THEORETICAL AND EXPERIMENTAL SELF-ASSEMBLY

by

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A Dissertation Presented to the
FACULTY OF THE GRADUATE SCHOOL
UNIVERSITY OF SOUTHERN CALIFORNIA
In Partial Fulfillment of the
Requirements for the Degree
DOCTOR OF PHILOSOPHY
(COMPUTER SCIENCE)

December 2008

Dedication

To my four grandparents. They made an intrepid journey to a foreign land, and paved the way for my own.

Acknowledgements

In this place I must record what cannot be expressed in quotations or references.
—Felix Klein

It is my good fortune to have Len Adleman for my dissertation advisor. He has been an unfailing source of inspiration and encouragement to me. In his conduct, I have found an ideal to aspire for. He has given generously of his time and his ideas. It is difficult for me to imagine a better advisor.

Ming-Deh Huang has been, at various times, my teacher, collaborator, mentor, and champion. His insightful comments have time and again opened up a whole new avenue of inquiry for me. I am thankful for having received the benefit of his sagacity and sanity.

From Nickolas Chelyapov, I have learnt much of what I know about how to perform experiments. I thank him for this, as well as for imbuing me with spirit, and fortifying me with much food and drink.

Erik Winfree has been kind enough to put a hand on my shoulder in difficult times, and urge me on. Interactions with him, and with people I have met through him, have played a significant role in my work.

Paul Rothemund has been like an elder brother. His own research feats have been cause for inspiration. I thank him for his constant support.

I thank Todd Brun, David Kempe, Robert Guralnick, Francis Bonahon, Thomas Geisser, Jason Fulman and Ko Honda for wonderful lectures. I am grateful for the opportunity to associate with these men of learning.

Dustin Reishus, Bilal Shaw, Pablo Moisset and Yuriy Brun have been my extended research family at USC. I thank them for their support. Dustin and Bilal helped me pick up the ropes of DNA self-assembly, and I owe them a debt of gratitude for that.

I thank Amrita Rajagopalan, Praveen Kumar, Joyita Dutta, Aniket Aga, Aditi Sarangi, Anita Iyer, Sachin Telang, Bhupesh Bansal, Ramakrishnan Iyer, Kaushik Roy Choudhury, Aditya Raghavan, Srihari Ramanathan, Sangeetha Somayajula, Parthiban Balasubramanian, Faizal Sainal, Diana Pinto, Sweta Anantharaman-Nair, Nirali Goradia, Janaki Iyer, Akshay Kedia, Anup Pancholi, Pankaj Golani, Gaurav Agarwal, Anirban Das, Arnab Kundu, Vidhya Navalpakkam, Debojyoti Dutta, Subashini Krishnamurthy, Badri Padukasahasram, Simran Agarwal, Iftikhar Burhanuddin, Nilesh Mishra, Vaibhav Bora and Susmita Chatterjee. They have been wonderful friends. I am grateful for their support through times of sorrow and joy, despair and aspiration. I have learnt much from their philosophies, their lives and their choices.

I thank IIT Kharagpur, and all my professors and friends there. I have fond memories of several teachers, at Our Lady of Remedy High School and other places, and thank them all for their love and dedication.

I thank my grandparents, uncles, aunts, cousins, nieces and nephews for so freely bestowing their love on me. I have learnt much from my brother Nikhil, and thank him for that. Last, I thank Amma and Appa, for more than I can express with words.

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Abstract

This thesis reports two contributions that have been prompted by a quest to better understand self-assembly.

Motivated by theoretical investigations of self-assembly, Adleman, Huang, Moisset, Reishus and I have investigated the mathematics of the "law of mass action." We believe that the law of mass action is of intrinsic mathematical interest, and may have deep connections to research in non-linear differential equations as well as algebraic geometry. One of our goals is to make the law of mass action available beyond chemistry. This has led us to a dynamical theory of sets of binomials over the complex numbers. A second goal is to present a mathematical consolidation of mass action chemistry. We have provided precise definitions, elucidated what can now be proved, and indicated what is only conjectured. This aspect of our work addresses the mathematical foundations of mass action chemistry.

My second contribution is to the emerging field of DNA self-assembly. It has been suggested that DNA self-assembly may lead to the manufacture of novel materials and computational devices. Chelyapov, Brun, Reishus, Shaw, Adleman and I have reported DNA complexes in the shape of triangles and in the pattern of hexagonal, planar tilings. Nikhil Gopalkrishnan, Adleman and I have reported DNA complexes in the shape of

cylinders and Möbius strips. The prevalent practice in the DNA self-assembly community appears to be to model DNA double helices as rigid cylinders and DNA lattices as rigid sheets. In contrast, our nanostructures were designed to avail of residual flexibilities in DNA double helices and DNA lattices.

Chapter 1

Introduction

> *Push one* [a sea-sponge] *through a fine-mesh sieve and its cells will separate from one another, turning clear aquarium water into a thick, cloudy liquid, like pea soup. Wait a few hours, however, and the cells will gradually find one another, stick together, and reassemble themselves into a whole sponge... In fact, the disaggregated cells of two different sponge species can be mixed, and the cells will sort themselves out and reassemble only with their own kind, re-creating sponges of the original two species.*
> —Boyce Rensberger, in the book *Life Itself*.

According to Adleman [2], "Self-assembly is the ubiquitous process by which objects autonomously assemble into complexes. Nature provides many examples: Atoms react to form molecules. Molecules react to form crystals and supramolecules. Cells sometimes coalesce to form organisms. Even heavenly bodies self-assemble into astronomical systems. It has been suggested that self-assembly will ultimately become an important technology, enabling the fabrication of great quantities of small objects such as computer circuits. ... Despite its importance, self-assembly is poorly understood." I have attempted to better understand self-assembly, by both theoretical and experimental investigations.

Our theoretical study of self-assembly is a continuation of the rich intellectual tradition of statistical mechanics, whose foundations were laid by Maxwell, Boltzmann and Gibbs in the late 19^{th} century. In more recent times, it has become apparent, thanks to the work of several researchers — von Neumann [33], Wang [34], Bennett [5], Wolfram [37], Adleman [1], Winfree [36], etc. — that self-assembly has connections with computer science and computational complexity theory. Hopefully, a study of self-assembly will reveal connections between statistical mechanics and computer science.

Historically, many phenomena in chemistry that we now recognize as self-assembly have been investigated with the aid of systems of chemical reactions. This suggests one approach to a theory of self-assembly lies through the study of systems of chemical reactions. Chapter 2 contains a manuscript prepared in collaboration with Adleman, Huang, Moisset and Reishus that makes a beginning along this direction. Our central assumption is the "law of mass action." Given a system of chemical reactions, this law describes how concentrations of chemical species evolve through time. We have extended this law beyond chemical reactions, so that it can apply to arbitrary sets of binomials. This allows us to ask the question, "When does a set of binomials represent a system of chemical reactions?" We propose mathematical abstractions of the law of conservation of energy, and of the atomic hypothesis. When we restrict our sets of binomials to "chemistry-like" systems — those that satisfy our version of the law of conservation of energy and the atomic hypothesis — the theory yields analogues to concepts like energy, entropy, and convergence to equilibrium. This work is discussed in greater detail in Section 2.1.

My experimental investigations of self-assembly have been carried out using molecules of deoxyribonucleic acid (DNA). Since DNA self-assembly is a relatively young discipline, I will outline the main ideas for readers unfamiliar with the area.

Seeman [29] appears to have been the first to investigate the self-assembly of DNA molecules. He availed of two properties of DNA that make it well-suited for self-assembly.

The first property is that DNA molecules can encode information. Each molecule of DNA is a polymer, i.e., a chain of similar units. Four different types of units are allowed in a DNA molecule. These are derived from the four "bases": adenine (denoted by the letter A), thymine (T), guanine (G), and cytosine (C). Thus, abstractly, each molecule of DNA can be thought of as a string over the alphabet $\{\mathrm{A}, \mathrm{T}, \mathrm{G}, \mathrm{C}\}$. Just as strings of 0's and 1's encode information in computers, strings over this alphabet of four characters can be made to encode information. A nuance is that because DNA molecules have a directionality, distinct strings encode distinct DNA molecules. Thus, GAAT and TAAG represent two different DNA molecules.

Remarkably, given a string over the alphabet $\{\mathrm{A}, \mathrm{T}, \mathrm{G}, \mathrm{C}\}$, it is possible to synthesize, with high purity and without much cost, billions of DNA molecules whose sequence of bases is that string. Of course, this is only true within certain technological constraints — the sequence can not be too long, some sequences are very hard to synthesize, etc. — but it is still very useful. The work of many researchers, notably Khurana, Letzinger, Caruthers and Mullis, has made this tour de force possible, and given us an opportunity to synthesize DNA molecules "programmed" with the information we wish.

The second property that makes DNA well-suited for self-assembly is that, under appropriate conditions, certain pairs of DNA molecules can wrap around each other via hydrogen-bond interactions to form a bimolecular complex in the shape of a double-helix. Importantly, DNA molecules are very selective about what other DNA molecules they will bind with. As a rule of thumb, the base A prefers to pair up with the base T, and the base G prefers to pair up with the base C. (Beware that this rule of thumb is not always accurate. For example, the stacking energies between adjacent base pairs play a crucial role. It is not a trivial computational problem, when given sequences for two DNA molecules, to determine the resulting tertiary, or even secondary, structures. Much of the art of experimental DNA self-assembly lies in avoiding exceptional conditions where such rules of thumb fail.)

So, you might think that the DNA molecule ATTC would bind with the DNA molecule TAAG. However, this is not quite right. The sequence needs to be reversed. So ATTC actually binds to GAAT. This comes about because DNA molecules prefer to bind in such a manner that the two binding molecules are aligned with opposing directionality. Sequences that are related in this manner are called "complementary" sequences.

Adleman [1] exploited these two properties of DNA, as well as the "polymerase chain reaction" — a technique to exponentially amplify small quantities of DNA — to show that interactions between DNA molecules could be used to solve computational problems. Winfree [36] clarified the relationship between DNA self-assembly and computation, and showed how computational ideas could be brought to the service of DNA self-assembly. Since then, researchers in DNA self-assembly have formed Sierpinski fractals [27], DNA octahedra [31], etc., and investigated self-replication [28], copying and counting [4], etc. Especially remarkable is Rothemund's invention of DNA origami [26], a method to create arbitrary shapes and patterns in two dimensions.

Chapter 3 contains my experimental contributions to DNA self-assembly. The first result concerns a hexagonal tiling. The repeating individual units of this tiling are triangular complexes of DNA molecules. This work is in collaboration with Nickolas Chelyapov, Yuriy Brun, Dustin Reishus, Bilal Shaw and Leonard Adleman. In Section 3.1, I present a jointly-authored article [8] describing this work. The second result concerns the self-assembly of cylinders and Möbius strips, by a method that extends Rothemund's method of DNA origami. This is joint work with Nikhil Gopalkrishnan and Leonard Adleman, and is presented in Section 3.2

Chapter 2

On the Mathematics of the Law of Mass Action

Good mathematicians see analogies between theorems or theories, the very best ones see analogies between analogies.
—Stefan Banach, as quoted by S. Ulam.

I have been working with Len Adleman, Ming-Deh Huang, Pablo Moisset and Dustin Reishus on a theory of self-assembly related to the law of mass action in chemistry. The rest of this chapter contains a manuscript that we have jointly prepared.

Abstract

In 1864, Waage and Guldberg formulated the "law of mass action." Since that time, chemists, chemical engineers, physicists and mathematicians have amassed a great deal of knowledge on the topic. In our view, sufficient understanding has been acquired to warrant a formal mathematical consolidation. A major goal of this consolidation is to solidify the mathematical foundations of mass action chemistry — to provide precise definitions, elucidate what can now be proved, and indicate what is only conjectured. In addition, we believe that the law of mass action is of intrinsic mathematical interest

and should be made available in a form that might transcend its application to chemistry alone. We are led to a dynamical theory of sets of binomials over the complex numbers.

2.1 Introduction

The study of mass action kinetics dates back at least to 1864, when Waage and Guldberg [15] formulated the "law of mass action." Since that time, a great deal of knowledge on the topic has been amassed in the form of empirical facts, physical theories and mathematical theorems by chemists, chemical engineers, physicists and mathematicians. In recent years, Horn and Jackson [17], and Feinberg [12] have made significant mathematical contributions, and these have guided our work.

It is our view that a critical mass of knowledge has been obtained, sufficient to warrant a formal mathematical consolidation. A major goal of this consolidation is to solidify the mathematical foundations of this aspect of chemistry — to provide precise definitions, elucidate what can now be proved, and indicate what is only conjectured. In addition, we believe that the law of mass action is of intrinsic mathematical interest and should be made available in a form that might transcend their application to chemistry alone.

To make the law of mass action available for consideration by researchers in areas other than chemistry, we present mass action kinetics in a new form, which we call event-systems. Our formulation begins with the observation that systems of chemical reactions can be represented by sets of binomials. This gives us an opportunity to extend the law of mass action to arbitrary sets of binomials. Once this extension is made, there is no reason to restrict ourselves to binomials with real coefficients. Hence, we are led to a dynamical theory of sets of binomials over the complex numbers. Possible mathematical applications of this theory include:

1. Binomials are objects of intrinsic mathematical interest [11]. For example, they occur in the study of toric varieties, and hence in string theory. With each set of binomials over the complex numbers, we associate a corresponding system of differential equations. Ideally, this dynamical viewpoint will help advance the theory of binomials, and enhance our understanding of their associated algebraic sets.

2. When we extend the study of the law of mass action to sets of binomials over the complex numbers, we can consider reactions that involve complex rates, complex concentrations, and move through complex time. Extending to the complex numbers gives us direct access to the powerful theorems of complex analysis. Though this clearly transcends conventional chemistry, it may have applications in pure mathematics.

   For example, in ongoing work, we seek to exploit an analogy between number theory and chemistry, where atoms are to molecules as primes are to numbers. We associate a distinct species with each natural number. Then each multiplication rule $m \times n = mn$ is encoded by a reaction where the species corresponding to the number m reacts with the species corresponding to the number n to form the species corresponding to the number mn. With an appropriate choice of specific rates of reactions the resulting event-system has the property that the sum of equilibrium concentrations of all species at complex temperature s is the value of the Riemann zeta function at

s. We hope to pursue this approach to study questions related to the distribution of the primes.

3. Systems of linear differential equations are well understood. In contrast, systems of ordinary non-linear differential equations can be notoriously intractable. Differential equations that arise from event-systems lie somewhere in between — more structured than arbitrary non-linear differential equations, but more challenging than linear differential equations. As such, they appear to be an important new class for consideration in the theory of ordinary differential equations.

