Abstract

Acknowledgements

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1 Introduction

1.1 Background and Motivation

1.2 Research Objective

A valid theoretical framework for discrimination of the two types of constraints in statistical properties of the production data

First formulate the binning methods here. Because this will describe the hypothesis underlining my thesis.

Hypothesis is a theoretical/conceptual framework that one uses as a starting point for the investigation. It is not made-up and it is based in facts. A research hypothesis is a well defined object.

two methods are indicative of two fundamentally different constraints acting on the manufacturing process, technological constraints on the one hand, and constraints related to material flow and production capacity on the other.

1.3 Research Plan and Thesis Organization

2 Methodology

The initial step of this master thesis work was to quantify the characteristics of two hypothetical types of constraints in industrial production: technology-driven constraints and load-driven constraints. I am planning to achieve this in two steps: first, by developing an abstract theoretical framework (the so-called Operations Research Model) to understand better the connection between each type of constraint and the statistical patterns created by them; and second, by analyzing the statistical properties of association networks over Time in a large data set from steel manufacturing.

2.1 Operations Research Model

Introduce proposed concepts. The art form of using this OR-model is really to bring the OR model in same shape with the previous pipeline used in real-life events analysis. In a shape where the data format is same as in the manufacturing data and the logic of the analysis is the same as in the manufacturing data.

A brief introduction for FBA and Association Networks and explanation for generating a data structure with OR-modeling in combination of those. More detailed information to be given in the Backgroud Information Section, guiding the readers who have knowledge of FBA and Association Network concepts to the Concept Implementation Section.

Using linear programming, generating sets of synthetic data, which allows to compare the statistical characteristics of their association network with the ones created from the real-world data set from steel manufacturing.

Briefly explaning *in silico analyses* attemps /numerical experiments from the generated data.
This part is not completed.

2.1.1 Steel Manufacturing Data Analysis

Association Networks

Beyond a simple network graph representation of a historical production data, formation of association networks is an insightful graph-based framework combining the tool: association rules and complex networks as Merten et al. (2020) performed in their article [6]. The relevant pipeline considers sequentially revealed events of a data set and results a graph that unfolds the non-random co-occurrence of specific events among the complete set that took place consecutively in the production period.

Assume we have a manufacturing data set with historical order, D, consists of k sequences and n events with mass values and sequence id's included as given in Table 2.1.

Event_ID	Mass	Sequence_ID
1	280	1
2	250	1
3	890	2
4	850	2
5	650	2
6	745	2
7	795	2
8	150	3
⋮	⋮	⋮
n-4	940	k-1
n-3	540	k
n-2	520	k
n-1	630	k
n	610	k

Table 2.1: Arbitrarily Created Data Set D.

Examining the data set, one can say that the events with mass values: 890, 850, 650, 745 or 540, 520, 630, 610 are close to each other, thus they are produced together and likely occur in the same sequences among the complete data. In a further step, they can be labeled with a value interval (the so-called binning size) that is common for every mass value with tiny difference to each other. Binning generation for the events allows us to investigate them in a mass production manner. Alternative binning methods will be addressed in the following subsection.

One can hypothetically argue that above-mentioned information patterns are probably deliberate planning choices based on the related constraints acting on the manufacturing process performance. However, forming prevailing arguments like those is not a simple task for large and complicated data sets since such a real-life data set may consist of more than $300,000$ events likely have various amount of events aggregated randomly in its large sequence groups.

To distinguish random co-occurrences from meaningful ones in production sequences and assess the complexity of production patterns before we create our network graphs, we extract the association rule from the set of sequences. With the similar approach as Merten et al. (2020) applied [6], an association rule measure known as "Lift" was picked and calculated for every possible pairwise subsets of events that occurred in the same sequences. By having a natural threshold of Lift measure 1. Lift can be computed by the ratio of pair items joint probability divided by the multiplication of each item's marginal probability as

$$Lift(A \leftrightarrow B) = \frac{P(A,B)}{P(A) * P(B)}, \tag{6}$$

thus, in the case of $Lift(A \leftrightarrow B) > 1$, B occurs likely if A occurs whereas $Lift(A \leftrightarrow B) < 1$, B unlikely occurs if A occurs. Indication of random and non-random co-occurrences as 0 and 1 in an adjacency matrix will provide the data structure to form a network as shown in Fig. 2.1.

