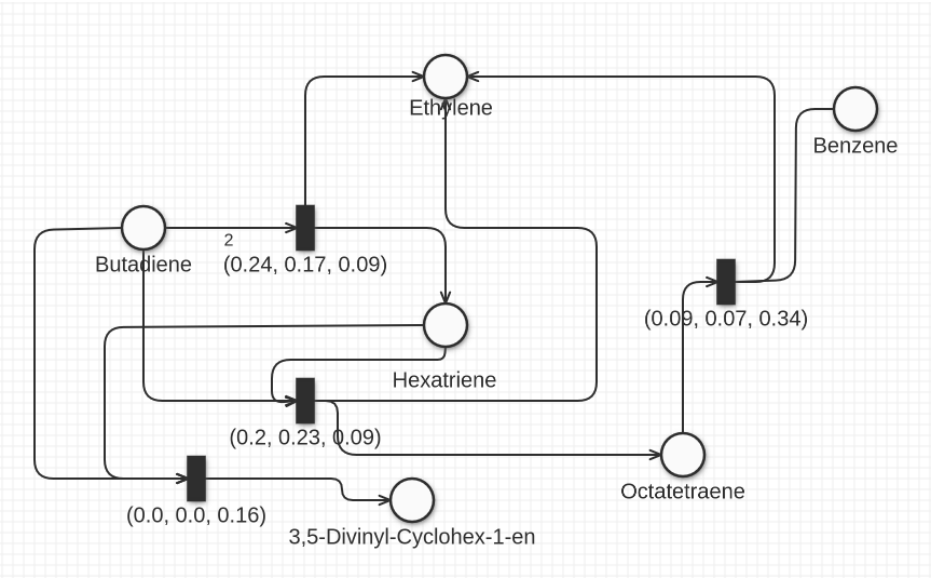
- Average: $el(41)=\begin{pmatrix}0.00\\0.00\\0.00\end{pmatrix}$
- Product: $el(41)=\begin{pmatrix}0.00\\0.00\\0.00\end{pmatrix}$

Edgelikelihood: Product



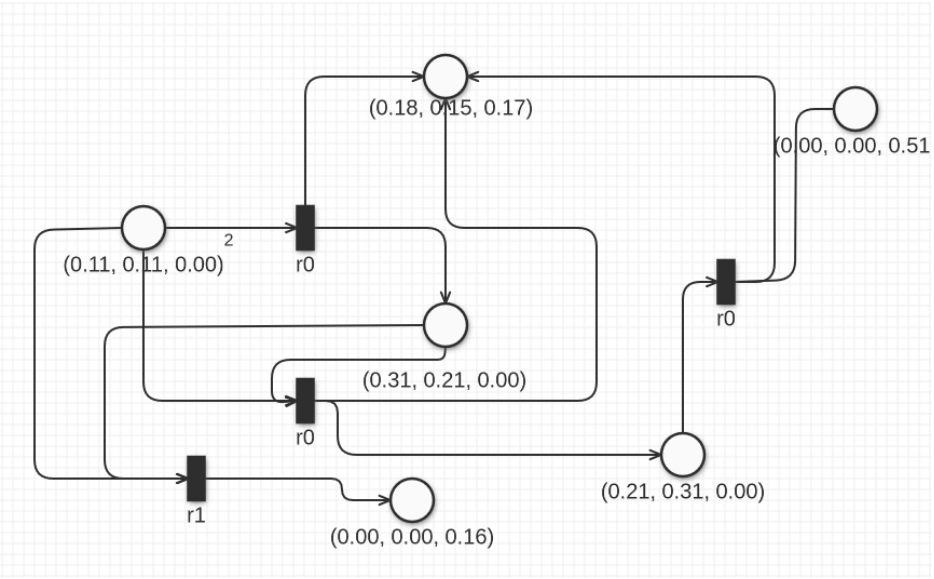
- 213: → Butadiene, $x_{213} = 3$
- 4: 2 Butadiene → Hexatriene + Ethylene, $x_4 = 1$, $p_{1,4} = 0.06$
- 37: Butadiene + Hexatriene → 3,5-Divinyl-Cyclohex-1-en, $x_{37} = 1$, $p_{3,37} = 0.16$
- 1: Ethylene → , $x_1 = 1$
- 36: 3,5-Divinyl-Cyclohex-1-en → , $x_{36} = 1$
- $z = 1000\ (0.06 + 0.16) – (1/0.06 + 1/0.16) = 197.08$

Edgelikelihood: Average



- 213: → Butadiene, $x_{213} = 3$
- 4: 2 Butadiene → Hexatriene + Ethylene, $x_4 = 1$, $p_{1,4} = 0.25$
- 23: Hexatriene + Butadiene → Octatetraene + Ethylene, $x_{23} = 1$, $p_{2,23} = 0.23$
- 42: Octatetraene → Benzene + Ethylene, $x_{42} = 1$, $p_{2,42} = 0.34$
- 1: Ethylene → , $x_1 = 3$
- 41: Benzene → , $x_{41} = 1$
- $z = 1000 * (0.24 + 0.23 + 0.34) – (1/0.24 + 1/0.23 + 1/0.34) = 798.54$

Species:



- 213: → Butadiene, $x_{213} = 3$
- 4: 2 Butadiene → Hexatriene + Ethylene, $x_4 = 1$, $p_{1,\text{Hexatriene}} = 0.31$
- 23: Hexatriene + Butadiene → Octatetraene + Ethylene, $x_{23} = 1$, $p_{2,\text{Octatetraene}} = 0.31$
- 42: Octatetraene → Benzene + Ethylene, $x_{42} = 1$, $p_{3,\text{Benzene}} = 0.51$
- 1: Ethylene → , $x_1 = 3$
- 41: Benzene → , $x_{41} = 1$
- $z_1 = 0.31 + 0.31 + 0.51$
- $z_2 = 3$
- $z_3 = 3$

Thesis Conclusion

- Differences characterized but abstracted
- Reconstruction from abstraction possible
- ILP Methods need consideration