In addition to their use in mathematics, event-systems provide a vehicle by which ideas in algebraic geometry may be made readily available to the study of mass action kinetics. As such, they may help solidify the foundations of this aspect of chemistry. We expand on this in Section 2.7.

Part of our motivation for this research comes from the emerging field of nanotechnology. To quote from [2], "Self-assembly is the ubiquitous process by which objects autonomously assemble into complexes. Nature provides many examples: Atoms react to form molecules. Molecules react to form crystals and supramolecules. Cells sometimes coalesce to form organisms. Even heavenly bodies self-assemble into astronomical systems. It has been suggested that self-assembly will ultimately become an important technology, enabling the fabrication of great quantities of small objects such as computer circuits… Despite its importance, self-assembly is poorly understood." Hopefully, the theory of event-systems is a step towards understanding this important process.

The paper is organized as follows:

In Section 2.2, we present the basic mathematical notations and definitions for the study of event-systems.

In Section 2.3, and all of the sections that follow, we restrict to finite event-systems. Theorem 2.3.3 demonstrates that the stoichiometric coefficients give rise to flow-invariant affine subspaces — "conservation classes."

In Section 2.4, and all of the sections that follow, we restrict to "physical event-systems." Though we have defined event-systems over the complex numbers, in this paper we focus on consolidating results from the mass action kinetics of reversible chemical reactions. Physical event-systems capture the idea that the specific rates of chemical reactions are always positive real numbers. The main result of this section is Theorem 2.4.5, which demonstrates that for physical event-systems, if initially all concentrations are non-negative, then they stay non-negative for all future real times so long as the solution exists. Further, the concentration of every species whose initial concentration is positive, stays positive.

In Section 2.5, and all the sections that follow, we restrict to "natural event-systems." Natural event-systems capture the concept of detailed balance from chemistry. In Theorem 2.5.1, we give four equivalent characterizations of natural event-systems; in particular, we show that natural event-systems are precisely those physical event-systems that have no "energy cycles." In Theorem 2.5.6, following Horn and Jackson [17], we show that natural event-systems have associated Lyapunov functions. This theorem is reminiscent of the second law of thermodynamics. The main result of this section is Theorem 2.5.15, which establishes that for natural event-systems, given non-negative initial conditions:

1. Solutions exist for all forward real times.

2. Solutions are uniformly bounded in forward real time.

3. All positive equilibria satisfy detailed balance.

4. Every conservation class containing a positive point also contains exactly one positive equilibrium point.

5. Every positive equilibrium point is asymptotically stable relative to its conservation class.

For systems of reversible reactions that satisfy detailed balance, must concentrations approach equilibrium? We believe this to be the case, but are unable to prove it. In 1972, an incorrect proof was offered [17, Lemma 4C]. This proof was retracted in 1974 [16]. To the best of our knowledge, this question in mass action kinetics remains unresolved [32, p. 10]. We pose it formally in Open Problem 1, and consider it the fundamental open question in the field.

In Section 2.6, we introduce the notion of "atomic event-systems." As the name suggests, this is an attempt to capture mathematically the atomic hypothesis that all species are composed of atoms. The main theorem of this section is Theorem 2.6.1, which establishes that for natural, atomic event-systems, solutions with positive initial conditions asymptotically approach positive equilibria. Hence, Open Problem 1 is resolved in the affirmative for this restricted class of event-systems.

2.2 Basic Definitions and Notation

Before formally defining event-systems, we give a very brief, informal introduction to chemical reactions. All reactions are assumed to take place at constant temperature in a well-stirred vessel of constant volume.

Consider

$$A + 2B \underset{\tau}{\overset{\sigma}{\rightleftharpoons}} C.$$

This chemical equation concerns the reacting species A, B and C. In the forward direction, one mole of A combines with two moles of B to form one mole of C. The symbol "σ" represents a real number greater than zero. It denotes, in appropriate units, the rate of the forward reaction when the reaction vessel contains one mole of A and one mole of B. It is called the specific rate of the forward reaction. In the reverse direction, one mole of C decomposes to form one mole of A and two moles of B. The symbol "τ" represents the specific rate of the reverse reaction. Chemists typically determine specific rates empirically. Though irreversible reactions (those with $\sigma = 0$ or $\tau = 0$) have been studied, they will not be considered in this paper.

Inspired by the law of mass action, we introduce a multiplicative notation for chemical reactions, as an alternative to the chemical equation notation. In our notation, each chemical reaction is represented by a binomial. Consider the following examples. On the left are chemical equations. On the right are the corresponding binomials.

$$\begin{array}{rcl}
X_2 \underset{1/2}{\overset{1/3}{\rightleftharpoons}} X_1 & \to & \frac{1}{3}X_2 - \frac{1}{2}X_1 \\
X_3 \underset{1/2}{\overset{1/3}{\rightleftharpoons}} X_1 + X_2 & \to & \frac{1}{3}X_3 - \frac{1}{2}X_1X_2 \\
2X_1 + 3X_6 \underset{\tau}{\overset{\sigma}{\rightleftharpoons}} 3X_1 + 2X_2 & \to & \sigma X_1^2X_6^3 - \tau X_1^3X_2^2
\end{array}$$

Our notation leads us to view every set of binomials over an arbitrary field $\mathbb{F}$ as a formal system of reversible reactions with specific rates in $\mathbb{F} \setminus \{0\}$. For our present purposes, we will restrict our attention to binomials over the complex numbers. With this in mind, we now define our notion of event-system.

Notation 1. Let $\mathbb{C}_\infty = \bigcup_{n=1}^{\infty} \mathbb{C}[X_1, X_2, \cdots, X_n]$. A monic monomial of $\mathbb{C}_\infty$ is a product of the form $\prod_{i=1}^{\infty} X_i^{e_i}$ where the e_i are non-negative integers all but finitely many of which are zero. We will write $\mathbb{M}_\infty$ to denote the set of all monic monomials of $\mathbb{C}_\infty$. More generally, if $S \subset \{X_1, X_2, \cdots\}$, we let $\mathbb{C}[S]$ be the ring of polynomials with indeterminants in S and we let $\mathbb{M}_S = \mathbb{M}_\infty \cap \mathbb{C}[S]$ (i.e. the monic monomials in $\mathbb{C}[S]$).

If $n \in \mathbb{Z}_{>0}$, $p \in \mathbb{C}[X_1, X_2, \cdots, X_n]$, and $\boldsymbol{a} = \langle a_1, a_2, \cdots, a_n\rangle \in \mathbb{C}^n$ then, as is usual, we will let $p(\boldsymbol{a})$ denote the value of p on argument $\boldsymbol{a}$.

Given two monic monomials $M = \prod_{i=1}^{\infty} X_i^{e_i}$ and $N = \prod_{i=1}^{\infty} X_i^{f_i}$ from $\mathbb{M}_\infty$, we will say M *precedes* N (and we will write $M \prec N$) iff $M \neq N$ and for the least i such that $e_i \neq f_i$, $e_i < f_i$.

It follows that 1 is a monic monomial of $\mathbb{C}_\infty$ and that each element of $\mathbb{C}_\infty$ is a $\mathbb{C}$-linear combination of finitely many monic monomials. We will be particularly concerned with the set of binomials $\mathbb{B}_\infty = \{\sigma M + \tau N \mid \sigma, \tau \in \mathbb{C} \setminus \{0\}$ and M, N are distinct monic monomials of $\mathbb{C}_\infty\}$.

Definition 2.2.1 (Event-system)**.** An event-system $\mathcal{E}$ is a nonempty subset of $\mathbb{B}_\infty$.

If $\mathcal{E}$ is an event-system, its elements will be called "$\mathcal{E}$-events" or just "events." Note that if $\sigma M + \tau N$ is an event then $M \neq N$.

Our map from chemical equations to events is as follows. A chemical equation

$$\sum_i a_i X_i \underset{\tau}{\overset{\sigma}{\rightleftharpoons}} \sum_j b_j X_j \quad \text{goes to:}$$

$$\begin{array}{lll} & 1. & \sigma \prod_i X_i^{a_i} - \tau \prod_j X_j^{b_j} \ \text{ if } \ \prod_i X_i^{a_i} \prec \prod_j X_j^{b_j} \\ \text{or} & 2. & \tau \prod_j X_j^{b_j} - \sigma \prod_i X_i^{a_i} \ \text{ if } \ \prod_j X_j^{b_j} \prec \prod_i X_i^{a_i} \end{array}$$

For example:

$$
\begin{array}{rcl}
X_1 \underset{1/3}{\overset{1/2}{\rightleftharpoons}} X_2 & \rightarrow & \frac{1}{3}X_2 - \frac{1}{2}X_1 \quad \text{(because } X_2 \prec X_1\text{)} \\
X_2 \underset{1/2}{\overset{1/3}{\rightleftharpoons}} X_1 & \rightarrow & \frac{1}{3}X_2 - \frac{1}{2}X_1 \\
X_1 \underset{-1/3}{\overset{-1/2}{\rightleftharpoons}} X_2 & \rightarrow & -\frac{1}{3}X_2 + \frac{1}{2}X_1 \\
X_1 \underset{1/3}{\overset{-1/2}{\rightleftharpoons}} X_2 & \rightarrow & \frac{1}{3}X_2 + \frac{1}{2}X_1 \\
X_1 + X_2 \underset{1/3}{\overset{1/2}{\rightleftharpoons}} X_3 & \rightarrow & \frac{1}{3}X_3 - \frac{1}{2}X_1X_2 \\
3X_1 + 2X_2 \underset{\tau}{\overset{\sigma}{\rightleftharpoons}} 2X_1 + 3X_6 & \rightarrow & \tau X_1^2X_6^3 - \sigma X_1^3X_2^2
\end{array}
$$

Note that our order of monomials is arbitrary. Any linear order would do. The order is necessary to achieve a one-to-one map from chemical reactions to events.

Our definition of event-systems allows for an infinite number of reactions, and an infinite number of reacting species. Indeed, polymerization reactions are commonplace in nature and, in principle, they are capable of creating arbitrarily long polymers (for example, DNA molecules).

The next definition introduces the notion of systems of reactions for which the number of reacting species is finite.

Definition 2.2.2 (Finite-dimensional event-system)**.** An event-system $\mathcal{E}$ is *finite-dimensional* iff there exists an $n \in \mathbb{Z}_{>0}$ such that $\mathcal{E} \subset \mathbb{C}[X_1, X_2, \cdots, X_n]$.

Definition 2.2.3 (Dimension of event-systems)**.** Let $\mathcal{E}$ be a finite-dimensional event-system. Then the least n such that $\mathcal{E} \subset \mathbb{C}[X_1, X_2, \cdots, X_n]$ is the *dimension* of $\mathcal{E}$.

Definition 2.2.4 (Physical event, Physical event-system)**.** A binomial $e \in \mathbb{B}_\infty$ is a *physical event* iff there exist $\sigma, \tau \in \mathbb{R}_{>0}$ and $M, N \in \mathbb{M}_\infty$ such that $M \prec N$ and $e = \sigma M - \tau N$. An event-system $\mathcal{E}$ is *physical* iff each $e \in \mathcal{E}$ is physical.

Chemical reaction systems typically have positive real forward and backward rates. Physical event-systems generalize this notion.

Definition 2.2.5. Let $n \in \mathbb{Z}_{>0}$. Let $\boldsymbol{\alpha} = \langle \alpha_1, \alpha_2, \ldots, \alpha_n \rangle \in \mathbb{C}^n$.

1. $\boldsymbol{\alpha}$ is a *non-negative point* iff for $i = 1, 2, \ldots, n$, $\alpha_i \in \mathbb{R}_{\geq 0}$.

2. $\boldsymbol{\alpha}$ is a *positive point* iff for $i = 1, 2, \ldots, n$, $\alpha_i \in \mathbb{R}_{>0}$.

3. $\boldsymbol{\alpha}$ is a *z-point* iff there exists an i such that $\alpha_i = 0$.

In chemistry, a system is said to have achieved detailed balance when it is at a point where the net flux of each reaction is zero. Given the corresponding event-system, points of detailed balance corresponds to points where each event evaluates to zero, and vice versa. We call such points "strong equilibrium points."

Definition 2.2.6 (Strong equilibrium point)**.** Let $\mathcal{E}$ be a finite-dimensional event-system of dimension n. $\boldsymbol{\alpha} \in \mathbb{C}^n$ is a *strong* $\mathcal{E}$*-equilibrium point* iff for all $e \in \mathcal{E}$, $e(\boldsymbol{\alpha}) = 0$.

In the language of algebraic geometry, when $\mathcal{E}$ is a finite-dimensional event-system, its corresponding algebraic set is precisely the set of its strong $\mathcal{E}$-equilibrium points.

It is widely believed that all "real" chemical reactions achieve detailed balance. We now introduce natural event-systems, a restriction of finite-dimensional, physical event-systems to those that can achieve detailed balance.

Definition 2.2.7 (Natural event-system)**.** A finite-dimensional event-system $\mathcal{E}$ is *natural* iff it is physical and there exists a positive strong $\mathcal{E}$-equilibrium point.

Our next goal is to introduce atomic event-systems: finite-dimensional event-systems obeying the atomic hypothesis that all species are composed of atoms. Towards this goal, we will define a graph for each finite-dimensional event-system. The vertices of this graph are the monomials from $\mathbb{M}_\infty$ and the edges are determined by the events. If a weight r is assigned to an edge, then r represents the energy released when a reaction corresponding to that edge takes place. For the purpose of defining atomic event-systems, the reader may ignore the weights; they are included here for use elsewhere in the paper (Definition 2.5.1).

Though graphs corresponding to systems of chemical reactions have been defined elsewhere (e.g. [12], [32, p. 10]), it is important to note that these definitions do not coincide with ours.

Definition 2.2.8 (Event-graph)**.** Let $\mathcal{E}$ be a finite-dimensional event-system. The event-graph $G_{\mathcal{E}} = \langle V, E, w\rangle$ is a weighted, directed multigraph such that:

1. $V = \mathbb{M}_\infty$
2. For all M_1, $M_2 \in \mathbb{M}_\infty$, for all $r \in \mathbb{C}$,

   $\langle M_1, M_2\rangle \in E$ and $r \in w\left(\langle M_1, M_2\rangle\right)$ iff

   there exist $e \in \mathcal{E}$ and $\sigma, \tau \in \mathbb{C}$ and $M, N, T \in \mathbb{M}_\infty$ such that $e = \sigma M + \tau N$ and $M \prec N$ and either

   (a) $M_1 = TM$ and $M_2 = TN$ and $r = \ln\left(-\frac{\sigma}{\tau}\right)$ or

   (b) $M_1 = TN$ and $M_2 = TM$ and $r = -\ln\left(-\frac{\sigma}{\tau}\right)$

Notice that two distinct weights r_1 and r_2 could be assigned to a single edge. For example, let $\mathcal{E} = \{X_1X_2 - 2X_1^2, X_2 - 5X_1\}$. Consider the edge in $G_{\mathcal{E}}$ from the monomial X_1^2 to the monomial X_1X_2. Weight $\ln 2$ is assigned to this edge due to the event $X_1X_2 - 2X_1^2$, with $T = 1$. Weight $\ln 5$ is also assigned to this edge due to the event $X_2 - 5X_1$, with $T = X_1$.