Events	1	2	3	...	n-1	n
1	0	1	0	...	0	0
2	1	0	0	...	0	0
3	0	0	0	...	0	0
⋮	⋮	⋮	⋮	⋱	⋮	⋮
n-1	0	0	0	...	0	1
n	0	0	0	...	1	0

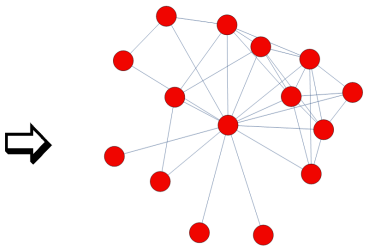


Figure 2.1: An Arbitrary Representation for Adjacency Matrix and Its Graph.

Binning Methods

What happens here is to bring the simulated data into a format that is compatible with my previous analysis of the real data.

Alternative binning methods for the production events underlie the developed hypothesis of this thesis work: Non-random features of the association networks derived from these two methods explained in the introduction part.

Considering the above-mentioned alternative binning tools, two distinguished network generation approach can be derived: Fixed Step Size network (FSSn),

it has graph nodes as binning members with equal bin sizes and Fixed Bucket Size network (FBSn), its nodes are binning members with equal event counts per bin. Forcing events to take place in the nodes with constant interval boundaries allows us to see how the aggregations take place within orders whereas defining a common bucket size for the network nodes results in arbitrary interval boundaries for each node but it makes possible to control their population.

D Labeled with FSS Bin Sizes

Event ID	Mass	FSS Bin Size	Sequence ID
1	280	200-299	1
2	250	200-299	1
3	890	800-899	2
4	850	800-899	2
⋮	⋮	⋮	⋮
n-2	520	500-599	k
n-1	630	600-699	k
n	610	600-699	k

D Labeled with FBS Bin Sizes

Event ID	Mass	FBS Bin Size	Sequence ID
1	280	200-599	1
2	250	200-599	1
3	890	630-899	2
4	850	630-899	2
⋮	⋮	⋮	⋮
n-2	520	200-599	k
n-1	630	630-899	k
n	610	600-629	k

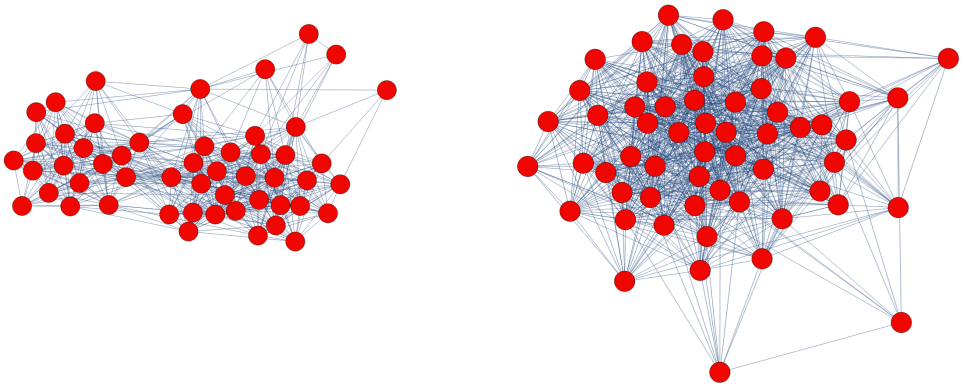


Figure 2.2: Graph Results For Two Different Network Approaches.

Network Metrics Analysis

Modularity Check

Different Types of Null Model

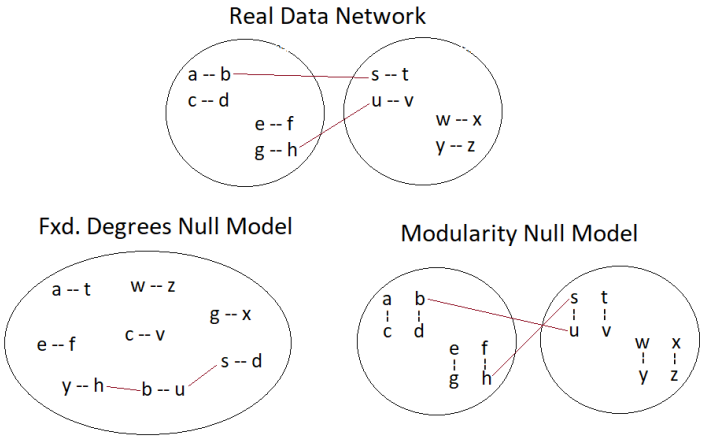


Figure 2.3: Formation of Different Null Models.

2.1.2 Flux Balance Analysis

The genome-scale integrated networks are necessary tools used by metabolic engineers on model generation, theoretical and computational analysis for microbial organisms since the network theory tools expand the feasible space for further analysis techniques in the field.