Definition 2.2.9. Let $\mathcal{E}$ be a finite-dimensional event-system. For all $M \in \mathbb{M}_\infty$, the *connected component* of M, denoted $C_{\mathcal{E}}(M)$, is the set of all $N \in \mathbb{M}_\infty$ such that there is a path in $G_{\mathcal{E}}$ from M to N.

It follows from the definition of "path" that every monomial belongs to its connected component.

Definition 2.2.10 (Atomic event-system)**.** Let $\mathcal{E}$ be a finite-dimensional event-system of dimension n. Let $S = \{X_1, X_2, \cdots, X_n\}$. Let $A_{\mathcal{E}} = \big\{X_i \in S \mid C_{\mathcal{E}}(X_i) = \{X_i\}\big\}$. $\mathcal{E}$ is *atomic* iff for all $M \in \mathbb{M}_S$, $C(M)$ contains a unique monomial in $\mathbb{M}_{A_{\mathcal{E}}}$.

If $\mathcal{E}$ is atomic then the members of $A_{\mathcal{E}}$ will be called *the atoms of* $\mathcal{E}$. It follows from the definition that in atomic event-systems, atoms are not decomposable, non-atoms are uniquely decomposable into atoms and events preserve atoms.

Since the set $\mathbb{M}_{\{X_1, X_2 \ldots, X_n\}}$ is infinite, it is not possible to decide whether $\mathcal{E}$ is atomic by exhaustively checking the connected component of every monomial in $\mathbb{M}_{\{X_1, X_2 \ldots, X_n\}}$. The following is sometimes helpful in deciding whether a finite-dimensional event-system is atomic (proof not provided).

Let $\mathcal{E}$ be an event-system of dimension n with no event of the form $\sigma + \tau N$. Let $B_{\mathcal{E}} = \{X_i \mid \text{For all } \sigma, \tau \in \mathbb{C} \setminus \{0\} \text{ and } N \in \mathbb{M}_\infty : \sigma X_i + \tau N \notin \mathcal{E}\}$. Then $\mathcal{E}$ is atomic iff there exist $M_1 \in C_{\mathcal{E}}(X_1) \cap \mathbb{M}_{B_{\mathcal{E}}}, M_2 \in C_{\mathcal{E}}(X_2) \cap \mathbb{M}_{B_{\mathcal{E}}}, \ldots, M_n \in C_{\mathcal{E}}(X_n) \cap \mathbb{M}_{B_{\mathcal{E}}}$ such that:

$$\text{For all } \sigma \prod_{i=1}^{n} X_i^{a_i} - \tau \prod_{i=1}^{n} X_i^{b_i} \in \mathcal{E}, \quad \prod_{i=1}^{n} M_i^{a_i} = \prod_{i=1}^{n} M_i^{b_i}. \tag{2.1}$$

We have shown (proof not provided) that if $\mathcal{E}$ and $B_{\mathcal{E}}$ are as above, and there exist $M_1 \in C_{\mathcal{E}}(X_1) \cap \mathbb{M}_{B_{\mathcal{E}}}, M_2 \in C_{\mathcal{E}}(X_2) \cap \mathbb{M}_{B_{\mathcal{E}}}, \ldots, M_n \in C_{\mathcal{E}}(X_n) \cap \mathbb{M}_{B_{\mathcal{E}}}$ and there exists $\sigma \prod_{i=1}^{n} X_i^{a_i} - \tau \prod_{i=1}^{n} X_i^{b_i} \in \mathcal{E}$ such that $\prod_{i=1}^{n} M_i^{a_i} \neq \prod_{i=1}^{n} M_i^{b_i}$, then $\mathcal{E}$ is not atomic. Hence, to check whether an event-system with no event of the form $\sigma+\tau N$ is atomic, it suffices to examine an arbitrary choice of $M_1 \in C_{\mathcal{E}}(X_1) \cap \mathbb{M}_{B_{\mathcal{E}}}, M_2 \in C_{\mathcal{E}}(X_2) \cap \mathbb{M}_{B_{\mathcal{E}}}, \ldots, M_n \in C_{\mathcal{E}}(X_n) \cap \mathbb{M}_{B_{\mathcal{E}}}$, if one exists, and check whether (2.1) above holds.

Example 1. Let $\mathcal{E} = \{X_2^2 - X_1^2\}$. Then $B_{\mathcal{E}} = \{X_1, X_2\}$. Let $M_1 = X_1$ and $M_2 = X_2$. Trivially, $M_1, M_2 \in \mathbb{M}_{B_{\mathcal{E}}}$, $M_1 \in C_{\mathcal{E}}(X_1)$ and $M_2 \in C_{\mathcal{E}}(X_2)$. Consider the event $X_2^2 - X_1^2$. Since $M_2^2 = X_2^2 \neq X_1^2 = M_1^2$, $\mathcal{E}$ is not atomic. Note that the event $X_2^2 - X_1^2$ does not preserve atoms.

Example 2. Let $\mathcal{E} = \{X_4^2 - X_2, X_5^2 - X_3, X_2X_3 - X_1\}$. Then $B_{\mathcal{E}} = \{X_4, X_5\}$. Let $M_1 = X_4^2X_5^2, M_2 = X_4^2, M_3 = X_5^2, M_4 = X_4, M_5 = X_5$. Clearly these are all in $\mathbb{M}_{B_{\mathcal{E}}}$. $X_5^2 - X_3 \in \mathcal{E}$ implies $M_3 \in C_{\mathcal{E}}(X_3)$. $X_4^2 - X_2 \in \mathcal{E}$ implies $M_2 \in C_{\mathcal{E}}(X_2)$. Since $(X_1, X_2X_3, X_2X_5^2, X_4^2X_5^2)$ is a path in $G_{\mathcal{E}}$, we have $M_1 \in C_{\mathcal{E}}(X_1)$. For the event $X_4^2 - X_2$, we have $M_4^2 = X_4^2 = M_2$. For the event $X_5^2 - X_3$, we have $M_5^2 = X_5^2 = M_3$. For the event $X_2X_3 - X_1$, we have $M_2M_3 = X_4^2X_5^2 = M_1$. Therefore, $\mathcal{E}$ is atomic.

Note that it is possible to have an atomic event-system where $A_{\mathcal{E}}$ is the empty set. For example:

Example 3. Let $\mathcal{E} = \{1 - X_1\}$. In this case, $S = \{X_1\}$ and $\mathbb{M}_S$ is the set $\{1, X_1, X_1^2, X_1^3, \ldots\}$. It is clear that $\mathbb{M}_S$ forms a single connected component C in $G_{\mathcal{E}}$. Hence, X_1 is not in $A_{\mathcal{E}}$, and $A_{\mathcal{E}} = \emptyset$. 1 is the only monomial in $\mathbb{M}_{A_{\mathcal{E}}}$. Since 1 is in C, $\mathcal{E}$ is atomic.

2.3 Finite Event-systems

The study of infinite event-systems is embryonic and appears to be quite challenging. In the rest of this paper only finite event-systems (i.e., where the set $\mathcal{E}$ is finite) will be considered. It is clear that all finite event-systems are finite-dimensional.

Definition 2.3.1 (Stoichiometric matrix)**.** Let $\mathcal{E} = \{e_1, e_2, \cdots, e_m\}$ be an event-system of dimension n. Let $i \leq n$ and $j \leq m$ be positive integers. Let $e_j = \sigma M + \tau N$, where $M \prec N$. Then $\gamma_{j,i}$ is the number of times X_i divides N minus the number of times X_i divides M. The *stoichiometric matrix* $\Gamma_{\mathcal{E}}$ of $\mathcal{E}$ is the $m \times n$ matrix of integers $\Gamma_{\mathcal{E}} = (\gamma_{j,i})_{m \times n}$.

Example 4. Let $e_1 = 0.5X_2^5 - 500X_1X_2^3X_7$. Let $\mathcal{E} = \{e_1\}$. Then $\gamma_{1,1} = 1$, $\gamma_{1,2} = -2$, $\gamma_{1,7} = 1$ and for all other i, $\gamma_{1,i} = 0$, hence $\Gamma_{\mathcal{E}} = \begin{pmatrix} 1 & -2 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}$.

Definition 2.3.2. Let $\mathcal{E} = \{e_1, \cdots, e_m\}$ be a finite event-system of dimension n. Then:

1. $\boldsymbol{P}_{\mathcal{E}}$ is the column vector $\langle P_1, P_2, \ldots, P_n \rangle^T = \Gamma_{\mathcal{E}}^T \langle e_1, e_2, \ldots, e_m \rangle^T$.

2. Let $\boldsymbol{\alpha} \in \mathbb{C}^n$. Then $\boldsymbol{\alpha}$ is an $\mathcal{E}$-equilibrium point iff for $i = 1, 2, \ldots, n : P_i(\boldsymbol{\alpha}) = 0$.

The P_i's arise from the Law of Mass Action in chemistry. For a system of chemical reactions, the P_i's are the right-hand sides of the differential equations that describe the concentration kinetics. Definition 2.3.2 extends the Law of Mass Action to arbitrary event-systems, and hence, arbitrary sets of binomials.

It follows from the definition that for finite event-systems, all strong equilibrium points are equilibrium points, but the converse need not be true.

Example 5. Let $e_1 = X_2 - X_1$ and $e_2 = X_2 - 2X_1$. Let $\mathcal{E} = \{e_1, e_2\}$. Then $\Gamma_{\mathcal{E}} = \begin{pmatrix} 1 & -1 \\ 1 & -1 \end{pmatrix}$ and $\boldsymbol{P}_{\mathcal{E}} = \begin{pmatrix} P_1 \\ P_2 \end{pmatrix} = \begin{pmatrix} 2X_2 - 3X_1 \\ 3X_1 - 2X_2 \end{pmatrix}$. Therefore $(2,3)$ is an $\mathcal{E}$-equilibrium point. Since $e_1(2,3) = 1$, $(2,3)$ is not a strong $\mathcal{E}$-equilibrium point.

Example 6. Let $e_1 = 6 - X_1X_2$ and $e_2 = 2X_2^2 - 9X_1$. Let $\mathcal{E} = \{e_1, e_2\}$. Then $\Gamma_{\mathcal{E}} = \begin{pmatrix} 1 & 1 \\ 1 & -2 \end{pmatrix}$ and $\boldsymbol{P}_{\mathcal{E}} = \begin{pmatrix} P_1 \\ P_2 \end{pmatrix} = \begin{pmatrix} 6 - X_1X_2 + 2X_2^2 - 9X_1 \\ 6 - X_1X_2 - 4X_2^2 + 18X_1 \end{pmatrix}$. The point $(2,3)$ is a strong equilibrium point because $e_1(2,3) = 0$ and $e_2(2,3) = 0$. Since $P_1(2,3) = e_1(2,3) + e_2(2,3) = 0$ and $P_2(2,3) = e_1(2,3) - 2e_2(2,3) = 0$, the point $(2,3)$ is also an equilibrium point.

The event-system in Example 5 is not natural, whereas the one in Example 6 is. In Theorem 2.5.7, it is shown that if $\mathcal{E}$ is a finite, natural event-system then all positive $\mathcal{E}$-equilibrium points are strong $\mathcal{E}$-equilibrium points.

Definition 2.3.3 (Event-process)**.** Let $\mathcal{E}$ be a finite event-system of dimension n. Let $\langle P_1, P_2, \ldots, P_n \rangle^T = \boldsymbol{P}_{\mathcal{E}}$. Let $\Omega \subseteq \mathbb{C}$ be a non-empty simply-connected open set. Let $\boldsymbol{f} = \langle f_1, f_2, \cdots, f_n \rangle$ where for $i = 1, 2, \ldots, n$, $f_i : \mathbb{C} \to \mathbb{C}$ is defined on Ω. Then $\boldsymbol{f}$ is an $\mathcal{E}$-process on Ω iff for $i = 1, 2, \ldots, n$:

1. f_i' exists on Ω.

2. $f_i' = P_i \circ f$ on Ω.

Note that $\mathcal{E}$-processes evolve through complex time, and hence generalize the idea of the time-evolution of concentrations in a system of chemical reactions.

Definition 2.3.3 immediately implies that if $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ is an $\mathcal{E}$-process on Ω, then for $i = 1, 2, \ldots, n$, f_i is holomorphic on Ω. In particular, for each i and all $\alpha \in \Omega$, there is a power series around α that agrees with f_i on a disk of non-zero radius.

Systems of chemical reactions sometimes obey certain conservation laws. For example, they may conserve mass, or the total number of each kind of atom. Event-systems also sometimes obey conservation laws.

Definition 2.3.4 (Conservation law, Linear conservation law)**.** Let $\mathcal{E}$ be a finite event-system of dimension n. A function $g : \mathbb{C}^n \to \mathbb{C}$ is a *conservation law of* $\mathcal{E}$ iff g is holomorphic on $\mathbb{C}^n$, $g(\langle 0, 0, \cdots, 0 \rangle) = 0$ and $\nabla g \cdot \boldsymbol{P}_{\mathcal{E}}$ is identically zero on $\mathbb{C}^n$. If g is a conservation law of $\mathcal{E}$ and g is linear (i.e. $\forall c \in \mathbb{C}, \forall \boldsymbol{\alpha}, \boldsymbol{\beta} \in \mathbb{C}^n, g(c\boldsymbol{\alpha} + \boldsymbol{\beta}) = cg(\boldsymbol{\alpha}) + g(\boldsymbol{\beta})$), then g is a *linear conservation law of* $\mathcal{E}$.

The event-system described in Example 5 has a linear conservation law $g(X_1, X_2) = X_1 + X_2$. The next theorem shows that conservation laws of $\mathcal{E}$ are dynamical invariants of $\mathcal{E}$-processes.