Introducing stoic. matrix. Explaining how the two graphs are formally obtained by manipulated the stoich. matrix, need to say the metabolite-centric network is $S*S^T$ and binarized while the reaction-centric network is S^T*S and binarized. Introduce the general idea of FBA is an optimization scheme in a steady-state solution space. Although the networks shown in Fig. 2.4 do not contain any information about directionality or effectiveness of the reactions to the system, the set of rules take place in networks can be represented in more detail and stoichiometrically by an m-by-r matrix formulation (the so-called Stoichiometric Matrix S), whereas its column elements represent reactions that play a role in the chemical transformation, and its row elements represent metabolites as

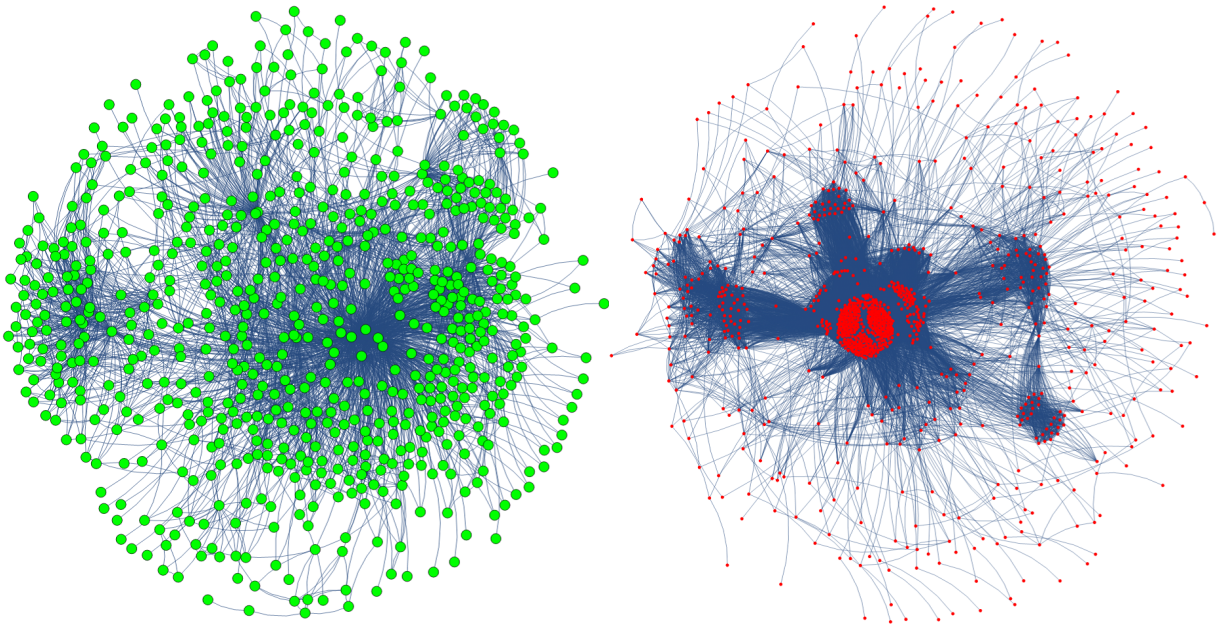
$$S = \begin{bmatrix} s_{11} & s_{12} & \dots & s_{1r} \\ s_{21} & s_{22} & \dots & s_{2r} \\ \vdots & \vdots & \ddots & \vdots \\ s_{m1} & s_{m2} & \dots & s_{mr} \end{bmatrix} = (s_{ij}) \in \mathbb{Z}^{mxr}, \tag{1}$$

Fig. 2.4 shows two differently constructed networks showing interactions between metabolites, intermediate or end products and metabolic reactions for a particular metabolism: Homo Sapien. In Fig. 2.4a the graph nodes stand for the metabolites, graph edges are the reactions, whereas in Fig. 2.4b the roles are reversed so that the metabolites are represented by the graph edges and the reactions are represented by the graph nodes.

Studying biological metabolic systems, generated models to achieve the cellular objectives like cell growth or ATP production bring the need of various tools to analyze reconstructed genome-scale networks. [1, 2]. One of the commonly used tools is Flux Balance Analysis (FBA). It is a constraint-based modeling approach to simulate microbial metabolisms and can be applied to biochemical-reaction networks containing the chemical transformations and flux exchanges in that particular network [3, 4].

while one can express the fluxes in a one-dimensional array (the so-called Flux Vector V) as

$$V = \begin{bmatrix} v_1 \\ v_2 \\ \vdots \\ v_r \end{bmatrix} = (v_i) \in \mathbb{R}. \tag{2}$$