Theorem 2.3.1. *For all finite event-systems $\mathcal{E}$, for all conservation laws g of $\mathcal{E}$, for all simply-connected open sets $\Omega \subseteq \mathbb{C}$, for all $\mathcal{E}$-processes $\boldsymbol{f}$ on Ω, there exists $k \in \mathbb{C}$ such that $g \circ \boldsymbol{f} - k$ is identically zero on Ω.*

Proof. Let n be the dimension of $\mathcal{E}$. Let $\langle P_1, P_2, \ldots, P_n \rangle^T = \boldsymbol{P}_{\mathcal{E}}$. For all $t \in \Omega$, by Definition 2.3.3, for $i = 1, 2, \ldots, n$, $f_i(t)$ and $f_i'(t)$ are defined. Further, by Definition 2.3.4, g is holomorphic on $\mathbb{C}^n$. Hence, $g \circ \boldsymbol{f}$ is holomorphic on Ω. Therefore, by the chain rule, $(g \circ \boldsymbol{f})'(t) = (\nabla g|_{\boldsymbol{f}(t)}) \cdot \langle f_1'(t), f_2'(t), \ldots, f_n'(t)\rangle$. By Definition 2.3.3, for all $t \in \Omega$, $\langle f_1'(t), f_2'(t), \ldots, f_n'(t)\rangle = \langle P_1(\boldsymbol{f}(t)), P_2(\boldsymbol{f}(t)), \ldots, P_n(\boldsymbol{f}(t))\rangle$. From these, it follows that $(g \circ \boldsymbol{f})'(t) = (\nabla g \cdot \boldsymbol{P}_{\mathcal{E}})(\boldsymbol{f}(t))$. But by Definition 2.3.4, $\nabla g \cdot \boldsymbol{P}_{\mathcal{E}}$ is identically zero. Hence, for all $t \in \Omega$, $(g \circ \boldsymbol{f})'(t) = 0$. In addition, Ω is a simply-connected open set. Therefore, by [3, Theorem 11], there exists $k \in \mathbb{C}$ such that $g \circ \boldsymbol{f} - k$ is identically zero on Ω. □

The next theorem shows a way to derive linear conservation laws of an event-system from its stoichiometric matrix.

Theorem 2.3.2. *Let $\mathcal{E}$ be a finite event-system of dimension n. For all $\boldsymbol{v} \in \ker \Gamma_{\mathcal{E}}$, $\boldsymbol{v} \cdot \langle X_1, \cdots, X_n\rangle$ is a linear conservation law of $\mathcal{E}$.*

Proof. Let $\Gamma = \Gamma_{\mathcal{E}}$, then $\ker \Gamma$ is orthogonal to the image of Γ^T. By the definition of $\boldsymbol{P} = \boldsymbol{P}_{\mathcal{E}}$, for all $\boldsymbol{w} \in \mathbb{C}^n$, $\boldsymbol{P}(\boldsymbol{w})$ lies in the image of Γ^T. Hence, for all $\boldsymbol{v} \in \ker \Gamma$, for all $\boldsymbol{w} \in \mathbb{C}^n$, $\boldsymbol{v} \cdot \boldsymbol{P}(\boldsymbol{w}) = 0$. But $\boldsymbol{v}$ is the gradient of $\boldsymbol{v} \cdot \langle X_1, \cdots, X_n\rangle$. It now follows from Definition 2.3.4 that $\boldsymbol{v} \cdot \langle X_1, \cdots, X_n\rangle$ is a linear conservation law of $\mathcal{E}$. □

Definition 2.3.5 (Primitive conservation law)**.** Let $\mathcal{E}$ be a finite event-system of dimension n. For all $\boldsymbol{v} \in \ker \Gamma_{\mathcal{E}}$, the linear conservation law $\boldsymbol{v} \cdot \langle X_1, X_2, \cdots, X_n\rangle$ is a *primitive conservation law.*

We can show (manuscript under preparation) that in physical event-systems all linear conservation laws are primitive and, in natural event-systems, all conservation laws arise from the primitive ones.

Definition 2.3.6 (Conservation class, Positive conservation class)**.** Let $\mathcal{E}$ be a finite event-system of dimension n. A coset of $(\ker \Gamma_{\mathcal{E}})^{\perp}$ is a *conservation class of $\mathcal{E}$*. If a conservation class of $\mathcal{E}$ contains a positive point, then the class is a *positive conservation class of $\mathcal{E}$*.

Equivalently, $\boldsymbol{\alpha}, \boldsymbol{\beta} \in \mathbb{C}^n$ are in the same conservation class if and only if they agree on all primitive conservation laws. Note that if H is a conservation class of $\mathcal{E}$ then it is closed in $\mathbb{C}^n$. The following theorem shows that the name "conservation class" is appropriate.

Theorem 2.3.3. *Let $\mathcal{E}$ be a finite event-system. Let $\Omega \subset \mathbb{C}$ be a simply-connected open set containing 0. Let $\boldsymbol{f}$ be an $\mathcal{E}$-process on Ω. Let H be a conservation class of $\mathcal{E}$ containing $\boldsymbol{f}(0)$. Then for all $t \in \Omega$, $\boldsymbol{f}(t) \in H$.*

Proof. Let $\mathcal{E}$, Ω, $\boldsymbol{f}$, H and t be as in the statement of this theorem. For all $\boldsymbol{v} \in \ker \Gamma_{\mathcal{E}}$, the primitive conservation law $\boldsymbol{v} \cdot \langle X_1, X_2, \cdots, X_n \rangle$ is a dynamical invariant of $\boldsymbol{f}$, from Theorem 2.3.2 and Theorem 2.3.1. Hence,

$$\boldsymbol{v} \cdot \langle f_1(0), f_2(0), \cdots, f_n(0) \rangle = \boldsymbol{v} \cdot \langle f_1(t), f_2(t), \cdots, f_n(t) \rangle$$

That is,

$$\boldsymbol{v} \cdot \langle f_1(0) - f_1(t), f_2(0) - f_2(t), \cdots, f_n(0) - f_n(t) \rangle = 0$$

Hence, $\boldsymbol{f}(t) - \boldsymbol{f}(0)$ is in $(\ker \Gamma_{\mathcal{E}})^{\perp}$. By Definition 2.3.6, $\boldsymbol{f}(t) \in H$. □

2.4 Finite Physical Event-systems

In this section, we investigate finite, physical event-systems — a generalization of systems of chemical reactions.

It is widely believed that systems of chemical reactions that begin with positive (respectively, non-negative) concentrations will have positive (respectively, non-negative) concentrations at all future times. This property has been addressed mathematically in numerous papers [14, p. 6],[12, Remark 3.4], [6, Theorem 3.2], [32, Lemma 2.1]. The notion of "system of chemical reactions" varies between papers. Several papers have provided no proof, incomplete proofs or inadequate proofs that this property holds for their systems. Sontag [32, Lemma 2.1] provides a lovely proof of this property for the systems he considers — zero deficiency reaction networks with one linkage class. We shall prove in Theorem 2.4.5 that the property holds for finite, physical event-systems. Finite, physical event-systems have a large intersection with the systems considered by Sontag, but each includes a large class of systems that the other does not. We remark that our methods of proof differ from Sontag's, but it is possible that Sontag's proof might be adaptable to our setting.

Lemma 2.4.4 and Lemma 2.4.11 are proved here because they apply to finite, physical event-systems. However, they are only invoked in subsequent sections. Lemma 2.4.4 relates $\mathcal{E}$-processes to solutions of ordinary differential equations over the reals. Lemma 2.4.11 establishes that if an $\mathcal{E}$-process defined on the positive reals starts at a real, non-negative point, then its ω-limit set is invariant and contains only real, non-negative points.

The next lemma shows that if two $\mathcal{E}$-processes evaluate to the same real point on a real argument then they must agree and be real-valued on an open interval containing that argument. The proof exploits the fact that $\mathcal{E}$-processes are analytic, by considering their power series expansions.

Lemma 2.4.1. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n, let $\Omega, \Omega' \subseteq \mathbb{C}$ be open and simply-connected, let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω and let $\boldsymbol{g} = \langle g_1, g_2, \ldots, g_n \rangle$ be an $\mathcal{E}$-process on Ω'. If $t_0 \in \Omega \cap \Omega' \cap \mathbb{R}$ and $\boldsymbol{f}(t_0) \in \mathbb{R}^n$ and $\boldsymbol{f}(t_0) = \boldsymbol{g}(t_0)$, then there exists an open interval $I \subseteq \mathbb{R}$ such that $t_0 \in I$ and for all $t \in I$:*

1. *$\boldsymbol{f}(t) = \boldsymbol{g}(t)$.*

2. *For $i = 1, 2, \ldots, n$: if $\sum_{j=0}^{\infty} c_j (z - t_0)^j$ is the Taylor series expansion of f_i at t_0 then for all $j \in \mathbb{Z}_{\geq 0}$, $c_j \in \mathbb{R}$.*

3. *$\boldsymbol{f}(t) \in \mathbb{R}^n$.*

Proof. Let $k \in \mathbb{Z}_{\geq 0}$. By Definition 2.3.3, $\boldsymbol{f}$ and $\boldsymbol{g}$ are vectors of functions analytic at t_0. For $i = 1, 2, \ldots, n$, let $f_i^{(k)}$ be the k^{th} derivative of f_i and let $\boldsymbol{f}^{(k)} = \langle f_1^{(k)}, f_2^{(k)}, \ldots, f_n^{(k)} \rangle$. Define $g_i^{(k)}$ and $\boldsymbol{g}^{(k)}$ similarly. To prove 1, it is enough to show that for $i = 1, 2, \ldots, n$, f_i and g_i have the same Taylor series around t_0. Let $\boldsymbol{V}_0 = \langle X_1, X_2, \ldots, X_n \rangle$. Let $\boldsymbol{V}_k = \mathrm{Jac}(\boldsymbol{V}_{k-1}) \boldsymbol{P}_{\mathcal{E}}$ (recall that if $\boldsymbol{H} = \langle h_1(X_1, X_2, \ldots, X_m)$, $h_2(X_1, X_2, \ldots, X_m)$, $\ldots$, $h_n(X_1, X_2, \ldots, X_m) \rangle$ is a vector of functions in m variables then $\mathrm{Jac}(\boldsymbol{H})$ is the $n \times m$ matrix $(\frac{\partial h_i}{\partial x_j})$, where $i = 1, 2, \ldots, n$ and $j = 1, 2, \ldots, m$). Let $\langle V_{k,1}, V_{k,2}, \ldots, V_{k,n} \rangle = \boldsymbol{V}_k$. We claim that $\boldsymbol{f}^{(k)} = \boldsymbol{V}_k \circ \boldsymbol{f}$ on Ω and $\boldsymbol{g}^{(k)} = \boldsymbol{V}_k \circ \boldsymbol{g}$ on Ω' and for $i = 1, 2, \ldots, n$, $V_{k,i} \in \mathbb{R}[X_1, X_2, \ldots, X_n]$. We prove the claim by induction on k. If $k = 0$, the proof is immediate. If $k \geq 1$, on Ω:

$$
\begin{aligned}
\boldsymbol{f}^{(k)} &= (\boldsymbol{f}^{(k-1)})' \\
&= (\boldsymbol{V}_{k-1} \circ \boldsymbol{f})' && \text{(Inductive hypothesis)} \\
&= (\mathrm{Jac}(\boldsymbol{V}_{k-1}) \circ \boldsymbol{f})\boldsymbol{f}' && \text{(Chain-rule of derivation)} \\
&= (\mathrm{Jac}(\boldsymbol{V}_{k-1}) \circ \boldsymbol{f})(\boldsymbol{P}_{\mathcal{E}} \circ \boldsymbol{f}) && (\boldsymbol{f} \text{ is an } \mathcal{E}\text{-process}) \\
&= (\mathrm{Jac}(\boldsymbol{V}_{k-1})\boldsymbol{P}_{\mathcal{E}}) \circ \boldsymbol{f} \\
&= \boldsymbol{V}_k \circ \boldsymbol{f}
\end{aligned}
$$

By a similar argument, we conclude that $\boldsymbol{g}^{(k)} = \boldsymbol{V}_k \circ \boldsymbol{g}$ on Ω'. By the inductive hypothesis, $\boldsymbol{V}_{k-1}$ is a vector of polynomials in $\mathbb{R}[X_1, X_2, \ldots, X_n]$. It follows that $\mathrm{Jac}(\boldsymbol{V}_{k-1})$ is an $n \times n$ matrix of polynomials in $\mathbb{R}[X_1, X_2, \ldots, X_n]$. Since $\mathcal{E}$ is physical, $\boldsymbol{P}_{\mathcal{E}}$ is a vector of polynomials in $\mathbb{R}[X_1, X_2, \ldots, X_n]$. Therefore, $\boldsymbol{V}_k = \mathrm{Jac}(\boldsymbol{V}_{k-1})\boldsymbol{P}_{\mathcal{E}}$ is a vector of polynomials in $\mathbb{R}[X_1, X_2, \ldots, X_n]$. This establishes the claim.

We have proved that $\boldsymbol{f}^{(k)} = \boldsymbol{V}_k \circ \boldsymbol{f}$ on Ω and $\boldsymbol{g}^{(k)} = \boldsymbol{V}_k \circ \boldsymbol{g}$ on Ω'. Since, by assumption, $t_0 \in \Omega \cap \Omega'$ and $\boldsymbol{f}(t_0) = \boldsymbol{g}(t_0)$, it follows that $\boldsymbol{f}^{(k)}(t_0) = \boldsymbol{g}^{(k)}(t_0)$. Therefore, for $i = 1, 2, \ldots, n$, f_i and g_i have the same Taylor series around t_0. For $i = 1, 2, \ldots, n$, let a_i be the radius of convergence of the Taylor series of f_i around t_0. Let $r_{\boldsymbol{f}} = \min_{i \in \{1,2,\ldots,n\}} a_i$. Define $r_{\boldsymbol{g}}$ similarly. Let $D \subseteq \Omega \cap \Omega'$ be some non-empty open disk centered at t_0 with radius $r \leq \min(r_{\boldsymbol{f}}, r_{\boldsymbol{g}})$. Since Ω and Ω' are open sets and $t_0 \in \Omega \cap \Omega'$, such a disk must exist. Letting $I = (t_0 - r, t_0 + r)$ completes the proof of 1.

By assumption, $\boldsymbol{f}(t_0) \in \mathbb{R}^n$, and we have proved that $\boldsymbol{f}^{(k)} = \boldsymbol{V}_k \circ \boldsymbol{f}$ and $\boldsymbol{V}_k$ is a vector of polynomials in $\mathbb{R}[X_1, X_2, \ldots, X_n]$. It follows that $\boldsymbol{f}^{(k)}(t_0) \in \mathbb{R}^n$. Therefore, for

$i = 1, 2, \ldots, n$, all coefficients in the Taylor series of f_i around t_0 are real. It follows that f_i is real valued on I, completing the proof of 3. $\square$

The next lemma is a kind of uniqueness result. It shows that if two $\mathcal{E}$-processes evaluate to the same real point at 0 then they must agree and be real-valued on every open interval containing 0 where both are defined. The proof uses continuity to extend the result of Lemma 2.4.1.