(a) Metabolic-centric Network (b) Reaction-centric Network

Figure 2.4: Network Representations for Homo Sapiens Metabolic Model

V contains flux exchange values for the corresponding reactions in the system and gives information about the flux distribution; hence, those can be both positive and negative real numbers. Definition of a mass balance ($S.V = 0$) constraint in the FBA enables us to analyze the metabolic network operations in a steady-state [3, 4].

$$S.V = \begin{bmatrix} s_{11}v_1 + s_{12}v_2 + \cdots + s_{1r}v_r \\ s_{21}v_1 + s_{22}v_2 + \cdots + s_{2r}v_r \\ \vdots \\ s_{m1}v_1 + s_{m2}v_2 + \cdots + s_{mr}v_r \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix}. \tag{3}$$

The higher amount of metabolite consideration in the set of rules, S, in other words, the larger matrix size by its rows amount means the more complex organization structure taken into account while preserving the steady-state in the whole system.

More than one steady-state solution might be present since it is impossible to identify all constraints in a cellular system [3]. Therefore, an optimization approach can be formulated to identify reaction network steady-states that maximize the biomass [3, 4] or control the production of specific metabolites [5] within a defined objective function under the consideration of the system constraints. According to Price et al. (2004), there are three main purposes to generate objective functions: to discover allowable characteristic properties in the

genome-scale network reconstruction; to mimic probable physiological functions like biomass or ATP production to be able to determine likely physiological states; and lastly, to design a genetic variant or sub-type to obtain a desired particular product [4].

The objective function can be thought as a production plan that gives an idea about the diversity of products that the relevant system can produce, and one can express its coefficients in a one-dimensional array as

$$O = \begin{bmatrix} o_1 & o_2 & \dots & o_r \end{bmatrix} = (o_i) \in \mathbb{R}. \tag{4}$$

As given in Eq.(5), the Objective Function, Z, rules the maximized output based on its non-zero coefficients, which are the decisive ones for the flux elements of V to be considered.

$$Z = O.V = (o_1 v_1 + o_2 v_2 + \cdots + o_r v_r) \in \mathbb{R}_{\geq 0}. \tag{5}$$

Stoichiometry and mass-balance are the constraints introduced so far in Eq.(1) and Eq.(3). In addition to those, upper and lower bounds are introduced for particular fluxes in V during the optimization process such that those are used in the reactions for uptake and secretion of any organic metabolite which are the nutrients are transported to the inside and the products are exported to the outside of the metabolic network. The rest of the fluxes in V are used in the exchange reactions, namely the intermediate reactions in the network. The constraints are decisive on the reactions for uptake and secretion whereas no limitation is considered in the exchange reactions. Quantification of imported nutrients and exported outputs (the so-called Resources and Wastes) by constraining them with upper and lower bounds, to fulfill a single objective function goal, might play a significant role in the whole optimization process.

The above-explained optimization process is a linear programming problem since the mass balance (Eq.(3)), the Objective Function (Eq.(5)), and the upper & lower bounds for fluxes are formulated by linear equations and the linear optimization result maximizes the structured objective function in the form of a flux distribution [3, 4]. Since each term in Eq.(5) is a produced biomass expression for the fluxes, the summation of those terms will give the overall growth of the system for a single network state.

Fluxes for Uptake and Secrete Reactions

Let

$$V^* = (v_1^*, v_2^*, \dots, v_x^*) = (a_i \leq v_i^* \leq b_i) \in V \tag{7}$$

is a set of fluxes picked from V to be limited with the bounds: a_i and b_i which are used in the reactions for uptake and secretion as previously introduced.

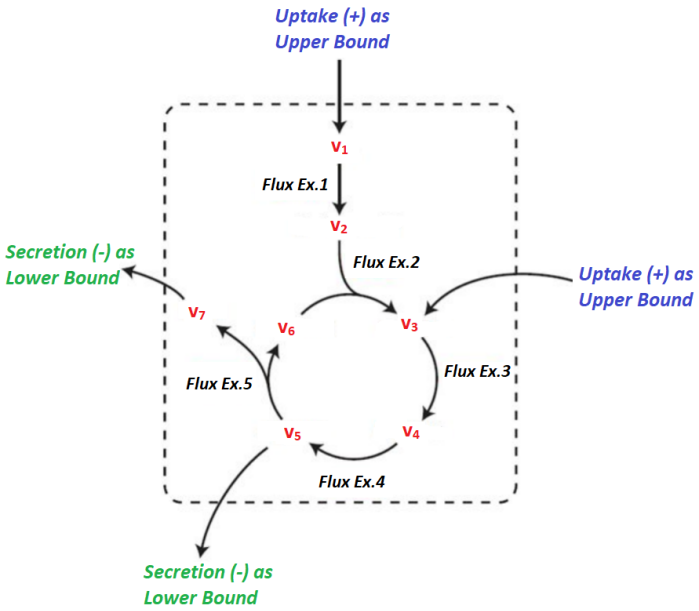


Figure 2.5: A Simplified Reaction-centric Network Sketch Shows The Reactions for Exchange, Uptake and Secretion.