Lemma 2.4.2. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n, let $\Omega, \Omega' \subseteq \mathbb{C}$ be open and simply-connected, let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω and let $\boldsymbol{g} = \langle g_1, g_2, \ldots, g_n \rangle$ be an $\mathcal{E}$-process on Ω'. If $0 \in \Omega \cap \Omega'$ and $\boldsymbol{f}(0) \in \mathbb{R}^n$ and $\boldsymbol{f}(0) = \boldsymbol{g}(0)$, then for all open intervals $I \subseteq \Omega \cap \Omega' \cap \mathbb{R}$ such that $0 \in I$, for all $t \in I$, $\boldsymbol{f}(t) = \boldsymbol{g}(t)$ and $\boldsymbol{f}(t) \in \mathbb{R}^n$.*

Proof. Assume there exists an open interval $I \subseteq \Omega \cap \Omega' \cap \mathbb{R}$ such that $0 \in I$ and $B = \{t \in I \mid \boldsymbol{f}(t) \neq \boldsymbol{g}(t) \text{ or } \boldsymbol{f}(t) \notin \mathbb{R}^n\} \neq \varnothing$. Let $B_P = B \cap \mathbb{R}_{\geq 0}$ and let $B_N = B \cap \mathbb{R}_{<0}$. Note that $B = B_P \cup B_N$, hence, $B_P \neq \varnothing$ or $B_N \neq \varnothing$. Suppose $B_P \neq \varnothing$ and let $t_P = \inf(B_P)$. By Lemma 2.4.1, there exists an $\varepsilon \in \mathbb{R}_{>0}$ such that $(-\varepsilon, \varepsilon) \cap B = \varnothing$. Hence, $t_P \geq \varepsilon > 0$. By definition of t_P, for all $t \in [0, t_P)$, $\boldsymbol{f}(t) = \boldsymbol{g}(t)$ and $\boldsymbol{f}(t) \in \mathbb{R}^n$. Since $\boldsymbol{f}$ and $\boldsymbol{g}$ are analytic at t_P, they are continuous at t_P. Therefore, $\boldsymbol{f}(t_P) = \boldsymbol{g}(t_P)$ and $\boldsymbol{f}(t_P) \in \mathbb{R}^n$. By Lemma 2.4.1, there exists an $\varepsilon' \in \mathbb{R}_{>0}$ such that for all $t \in (t_P - \varepsilon', t_P + \varepsilon')$, $\boldsymbol{f}(t) = \boldsymbol{g}(t)$ and $\boldsymbol{f}(t) \in \mathbb{R}^n$, contradicting t_P being the infimum of B_P. Therefore, $B_P = \varnothing$. Using a similar agument, we can prove that $B_N = \varnothing$. Therefore, $B = \varnothing$, and for all $t \in I$, $\boldsymbol{f}(t_P) = \boldsymbol{g}(t_P)$ and $\boldsymbol{f}(t_P) \in \mathbb{R}^n$. $\square$

The next lemma is a convenient technical result that lets us ignore the choice of origin for the time variable.

Lemma 2.4.3. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n, let $\Omega, \widetilde{\Omega} \subseteq \mathbb{C}$ be open and simply connected, let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω and let $\tilde{\boldsymbol{f}} = \langle \tilde{f}_1, \tilde{f}_2, \ldots, \tilde{f}_n \rangle$ be an $\mathcal{E}$-process on $\widetilde{\Omega}$. Let $u \in \Omega$ and $\tilde{u} \in \widetilde{\Omega}$ and $\boldsymbol{\alpha} \in \mathbb{R}^n$. Let $I \subseteq \mathbb{R}$ be an open interval. If*

1. $\boldsymbol{f}(u) = \tilde{\boldsymbol{f}}(\tilde{u}) = \boldsymbol{\alpha}$ *and*

2. $0 \in I$ *and*

3. *for all* $s \in I$, $u + s \in \Omega$ *and* $\tilde{u} + s \in \widetilde{\Omega}$

then for all $t \in I$, $\boldsymbol{f}(u + t) = \tilde{\boldsymbol{f}}(\tilde{u} + t)$.

Proof. Suppose $\boldsymbol{f}(u) = \tilde{\boldsymbol{f}}(\tilde{u}) = \boldsymbol{\alpha} \in \mathbb{R}^n$. Let $\Omega_u = \{z \in \mathbb{C} \mid u + z \in \Omega\}$ and $\widetilde{\Omega}_{\tilde{u}} = \{z \in \mathbb{C} \mid \tilde{u} + z \in \widetilde{\Omega}\}$. Let $\boldsymbol{h} = \langle h_1, h_2, \ldots, h_n \rangle$ where for $i = 1, 2, \ldots, n$, $h_i : \Omega_u \to \mathbb{C}$ is such that for all $z \in \Omega_u$, $h_i(z) = f_i(u + z)$ and let $\tilde{\boldsymbol{h}} = \langle \tilde{h}_1, \tilde{h}_2, \ldots, \tilde{h}_n \rangle$ where for $i = 1, 2, \ldots, n$, $\tilde{h}_i : \widetilde{\Omega}_{\tilde{u}} \to \mathbb{C}$ is such that for all $z \in \widetilde{\Omega}_{\tilde{u}}$, $\tilde{h}_i(z) = \tilde{f}_i(\tilde{u} + z)$. Since $u + z$ is differentiable on Ω_u and for $i = 1, 2, \ldots, n$, f_i is differentiable on Ω, it follows that for $i = 1, 2, \ldots, n$, h_i is differentiable on Ω_u. Further, for $i = 1, 2, \ldots, n$, for all $z \in \Omega_u$, $h_i'(z) = f_i'(u + z) = \boldsymbol{P}_{\mathcal{E}}(f_i(u + z)) = \boldsymbol{P}_{\mathcal{E}}(h_i(z))$, so $\boldsymbol{h}$ is an $\mathcal{E}$-process on Ω_u. Similarly, $\tilde{\boldsymbol{h}}$ is an $\mathcal{E}$-process on $\widetilde{\Omega}_{\tilde{u}}$. Note that $0 \in \Omega_u \cap \widetilde{\Omega}_{\tilde{u}}$ because $u \in \Omega$ and $\tilde{u} \in \widetilde{\Omega}$ and that $\boldsymbol{h}(0) = \tilde{\boldsymbol{h}}(0) = \boldsymbol{\alpha}$ because $\boldsymbol{f}(u) = \tilde{\boldsymbol{f}}(\tilde{u}) = \boldsymbol{\alpha}$. By Lemma 2.4.2, for all open intervals $I \subseteq \Omega_u \cap \widetilde{\Omega}_{\tilde{u}} \cap \mathbb{R}$ such that $0 \in I$, for all $t \in I$, $\boldsymbol{h}(t) = \tilde{\boldsymbol{h}}(t)$, so $\boldsymbol{f}(u + t) = \tilde{\boldsymbol{f}}(\tilde{u} + t)$. $\square$

Because event-systems are defined over the complex numbers, we have access to results from complex analysis. However, there is a considerable body of results regarding ordinary differential equations over the reals. Definition 2.4.1 and Lemma 2.4.4 establish a relationship between $\mathcal{E}$-processes and solutions to systems of ordinary differential equations over the reals.

Definition 2.4.1 (Real event-process)**.** Let $\mathcal{E}$ be a finite, physical event-system of dimension n. Let $\langle P_1, P_2, \ldots, P_n\rangle^T = \boldsymbol{P}_{\mathcal{E}}$. Let $I \subseteq \mathbb{R}$ be an interval. Let $\boldsymbol{h} = \langle h_1, h_2, \ldots, h_n\rangle$ where for $i = 1, 2, \ldots, n$, $h_i : \mathbb{R} \to \mathbb{R}$ is defined on I. Then $\boldsymbol{h}$ is a real-$\mathcal{E}$-process on I iff for $i = 1, 2, \ldots, n$:

1. h_i' exists on I.

2. $h_i' = P_i \circ \boldsymbol{h}$ on I.

Lemma 2.4.4 (All real-$\mathcal{E}$-processes are restrictions of $\mathcal{E}$-processes)**.** *Let $\mathcal{E}$ be a finite, physical event-system of dimension n. Let $I \subseteq \mathbb{R}$ be an interval. Let $\boldsymbol{h} = \langle h_1, h_2, \ldots, h_n\rangle$ be a real-$\mathcal{E}$-process on I. Then there exist an open, simply-connected $\Omega \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\boldsymbol{f}$ on Ω such that:*

1. $I \subset \Omega$

2. For all $t \in I : \boldsymbol{f}(t) = \boldsymbol{h}(t)$.

Proof. Let $\boldsymbol{P} = \langle P_1, P_2, \ldots, P_n\rangle = \boldsymbol{P}_{\mathcal{E}}$. For $i = 1, 2, \ldots, n$, P_i is a polynomial and therefore analytic on $\mathbb{C}^n$. By Cauchy's existence theorem for ordinary differential equations with analytic right-hand sides [19], for all $a \in I$, there exist a non-empty open disk $D_a \subseteq \mathbb{C}$ centered at a and functions $f_{a,1}, f_{a,2}, \ldots, f_{a,n}$ analytic on D_a such that for $i = 1, 2, \ldots, n$:

1. $f_{a,i}(a) = h_i(a)$

2. $f'_{a,i}$ exists on D_a and for all $t \in D_a : f'_{a,i}(t) = P_i(f_{a,1}(t), f_{a,2}(t), \ldots, f_{a,n}(t))$. That is, $\boldsymbol{f}_a = \langle f_{a,1}, f_{a,2}, \ldots, f_{a,n} \rangle$ is an $\mathcal{E}$-process on D_a.

Claim: For all $a \in I$, there exists $\delta_a \in \mathbb{R}_{>0}$ such that for all $t \in I \cap (a - \delta_a, a + \delta_a)$: $\boldsymbol{f}_a(t) = \boldsymbol{h}(t)$. To see this, by Lemma 2.4.1, for all $a \in I$ there exists $\beta_a \in \mathbb{R}_{>0}$ such that for all $t \in (a - \beta_a, a + \beta_a) \cap D_a$, $\boldsymbol{f}_a(t) \in \mathbb{R}^n$. Let $I_a = (a - \beta_a, a + \beta_a) \cap D_a$. Note that $\boldsymbol{f}_a|_{I_a}$ is a real-$\mathcal{E}$-process on I_a . By the theorem of uniqueness of solutions to differential equations with $\mathcal{C}^1$ right-hand sides [24], there exists $\gamma_a \in \mathbb{R}_{>0}$ such that for all $t \in (a - \gamma_a, a + \gamma_a) \cap I_a \cap I$, $\boldsymbol{f}_a(t) = \boldsymbol{h}(t)$. Clearly, we can choose $\delta_a \in \mathbb{R}_{>0}$ such that $(a - \delta_a, a + \delta_a) \subseteq (a - \gamma_a, a + \gamma_a) \cap I_a$. This establishes the claim.

For all $a \in I$, let $\delta_a \in \mathbb{R}_{>0}$ be such that for all $t \in I \cap (a - \delta_a, a + \delta_a) : \boldsymbol{f}_a(t) = \boldsymbol{h}(t)$. Let $\widehat{D}_a$ be an open disk centered at a of radius δ_a.

Claim: For all $a_1, a_2 \in I$, for all $t \in \widehat{D}_{a_1} \cap \widehat{D}_{a_2}$: $\boldsymbol{f}_{a_1}(t) = \boldsymbol{f}_{a_2}(t)$. To see this, suppose $\widehat{D}_{a_1} \cap \widehat{D}_{a_2} \neq \varnothing$. Let $J = \widehat{D}_{a_1} \cap \widehat{D}_{a_2} \cap \mathbb{R}$. Since $\widehat{D}_{a_1}$ and $\widehat{D}_{a_2}$ are open disks centered on the real line, J is a non-empty open real interval. For all $t \in J$, by the claim above, $\boldsymbol{f}_{a_1}(t) = \boldsymbol{h}(t)$ and $\boldsymbol{f}_{a_2}(t) = \boldsymbol{h}(t)$. Hence, $\boldsymbol{f}_{a_1}(t) = \boldsymbol{f}_{a_2}(t)$. Since J is a non-empty interval, J contains an accumulation point. Since $\boldsymbol{f}_{a_1}$ and $\boldsymbol{f}_{a_2}$ are analytic on $\widehat{D}_{a_1} \cap \widehat{D}_{a_2}$ and $\widehat{D}_{a_1} \cap \widehat{D}_{a_2}$ is simply connected, for all $t \in \widehat{D}_{a_1} \cap \widehat{D}_{a_2} : \boldsymbol{f}_{a_1}(t) = \boldsymbol{f}_{a_2}(t)$. This establishes the claim.

Let $\Omega = \bigcup_{a \in I} \widehat{D}_a$. Clearly, $I \subset \Omega$. Ω is a union of open discs, and is therefore open.

For all $t \in \Omega$, there exists $a \in I$ such that $t \in \widehat{D}_a$. Since $\widehat{D}_a$ is a disk, t and a are path-connected in Ω. Since I is path-connected, and $I \subseteq \Omega$, it follows that Ω is path-connected.

To see that Ω is simply-connected, consider the function $R : [0,1] \times \Omega \to \Omega$ given by $(u, z) \mapsto \mathrm{Re}(z) + i\,\mathrm{Im}(z)(1-u)$. Observe that R is continuous on $[0,1] \times \Omega$, and for all $z \in \Omega$: $R(0,z) = z$, $R(1,\Omega) \subset \Omega$, and for all $u \in [0,1]$, for all $z \in \Omega \cap \mathbb{R} : R(u,z) \in \Omega$. Therefore, R is a deformation retraction. Note that $R(0,\Omega) = \Omega$ and $R(1,\Omega) \subseteq \mathbb{R}$, and Ω is path-connected together imply that $R(1,\Omega)$ is a real interval. Hence, $R(1,\Omega)$ is simply-connected. Since R was a deformation retraction, Ω is simply-connected.

Let $\boldsymbol{f} : \Omega \to \mathbb{C}^n$ be the unique function such that for all $a \in I$, for all $t \in \widehat{D}_a : \boldsymbol{f}(t) = \boldsymbol{f}_a(t)$. By the claim above and from the definition of Ω, $\boldsymbol{f}$ is well-defined.

Observe that for all $t \in I$,

$$\begin{aligned} \boldsymbol{h}(t) &= \boldsymbol{f}_t(t) && \text{(Definition of } \boldsymbol{f}_t\text{)} \\ &= \boldsymbol{f}(t) && (I \subset \Omega \text{ and definition of } \boldsymbol{f}). \end{aligned}$$

Claim: $\boldsymbol{f}$ is an $\mathcal{E}$-process on Ω. From the definitions of Ω and $\boldsymbol{f}$, for all $t \in \Omega$, there exists $a \in I$ such that $t \in \widehat{D}_a$ and for all $s \in \widehat{D}_a$, $\boldsymbol{f}(s) = \boldsymbol{f}_a(s)$. Since $\boldsymbol{f}_a$ is an $\mathcal{E}$-process on $\widehat{D}_a$, the claim follows. □

In Theorem 2.4.5, we prove that if $\mathcal{E}$ is a finite, physical event-system, then $\mathcal{E}$-processes that begin at positive (respectively non-negative) points remain positive (respectively non-negative) through all forward real time where they are defined. In fact, Theorem 2.4.5

establishes more detail about $\mathcal{E}$-processes. In particular, if at some time a species' concentration is positive, then it will be positive at subsequent times.

Theorem 2.4.5. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n, let $\Omega \subseteq \mathbb{C}$ be open and simply-connected, and let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω. If $I \subseteq \Omega \cap \mathbb{R}_{\geq 0}$ is connected and $0 \in I$ and $\boldsymbol{f}(0)$ is a non-negative point then for $k = 1, 2, \ldots, n$ either:*

1. *For all $t \in I$, $f_k(t) = 0$, or*

2. *For all $t \in I \cap \mathbb{R}_{>0}$, $f_k(t) \in \mathbb{R}_{>0}$.*

The proof of Theorem 2.4.5 is highly technical, and relies on a detailed examination of the vector of polynomials $\boldsymbol{P}_{\mathcal{E}}$. This allows us to show (Lemma 2.4.8) that if $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ is an $\mathcal{E}$-process that at real time t_0 is non-negative, then each f_i is "right non-negative." That is, the Taylor series expansion of f_i around t_0 has real coefficients and the first non-zero coefficient, if any, is positive. Further, (Lemma 2.4.10) if $f_i(t_0) = 0$ and its Taylor series expansion has a non-zero coefficient, then there exists k such that $f_k(t_0) = 0$ and the first derivative of f_k with respect to time is positive at t_0.

Definition 2.4.2. Let $n \in \mathbb{Z}_{>0}$ and let $k \in \{1, 2, \ldots, n\}$. A polynomial $f \in \mathbb{R}[X_1, X_2, \ldots, X_n]$ is *non-nullifying with respect to k* iff there exist $m \in \mathbb{N}$, $c_1, c_2, \cdots, c_m \in \mathbb{R}_{>0}$, $M_1, M_2, \ldots, M_m \in \mathbb{M}_{\{X_1, X_2, \ldots, X_n\}}$ and $h \in \mathbb{R}[X_1, X_2, \ldots, X_n]$ such that $f = \sum_{i=1}^{m} c_i M_i + X_k h$.

Observe that for all k, the polynomial 0 is non-nullifying with respect to k.

Lemma 2.4.6. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n. Let $\langle P_1, P_2, \ldots, P_n \rangle = \boldsymbol{P}_{\mathcal{E}}$. Then, for all $i \in \{1, 2, \ldots, n\}$, P_i is non-nullifying with respect to i.*

Proof. Let $m = |\mathcal{E}|$. Let $(\gamma_{j,i})_{m\times n} = \Gamma_{\mathcal{E}}$. Since $\mathcal{E}$ is physical, there exist $\sigma_1, \sigma_2, \ldots, \sigma_m$, $\tau_1, \tau_2, \ldots, \tau_m \in \mathbb{R}_{>0}$ and $M_1, M_2, \ldots, M_m, N_1, N_2, \ldots, N_m \in \mathbb{M}_\infty$ such that for $j = 1, 2, \ldots, m : M_j \prec N_j$ and $\{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2, \tau_2 N_2, \ldots, \sigma_m M_m - \tau_m N_m\} = \mathcal{E}$. Let $i \in \{1, 2, \ldots, n\}$.

From the definition of $\boldsymbol{P}_{\mathcal{E}}$, $P_i = \sum_{j=1}^{m} \gamma_{j,i}(\sigma_j M_j - \tau_j N_j)$. It is sufficient to prove that for $j = 1, 2, \ldots, m : \gamma_{j,i}(\sigma_j M_j - \tau_j N_j)$ is non-nullifying with respect to i. Let $j \in \{1, 2, \ldots, m\}$. If $\gamma_{j,i} = 0$ then $\gamma_{j,i}(\sigma_j M_j - \tau_j N_j) = 0$ which is non-nullifying with respect to i. If $\gamma_{j,i} > 0$ then, from the definition of $\Gamma_{\mathcal{E}}$, $X_i \mid N_j$ and

$$\gamma_{j,i}(\sigma_j M_j - \tau_j N_j) = \gamma_{j,i}\sigma_j M_j + X_i \left(-\gamma_{j,i}\tau_j \frac{N_j}{X_i}\right)$$

which is non-nullifying with respect to i since $\gamma_{j,i}\sigma_j > 0$. Similarly, if $\gamma_{j,i} < 0$ then $X_i \mid M_j$ and

$$\gamma_{j,i}(\sigma_j M_j - \tau_j N_j) = -\gamma_{j,i}\tau_j N_j + X_i \gamma_{j,i}\sigma_j \frac{M_j}{X_i}$$

which is non-nullifying with respect to i since $-\gamma_{j,i}\tau_j > 0$. Hence, P_i is non-nullifying with respect to i. $\square$

Definition 2.4.3. Let $t_0 \in \mathbb{C}$, let $f : \mathbb{C} \to \mathbb{C}$ be analytic at t_0 and let $f(t) = \sum_{k=0}^{\infty} c_k (t - t_0)^k$ be the Taylor series expansion of f around t_0. Then $O(f, t_0)$ is the least k such that $c_k \neq 0$. If for all k, $c_k = 0$, then $O(f, t_0) = \infty$.

Definition 2.4.4 (Right non-negative)**.** Let $t_0 \in \mathbb{R}$, let $f : \mathbb{C} \to \mathbb{C}$ be analytic at t_0 and let $f(t) = \sum_{k=0}^{\infty} c_k (t - t_0)^k$ be the Taylor series expansion of f around t_0. Then f is *RNN at* t_0 iff both:

1. For all $k \in \mathbb{N}$, $c_k \in \mathbb{R}$ and

2. Either $O(f, t_0) = \infty$ or $c_{O(f,t_0)} \in \mathbb{R}_{>0}$.

Lemma 2.4.7. *Let $t_0 \in \mathbb{C}$. Let $f, g : \mathbb{C} \to \mathbb{C}$ be functions analytic at t_0. Then:*

1. $O(f \cdot g, t_0) = O(f, t_0) + O(g, t_0)$.

2. If $t_0 \in \mathbb{R}$ and f, g are RNN at t_0 then $f \cdot g$ is RNN at t_0.

The proof is obvious.

Lemma 2.4.8. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n, let $\Omega \subseteq \mathbb{C}$ be open and simply-connected and let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω. For all $t_0 \in \Omega \cap \mathbb{R}$, if $\boldsymbol{f}(t_0) \in \mathbb{R}^n_{\geq 0}$ then for $i = 1, 2, \ldots, n : f_i$ is RNN at t_0.*

Proof. Suppose $t_0 \in \Omega \cap \mathbb{R}$ and $\boldsymbol{f}(t_0) \in \mathbb{R}^n_{\geq 0}$. Let $\boldsymbol{P} = \langle P_1, P_2, \ldots, P_n \rangle = \boldsymbol{P}_{\mathcal{E}}$. Let $C = \{i \mid f_i \text{ is not RNN at } t_0\}$.

For the sake of contradiction, suppose $C \neq \varnothing$. Let $m = \min_{i \in C} O(f_i, t_0)$. Let $k \in C$ be such that $O(f_k, t_0) = m$. Let $f_k(t) = \sum_{i=0}^{\infty} a_i (t - t_0)^i$ be the Taylor series expansion of f_k around t_0. Since $\mathcal{E}$ is physical and $t_0 \in \mathbb{R}$ and $\boldsymbol{f}(t_0) \in \mathbb{R}^n_{\geq 0}$, it follows from Lemma 2.4.1.2 that for all $i \in \mathbb{N}$, $a_i \in \mathbb{R}$. Further:

$$a_0 = a_1 = \ldots = a_{m-1} = 0 \qquad (O(f_k, t_0) = m.) \tag{2.2}$$

$$a_m \in \mathbb{R}_{<0} \qquad (f_k \text{ is not RNN at } t_0.) \tag{2.3}$$

Since $\boldsymbol{f}(t_0) \in \mathbb{R}^n_{\geq 0}$ and $a_m \in \mathbb{R}_{<0}$ and $a_0 = f_k(t_0)$, it follows that $m > 0$.

Consider $f_k' = P_k \circ \boldsymbol{f}$. By differentiation, the Taylor series expansion of f_k' at t_0 is:

$$f_k'(t) = \sum_{i=0}^{\infty}(i+1)a_{i+1}(t-t_0)^i. \tag{2.4}$$

From Lemma 2.4.6, P_k is non-nullifying. Hence, there exist $l \in \mathbb{N}$, $b_1, b_2, \dots, b_l \in \mathbb{R}_{>0}$, $M_1, M_2, \dots, M_l \in \mathbb{M}_{\{X_1, X_2, \dots, X_n\}}$ and $h \in \mathbb{R}[X_1, X_2, \dots, X_n]$ such that $P_k = \sum_{j=1}^{l} b_j M_j + X_k \cdot h$. Then for all $t \in \Omega$:

$$f_k'(t) = P_k \circ \boldsymbol{f}(t) = \sum_{j=1}^{l} b_j M_j \circ \boldsymbol{f}(t) + f_k(t) \cdot (h \circ \boldsymbol{f}(t)) \tag{2.5}$$

Since h is a polynomial, $h \circ \boldsymbol{f}$ is analytic at t_0. Therefore, $f_k \cdot (h \circ \boldsymbol{f})$ is analytic at t_0. Let $\sum_{i=0}^{\infty} c_i (t-t_0)^i$ be the Taylor series expansion of $f_k \cdot (h \circ \boldsymbol{f})$ at t_0. Similarly, for $j = 1, 2, \dots, l$, $b_j M_j \circ \boldsymbol{f}$ is analytic at t_0. Let $\sum_{i=0}^{\infty} d_{j,i}(t-t_0)^i$ be the Taylor series expansion of $b_j M_j \circ \boldsymbol{f}$ at t_0. From (2.4),(2.5), equating Taylor series coefficients, for $i = 0, 1, \dots, m-1$:

$$(i+1)a_{i+1} = c_i + \sum_{j=1}^{l} d_{j,i} \tag{2.6}$$

From Lemma 2.4.7.1,

$$O(f_k \cdot (h \circ \boldsymbol{f}), t_0) = O(f_k, t_0) + O(h \circ \boldsymbol{f}, t_0) \geq O(f_k, t_0) = m$$

Hence,

$$c_0 = c_1 = \ldots = c_{m-1} = 0. \tag{2.7}$$

From (2.2), (2.6), (2.7), for $i = 0, 1, \ldots, m-2$:

$$\sum_{j=1}^{l} d_{j,i} = 0 \tag{2.8}$$

Since $m > 0$, from (2.3), (2.6), (2.7):

$$\sum_{j=1}^{l} d_{j,m-1} = ma_m \in \mathbb{R}_{<0} \tag{2.9}$$

Let $i_0 = \min_{j=1,2,\ldots,l}\{O(b_j M_j \circ \boldsymbol{f}, t_0)\}$. From (2.9), it follows that $i_0 \le m-1$.

Case 1: For $j = 1, 2, \ldots, l : d_{j,i_0} \in \mathbb{R}_{\ge 0}$. From the definition of i_0 it follows that $\sum_{j=1}^{l} d_{j,i_0} \in \mathbb{R}_{>0}$. If $i_0 < m-1$, this contradicts (2.8). If $i_0 = m-1$, this contradicts (2.9).

Case 2: There exists $j_0 \in \{1, 2, \ldots, l\}$ such that $d_{j_0,i_0} \in \mathbb{R}_{<0}$. From the definition of i_0, $O(b_{j_0} M_{j_0}, t_0) = i_0 \le m-1$. Therefore, for each i such that $X_i \mid M_{j_0}$, $O(f_i, t_0) \le m-1$. From the definitions of C and m, this implies that for each i such that $X_i \mid M_{j_0}$, f_i is RNN at t_0. Since $b_{j_0} \in \mathbb{R}_{>0}$, it follows that $b_{j_0} M_{j_0} \circ \boldsymbol{f}$ is a product of RNN functions. Hence, by Lemma 2.4.7.2, $b_{j_0} M_{j_0} \circ \boldsymbol{f}$ is RNN at t_0 and $d_{j_0,i_0} \in \mathbb{R}_{>0}$, a contradiction.

Hence, for $i = 1, 2, \ldots, n$, f_i is RNN at t_0. $\square$

Lemma 2.4.9. *Let $t_0 \in \mathbb{R}$ and let f be a function RNN at t_0. There exists an $\varepsilon \in \mathbb{R}_{>0}$ such that either for all $t \in (t_0, t_0+\varepsilon)$, $f(t) \in \mathbb{R}_{>0}$ or for all $t \in (t_0, t_0+\varepsilon)$, $f(t) = 0$.*

Proof. Let $m = O(f, t_0)$. If $m = \infty$, f is identically zero and the lemma follows immediately. Otherwise, let $f^{(m)}$ denote the m^{th} derivative of f. Since f is RNN at t_0 and has order m, $f^{(m)}(t_0) \in \mathbb{R}_{>0}$. Since f is analytic at t_0, $f^{(m)}$ is analytic at t_0, and hence continuous at t_0. By continuity, there exists $\varepsilon \in \mathbb{R}_{>0}$ such that for all $\tau \in [t_0, t_0+\varepsilon] : f^{(m)}(\tau) \in \mathbb{R}_{>0}$. From Taylor's theorem, for all $t \in (t_0, t_0+\varepsilon)$, there exists $\tau \in [t_0, t_0+\varepsilon]$ such that:

$$f(t) = \frac{(t-t_0)^m}{m!} f^{(m)}(\tau)$$

Therefore, $f(t) \in \mathbb{R}_{>0}$. $\square$

Note that Lemma 2.4.8 and Lemma 2.4.9 together already imply that if $\mathcal{E}$ is a finite, physical event-system, then $\mathcal{E}$-processes that begin at non-negative points remain non-negative through all forward real time where they are defined. This result is weaker than Theorem 2.4.5.

Lemma 2.4.10. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n, let $\Omega \subseteq \mathbb{C}$ be open and simply-connected, let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω. Let $t_0 \in \Omega$. If $\boldsymbol{f}(t_0)$ is non-negative and there exists $j \in \{1, 2, \ldots, n\}$ such that $0 < O(f_j, t_0) < \infty$ then there exists $k \in \{1, 2, \ldots, n\}$ such that $O(f_k, t_0) = 1$.*

Proof. Suppose $\boldsymbol{f}(t_0) \in \mathbb{R}^n_{\geq 0}$. Let $C = \{i \mid 0 < O(f_i, t_0) < \infty\}$. Suppose $C \neq \varnothing$. Let $m = \min_{i \in C} O(f_i, t_0)$. There exists $k \in C$ such that $O(f_k, t_0) = m$.