Upper and Lower Bounds

Objective Functions

2.2 Applications and Results of the Developed Concepts

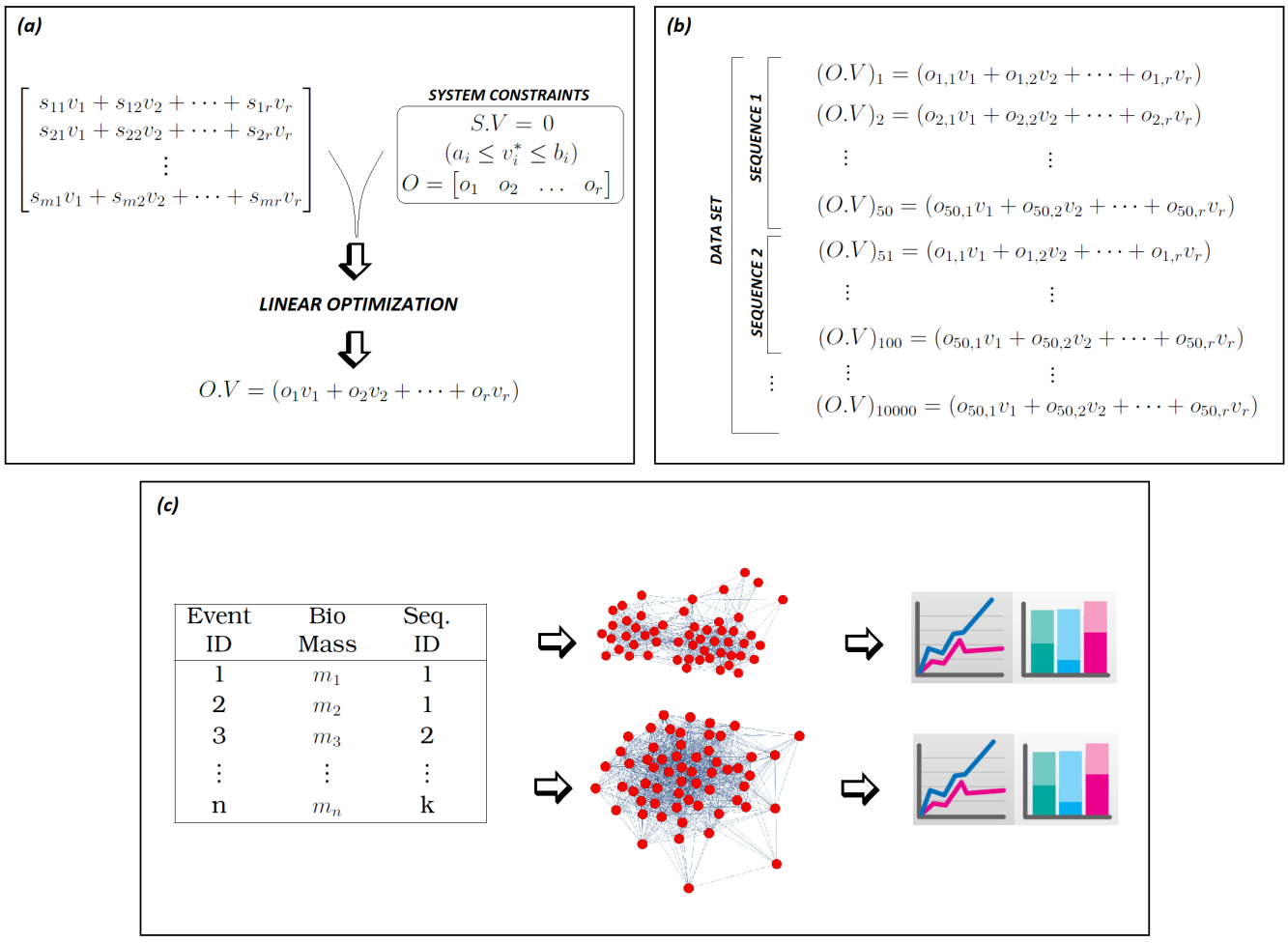


Figure 2.6: Complete Framework Sketch.

3 Conclusion And Outlook

3.1 Thesis Contribution

3.2 Outlook

4 Bibliography

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5 Supplements