Let $\boldsymbol{P} = \langle P_1, P_2, \ldots, P_n \rangle = \boldsymbol{P}_{\mathcal{E}}$. From Lemma 2.4.6, P_k is non-nullifying with respect to k. Hence, there exist $l \in \mathbb{N}$, $b_1, b_2, \ldots, b_l \in \mathbb{R}_{>0}$, $M_1, M_2, \ldots, M_l \in \mathbb{M}_{\{X_1, X_2, \ldots, X_n\}}$ and $h \in \mathbb{R}[X_1, X_2, \ldots, X_n]$ such that $P_k = \sum_{j=1}^{l} b_j M_j + X_k \cdot h$.

For all $t \in \Omega$: $f_k'(t) = P_k \circ \boldsymbol{f}(t) = \sum_{j=1}^{l} b_j M_j \circ \boldsymbol{f}(t) + f_k(t) \cdot (h \circ \boldsymbol{f}(t))$. From Lemma 2.4.7.1, $O(f_k \cdot (h \circ \boldsymbol{f}), t_0) = O(f_k, t_0) + O(h \circ \boldsymbol{f}, t_0) \geq O(f_k, t_0) = m$. It follows that:

$$m - 1 = O(f_k', t_0) = O(\sum_{j=1}^{l} b_j M_j \circ \boldsymbol{f}, t_0) \tag{2.10}$$

From Lemma (2.4.7.2) and Lemma (2.4.8), for $j = 1, 2, \ldots, l : b_j M_j \circ \boldsymbol{f}$ is RNN at t_0. It follows that $O(\sum_{j=1}^{l} b_j M_j \circ \boldsymbol{f}, t_0) = \min_{j=1,2,\ldots,l} O(b_j M_j \circ \boldsymbol{f}, t_0)$. From Equation (2.10), $m - 1 = \min_{j=1,2,\ldots,l} O(b_j M_j \circ \boldsymbol{f}, t_0)$. Hence, there exists j_0 such that $O(b_{j_0} M_{j_0} \circ \boldsymbol{f}, t_0) = m - 1$. From Lemma (2.4.7.1), for all i such that $X_i \mid M_{j_0}$, $O(f_i, t_0) \leq m - 1$. From the definition of m, for all i such that $X_i \mid M_{j_0}$, $O(f_i, t_0) = 0$. It follows that $m - 1 = O(b_{j_0} M_{j_0} \circ \boldsymbol{f}, t_0) = 0$. Hence, $m = 1$. $\square$

We are now ready to prove Theorem 2.4.5.

Proof of Theorem 2.4.5. Suppose $I \subseteq \Omega \cap \mathbb{R}_{\geq 0}$ is connected and $0 \in I$ and $\boldsymbol{f}(0)$ is a non-negative point. If $I \cap \mathbb{R}_{>0} = \varnothing$, the theorem is immediate. Suppose $I \cap \mathbb{R}_{>0} \neq \varnothing$.

It is clear that for all k, $O(f_k, 0) = \infty$ iff for all $t \in I$, $f_k(t) = 0$. Let $C = \{i \mid O(f_i, 0) \neq \infty\}$. From Lemma (2.4.8) and Lemma (2.4.9), for all $k \in C$, there exists $\varepsilon_k \in I \cap \mathbb{R}_{>0}$ such that for all $t \in (0, \varepsilon_k) : f_k(t) \in \mathbb{R}_{>0}$.

Suppose for the sake of contradiction that there exist $i \in C$ and $t \in I \cap \mathbb{R}_{>0}$ such that $f_i(t) \notin \mathbb{R}_{>0}$. From Lemma (2.4.2), $f_i(t) \in \mathbb{R}$. Since $f_i(\varepsilon_i/2) \in \mathbb{R}_{>0}$ and $f_i(t) \in \mathbb{R}_{\leq 0}$, by continuity there exists $t' \in I \cap \mathbb{R}_{>0}$ such that $f_i(t') = 0$.

Let $t_0 = \inf\{t \in I \cap \mathbb{R}_{>0} \mid \text{There exists } i \in C \text{ with } f_i(t) = 0\}$. It follows that:

1. $t_0 \in \mathbb{R}_{>0}$ because $t_0 \geq \min_{i \in C}\{\varepsilon_i\}$.

2. $\boldsymbol{f}(t_0) \in \mathbb{R}^n_{\geq 0}$, from the definition of t_0.

3. There exists $i_1 \in C$ such that $O(f_{i_1}, t_0) = 1$. This follows because there exist $i_0 \in C$ and $T \subseteq I \cap \mathbb{R}_{>0}$ such that $t_0 = \inf(T)$ and for all $t \in T$: $f_{i_0}(t) = 0$. By continuity, $f_{i_0}(t_0) = 0$. Hence, $O(f_{i_0}, t_0) > 0$. Since $i_0 \in C$, $O(f_{i_0}, 0) \neq \infty$. By connectedness of I, $O(f_{i_0}, t_0) \neq \infty$. Therefore, $0 < O(f_{i_0}, t_0) < \infty$. Since $\boldsymbol{f}(t_0) \in \mathbb{R}^n_{\geq 0}$, by Lemma (2.4.10), there exists $i_1 \in \{1, 2, \ldots, n\}$ such that $O(f_{i_1}, t_0) = 1$. Assume $i_1 \notin C$. Then $O(f_{i_1}, 0) = \infty$. By connectedness of I, $O(f_{i_1}, t_0) = \infty$, contradicting that $O(f_{i_1}, t_0) = 1$. Hence, $i_1 \in C$.

Hence, $f_{i_1}(t_0) = 0$. Since $\boldsymbol{f}(t_0) \in \mathbb{R}^n_{\geq 0}$, by Lemma (2.4.8) $f'_{i_1}(t_0) \in \mathbb{R}_{>0}$.

From the definition of t_0, for all $t \in (0, t_0)$, $f_{i_1}(t) \in \mathbb{R}_{>0}$. Since $t_0 \in \mathbb{R}_{>0}$,

$$f'_{i_1}(t_0) = \lim_{h \to 0^+} \frac{f_{i_1}(t_0) - f_{i_1}(t_0 - h)}{h} = \lim_{h \to 0^+} \frac{-f_{i_1}(t_0 - h)}{h} \in \mathbb{R}_{\leq 0},$$

a contradiction. The theorem follows. □

There is a notion in chemistry that, for systems of chemical reactions, concentrations evolve through time to reach equilibrium. In later sections of this paper, we will investigate this notion. In the remainder of this section of the paper, we will prepare for that investigation.

Definition 2.4.5. Let $\mathcal{E}$ be a finite event-system of dimension n, let $\Omega \subseteq \mathbb{C}$ be open, simply connected and such that $\mathbb{R}_{\geq 0} \subseteq \Omega$, let $\boldsymbol{f}$ be an $\mathcal{E}$-process on Ω, and let $\boldsymbol{q} \in \mathbb{C}^n$. Then $\boldsymbol{q}$ is an *ω-limit point of $\boldsymbol{f}$* iff for all $\varepsilon \in \mathbb{R}_{>0}$ there exists a sequence of non-negative reals $\{t_i\}_{i \in \mathbb{Z}_{>0}}$ such that $t_i \to \infty$ as $i \to \infty$ and for all $i \in \mathbb{Z}_{>0}$, $\|\boldsymbol{f}(t_i) - \boldsymbol{q}\|_2 < \varepsilon$.

Sometimes, an ω-limit is defined by the existence of a single sequence of times such that the value approaches the limit. The above definition is easily seen to be equivalent.

Definition 2.4.6. Let $\mathcal{E}$ be a finite event-system of dimension n and let $S \subseteq \mathbb{C}^n$. S is an *invariant set of $\mathcal{E}$* iff for all $\boldsymbol{q} \in S$, for all open, simply-connected $\Omega \subseteq \mathbb{C}$, for all $\mathcal{E}$-processes $\boldsymbol{f}$ on Ω, if $0 \in \Omega$ and $\boldsymbol{f}(0) = \boldsymbol{q}$ then for all $t \in \mathbb{R}_{\geq 0}$ such that $[0, t] \subseteq \Omega$, $\boldsymbol{f}(t) \in S$.

Lemma 2.4.11. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n, let $\Omega \subseteq \mathbb{C}$ be open and simply connected, and let $\boldsymbol{f}$ be an $\mathcal{E}$-process on Ω. If $\mathbb{R}_{\geq 0} \subseteq \Omega$ and $\boldsymbol{f}(0)$ is a non-negative point, then the set of all ω-limit points of $\boldsymbol{f}$ is an invariant set of $\mathcal{E}$ and is contained in $\mathbb{R}^n_{\geq 0}$.*

Proof. Let S be the set of all ω-limit points of $\boldsymbol{f}$. By Lemma 2.4.5, for all $t \in \mathbb{R}_{\geq 0}$, $\boldsymbol{f}(t) \in \mathbb{R}^n_{\geq 0}$, hence $S \subseteq \mathbb{R}^n_{\geq 0}$.

Let $\boldsymbol{q} \in S$, let $\widetilde{\Omega} \subseteq \mathbb{C}$ be open, simply-connected, and such that $0 \in \widetilde{\Omega}$, and let $\boldsymbol{h}$ be an $\mathcal{E}$-process on $\widetilde{\Omega}$ such that $\boldsymbol{h}(0) = \boldsymbol{q}$. Suppose $u \in \mathbb{R}_{\geq 0}$ and $[0, u] \subseteq \widetilde{\Omega}$. Since $\mathcal{E}$ is finite and physical, $\boldsymbol{P}_{\mathcal{E}}|_{\mathbb{R}^n}$ can be viewed as a map $\boldsymbol{F} : \mathbb{R}^n \to \mathbb{R}^n$ of class $\mathcal{C}^1$. By Lemma 2.4.2, for all $t \in [0, u]$, $\boldsymbol{h}(t) \in \mathbb{R}^n$, so $\boldsymbol{h}|_{[0,u]}$ can be viewed as a map $\boldsymbol{X} : [0, u] \to \mathbb{R}^n$ such that $\boldsymbol{X}' = \boldsymbol{F}(\boldsymbol{X})$. By [24, p. 147], there exists a neighborhood $U \subset \mathbb{R}^n$ of $\boldsymbol{q}$ and a constant K such that for all $\boldsymbol{\alpha} \in U$, there exists a unique real-$\mathcal{E}$-process $\boldsymbol{\rho}_{\boldsymbol{\alpha}}$ defined on $[0, u]$ with $\boldsymbol{\rho}_{\boldsymbol{\alpha}}(0) = \boldsymbol{\alpha}$ and $\|\boldsymbol{\rho}_{\boldsymbol{\alpha}}(u) - \boldsymbol{h}(u)\|_2 \leq K\|\boldsymbol{\alpha} - \boldsymbol{q}\|_2 \exp(Ku)$. Observe that necessarily $K \in \mathbb{R}_{\geq 0}$. By Lemma 2.4.4 for all $\boldsymbol{\alpha} \in U$ there exists an open, simply-connected $\Omega_{\boldsymbol{\alpha}} \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\boldsymbol{\varrho}_{\boldsymbol{\alpha}}$ on $\Omega_{\boldsymbol{\alpha}}$ such that $[0, u] \subseteq \Omega_{\boldsymbol{\alpha}}$ and for all $t \in [0, u]$, $\boldsymbol{\varrho}_{\boldsymbol{\alpha}}(t) = \boldsymbol{\rho}_{\boldsymbol{\alpha}}(t)$. Therefore, $\|\boldsymbol{\varrho}_{\boldsymbol{\alpha}}(u) - \boldsymbol{h}(u)\|_2 \leq K\|\boldsymbol{\alpha} - \boldsymbol{q}\|_2 \exp(Ku)$.

Let $\varepsilon \in \mathbb{R}_{>0}$ and let $\delta_1, \delta_2 \in \mathbb{R}_{>0}$ be such that $K\delta_1 \exp(Ku) \leq \varepsilon$ and the open ball centered at $\boldsymbol{q}$ of radius δ_2 is contained in U. Let $\delta = \min(\delta_1, \delta_2)$. Since $\boldsymbol{q}$ is an ω-limit point of $\boldsymbol{f}$, there exists a sequence of non-negative reals $\{t_i\}_{i \in \mathbb{Z}_{>0}}$ such that $t_i \to \infty$ as $i \to \infty$ and for all $i \in \mathbb{Z}_{>0}$, $\|\boldsymbol{f}(t_i) - \boldsymbol{q}\|_2 < \delta$. Then for all $i \in \mathbb{Z}_{>0}$, $\boldsymbol{f}(t_i) \in U$, so by Lemma 2.4.3 for all $t \in [0, u]$, $\boldsymbol{f}(t_i + t) = \boldsymbol{\varrho}_{\boldsymbol{f}(t_i)}(t)$. Then

$$\begin{aligned}
\|\boldsymbol{f}(t_i + u) - \boldsymbol{h}(u)\|_2 &= \|\boldsymbol{\varrho}_{\boldsymbol{f}(t_i)}(u) - \boldsymbol{h}(u)\|_2 \\
&\leq K\|\boldsymbol{f}(t_i) - \boldsymbol{q}\|_2 \exp(Ku) \\
&\leq K\delta \exp(Ku) \\
&\leq \varepsilon
\end{aligned}$$

Thus $\boldsymbol{h}(u)$ is an ω-limit point of $\boldsymbol{f}$, so S is an invariant set of $\mathcal{E}$. $\square$

2.5 Finite Natural Event-systems

In this section, we focus on finite, natural event-systems — a subclass of finite, physical event-systems which has much in common with systems of chemical reactions that obey detailed balance.

In chemical reactions, the total bond energy of the reactants minus the total bond energy of the products is a measure of the heat released. For example, in the reaction, $\sigma X_2 - \tau X_1$, $\ln\left(\frac{\sigma}{\tau}\right)$ is taken to be the quantity of heat released. If there are multiple reaction paths that take the same reactants to the same products, then the quantity of heat released along each path must be the same.

The finite, physical event-system $\mathcal{E} = \{2X_2 - X_1, X_2 - X_1\}$ does not behave like a chemical reaction system since, when X_2 is converted to X_1 by the first reaction, $\ln(2)$ units of heat are released; however, when X_2 is converted to X_1 by the second reaction, $\ln(1) = 0$ units of heat are released. When an event-system admits a pair of paths from the same reactants to the same products but with different quantities of heat released, we say that the system has an "energy cycle."

Definition 2.5.1 (Energy cycle)**.** Let $\mathcal{E}$ be a finite, physical event-system. $\mathcal{E}$ has an energy cycle iff $G_{\mathcal{E}}$ has a cycle of non-zero weight.

Example 7. For the physical event-system $\mathcal{E}_1 = \{2X_2 - X_1, X_2 - X_1\}$, the event $X_2 - X_1$ induces an edge $\langle X_2, X_1\rangle$ in the event graph with weight $\ln\left(\frac{1}{1}\right) = 0$. The event $2X_2 - X_1$ induces an edge $\langle X_1, X_2\rangle$ with weight $-\ln\left(\frac{2}{1}\right) = -\ln(2)$. The weight of the cycle from X_2 to X_1 and back to X_2 using these two edges, is $-\ln(2) \neq 0$. Hence, $\mathcal{E}_1$ has an energy cycle by Definition 2.5.1.

Example 8. For the physical event-system $\mathcal{E}_2 = \{X_2 - X_1, 2X_3X_4 - X_2X_3, X_4X_5 - X_1X_5\}$, the cycle $\langle X_3X_4X_5, X_2X_3X_5, X_1X_3X_5, X_3X_4X_5\rangle$ is induced by the sequence of events $2X_3X_4 - X_2X_3, X_2 - X_1, X_4X_5 - X_1X_5$ and has corresponding weight $\ln\frac{2}{1} + \ln\frac{1}{1} + \ln\frac{1}{1} = \ln(2) \neq 0$. Hence, $\mathcal{E}_2$ has an energy cycle.

The following theorem gives multiple characterizations of natural event-systems.

Theorem 2.5.1. *Let $\mathcal{E}$ be a finite, physical event-system of dimension n. The following are equivalent:*

1. *$\mathcal{E}$ is natural.*

2. *$\mathcal{E}$ has a strong equilibrium point that is not a z-point. (i.e. there exists $\boldsymbol{\alpha} \in \mathbb{C}^n$ such that for all $i = 1$ to n, $\alpha_i \neq 0$ and for all $e \in \mathcal{E}$, $e(\boldsymbol{\alpha}) = 0$.)*

3. *$\mathcal{E}$ has no energy cycles.*

4. *If $\mathcal{E} = \{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2 - \tau_2 N_2, \ldots, \sigma_m M_m - \tau_m N_m\}$ and for all $j = 1$ to m, $M_j \prec N_j$ and $\sigma_j, \tau_j > 0$ then there exists $\boldsymbol{\alpha} \in \mathbb{R}^n$ such that $\Gamma_{\mathcal{E}}\boldsymbol{\alpha} = \left\langle \ln\left(\frac{\sigma_1}{\tau_1}\right), \ldots, \ln\left(\frac{\sigma_m}{\tau_m}\right)\right\rangle^T$.*

To prove Theorem 2.5.1, we will use the following lemma.

Lemma 2.5.2. *Let $\mathcal{E} = \{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2 - \tau_2 N_2, \ldots, \sigma_m M_m - \tau_m N_m\}$ be a finite, physical event-system of dimension n such that for all $j = 1$ to m, $\sigma_j, \tau_j > 0$ and $M_j \prec N_j$. Then for all $\boldsymbol{\alpha} = \langle \alpha_1, \alpha_2, \ldots, \alpha_n\rangle^T \in \mathbb{R}^n$, $\Gamma_{\mathcal{E}} \cdot \boldsymbol{\alpha} = \left\langle \ln\left(\frac{\sigma_1}{\tau_1}\right), \ln\left(\frac{\sigma_2}{\tau_2}\right), \ldots, \ln\left(\frac{\sigma_m}{\tau_m}\right)\right\rangle^T$ iff $\langle e^{\alpha_1}, \cdots, e^{\alpha_n}\rangle$ is a positive strong $\mathcal{E}$-equilibrium point.*

Proof. Let $\mathcal{E} = \{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2 - \tau_2 N_2, \ldots, \sigma_m M_m - \tau_m N_m\}$ and for all $j = 1$ to m, $M_j \prec N_j$ and $\sigma_j, \tau_j > 0$. Let $\Gamma = \Gamma_{\mathcal{E}}$. For all $\boldsymbol{\alpha} = \langle \alpha_1, \ldots, \alpha_n \rangle \in \mathbb{R}^n$,

$$\Gamma\boldsymbol{\alpha} = \left\langle \ln\left(\frac{\sigma_1}{\tau_1}\right), \ln\left(\frac{\sigma_2}{\tau_2}\right), \ldots, \ln\left(\frac{\sigma_m}{\tau_m}\right) \right\rangle^T$$

$$\Leftrightarrow \sum_{i=1}^{n} \gamma_{j,i}\alpha_i = \ln\left(\sigma_j/\tau_j\right), \forall j = 1, 2, \ldots, m$$

$$\Leftrightarrow \prod_{i=1}^{n} \left(\mathrm{e}^{\alpha_i}\right)^{\gamma_{j,i}} = \sigma_j/\tau_j, \forall j = 1, 2, \ldots, m \qquad \text{(Exponentiation.)}$$

$$\Leftrightarrow N_j\left(\langle \mathrm{e}^{\alpha_1}, \ldots, \mathrm{e}^{\alpha_n} \rangle\right) / M_j\left(\langle \mathrm{e}^{\alpha_1}, \ldots, \mathrm{e}^{\alpha_n} \rangle\right) = \sigma_j/\tau_j, \forall j = 1, 2, \ldots, m \qquad \text{(Definition of } \Gamma.)$$

$$\Leftrightarrow \sigma_j M_j\left(\langle \mathrm{e}^{\alpha_1}, \ldots, \mathrm{e}^{\alpha_n} \rangle\right) - \tau_j N_j\left(\langle \mathrm{e}^{\alpha_1}, \ldots, \mathrm{e}^{\alpha_n} \rangle\right) = 0, \forall j = 1, 2, \ldots, m$$

$\Leftrightarrow \langle \mathrm{e}^{\alpha_1}, \ldots, \mathrm{e}^{\alpha_n} \rangle$ is a positive strong $\mathcal{E}$-equilibrium point.

□

Proof of Theorem 2.5.1. **(4) ⇒ (1)** : Follows from Lemma 2.5.2.

(1) ⇒ (2) : Follows immediately from definitions.

(2) ⇒ (3) :

Consider an arbitrary cycle $\mathcal{C}$ in $G_{\mathcal{E}}$ given by the sequence of k edges $\{\langle v_0, v_1 \rangle, \langle v_1, v_2 \rangle, \ldots, \langle v_{k-1}, v_k = v_0 \rangle\}$ with corresponding weights $r_1, r_2, \ldots, r_k$. By Definition 2.2.8, for $i = 1, 2, \ldots, k$, there exist $T_i \in \mathbb{M}_\infty$ and $e_i \in \mathcal{E}$ with $e_i = \sigma_i M_i - \tau_i N_i$ where $\sigma_i, \tau_i > 0$ and $M_i, N_i \in \mathbb{M}_\infty$ and $M_i \prec N_i$ such that either

1) $v_{i-1} = T_i M_i$ and $v_i = T_i N_i$ and $r_i = \ln \frac{\sigma_i}{\tau_i} \in w\left(\langle v_{i-1}, v_i \rangle\right)$ or

2) $v_{i-1} = T_i N_i$ and $v_i = T_i M_i$ and $r_i = -\ln \frac{\sigma_i}{\tau_i} \in w(\langle v_{i-1}, v_i \rangle)$

Hence, there exists a vector $\boldsymbol{b} = \langle b_1, b_2, \ldots, b_k \rangle$ with $b_i = 0$ or 1 such that:

$$\prod_{i=1}^{k} M_i^{b_i} N_i^{1-b_i} = \prod_{i=1}^{k} M_i^{1-b_i} N_i^{b_i} \tag{2.11}$$

$$w(\mathcal{C}) = \sum_{i=1}^{k} r_i = \sum_{i=1}^{k} (2b_i - 1) \ln \left(\frac{\sigma_i}{\tau_i} \right) \tag{2.12}$$

Let $\boldsymbol{\alpha}$ be a strong equilibrium point of $\mathcal{E}$ that is not a z-point. Then, by Definition 2.2.6, for $i = 1$ to k, $\sigma_i M_i(\boldsymbol{\alpha}) - \tau_i N_i(\boldsymbol{\alpha}) = 0$

$\Rightarrow \sigma_i M_i(\boldsymbol{\alpha}) = \tau_i N_i(\boldsymbol{\alpha})$ for $i = 1$ to k

$\Rightarrow (\sigma_i M_i(\boldsymbol{\alpha}))^{b_i} = (\tau_i N_i(\boldsymbol{\alpha}))^{b_i}$ and $(\tau_i N_i(\boldsymbol{\alpha}))^{1-b_i} = (\sigma_i M_i(\boldsymbol{\alpha}))^{1-b_i}$ for $i = 1$ to k

$\Rightarrow (\sigma_i M_i(\boldsymbol{\alpha}))^{b_i} (\tau_i N_i(\boldsymbol{\alpha}))^{1-b_i} = (\sigma_i M_i(\boldsymbol{\alpha}))^{1-b_i} (\tau_i N_i(\boldsymbol{\alpha}))^{b_i}$ for $i = 1$ to k

$\Rightarrow \prod_{i=1}^{k} (\sigma_i M_i(\boldsymbol{\alpha}))^{b_i} (\tau_i N_i(\boldsymbol{\alpha}))^{1-b_i} = \prod_{i=1}^{k} (\sigma_i M_i(\boldsymbol{\alpha}))^{1-b_i} (\tau_i N_i(\boldsymbol{\alpha}))^{b_i}$

$\Rightarrow \prod_{i=1}^{k} {\sigma_i}^{b_i} {\tau_i}^{1-b_i} = \prod_{i=1}^{k} {\sigma_i}^{1-b_i} {\tau_i}^{b_i}$ [From Equation (1) and since $\boldsymbol{\alpha}$ is not a z-point]

$\Rightarrow \prod_{i=1}^{k} \frac{{\sigma_i}^{b_i} {\tau_i}^{1-b_i}}{{\sigma_i}^{1-b_i} {\tau_i}^{b_i}} = 1$

$\Rightarrow \sum_{i=1}^{k} (2b_i - 1) \ln \left(\frac{\sigma_i}{\tau_i} \right) = 0$ [Taking logarithm]

$\Rightarrow w(\mathcal{C}) = 0$ [From Equation (2)]

Hence, $\mathcal{E}$ has no energy cycle.

(3) $\Rightarrow$ (4) :

Let $\mathcal{E} = \{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2 - \tau_2 N_2, \ldots, \sigma_m M_m - \tau_m N_m\}$ and for all $j = 1$ to m, $M_j \prec N_j$ and $\sigma_j, \tau_j > 0$. Let $\Gamma = \Gamma_{\mathcal{E}}$. We shall prove that if the linear equation $\Gamma \boldsymbol{\alpha} = \langle \ln(\sigma_1/\tau_1), \ldots, \ln(\sigma_m/\tau_m) \rangle^T$ has no solution in $\mathbb{R}^n$ then $\mathcal{E}$ has an energy cycle. For $j = 1$ to m, let Γ_j be the j^{th} row of Γ. If the system of linear equations $\Gamma \boldsymbol{\alpha} = \langle \ln(\sigma_1/\tau_1), \ldots, \ln(\sigma_m/\tau_m) \rangle^T$ has no solution in $\mathbb{R}^n$ then, from linear algebra [25,

p. 164, Theorem] and the fact that Γ is a matrix of integers, it follows that there exists l, there exist (not necessarily distinct) integers $j_1, j_2, \ldots, j_l \in \{1, 2, \ldots, m\}$, there exist $a_1, a_2, \ldots, a_l \in \{+1, -1\}$ such that:

$$a_1\Gamma_{j_1} + a_2\Gamma_{j_2} + \cdots + a_l\Gamma_{j_l} = \mathbf{0} \tag{2.13}$$

$$a_1 \ln(\sigma_{j_1}/\tau_{j_1}) + a_2 \ln(\sigma_{j_2}/\tau_{j_2}) + \cdots + a_l \ln(\sigma_{j_l}/\tau_{j_l}) \neq 0 \tag{2.14}$$

Consider the sequence $\mathcal{C}$ of $l+1$ vertices in the event-graph defined recursively by

$$v_0 = \prod_{i=1, a_i=+1}^{l} M_{j_i} \prod_{i=1, a_i=-1}^{l} N_{j_i}$$

and for $i = 1$ to l,

$$v_i = \frac{v_{i-1} N_{j_i}^{a_i}}{M_{j_i}^{a_i}}$$

Observe that by (3),

$$\prod_{i=1}^{l} \left(\frac{N_{j_i}}{M_{j_i}} \right)^{a_i} = 1$$

Hence,

$$v_0 = \prod_{i=1, a_i=+1}^{l} M_{j_i}^{a_i} \prod_{i=1, a_i=-1}^{l} N_{j_i}^{-a_i} = \prod_{i=1, a_i=+1}^{l} N_{j_i}^{a_i} \prod_{i=1, a_i=-1}^{l} M_{j_i}^{-a_i} = v_l$$

Hence, $\mathcal{C}$ is a cycle. Further, for $i = 1$ to l,

$a_i \ln \frac{\sigma_{j_i}}{\tau_{j_i}} \in w\left(\langle v_{i-1}, v_i\rangle\right)$

From Equation (4),

$$w\left(\mathcal{C}\right) = a_1 \ln\left(\sigma_{j_1}/\tau_{j_1}\right) + a_2 \ln\left(\sigma_{j_2}/\tau_{j_2}\right) + \cdots + a_l \ln\left(\sigma_{j_l}/\tau_{j_l}\right) \neq 0$$

Hence, $\mathcal{C}$ is an energy cycle. $\square$

Horn and Jackson [17] and Feinberg [12] have proved that chemical reaction networks with appropriate properties admit Lyapunov functions. While finite, natural event-systems are closely related to the chemical reaction networks considered by Horn and Jackson and by Feinberg, they are not identical. Consequently, we will prove the existence of Lyapunov functions for finite, natural event-systems (Theorem 2.5.6).

The Lyapunov function is analogous in form and properties to "Entropy of the Universe" in thermodynamics. The Lyapunov function composed with an event-process is monotonic with respect to time, providing an analogy to the second law of thermodynamics.

Definition 2.5.2. Let $\mathcal{E}$ be a finite, natural event-system of dimension n with positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c} = \langle c_1, c_2, \ldots, c_n\rangle$. Then $g_{\mathcal{E},\boldsymbol{c}} : \mathbb{R}^n_{>0} \to \mathbb{R}$ is given by

$$g_{\mathcal{E},\boldsymbol{c}}\left(x_1, x_2, \ldots, x_n\right) = \sum_{i=1}^{n} \left(x_i \left(\ln\left(x_i\right) - 1 - \ln\left(c_i\right)\right) + c_i\right)$$

The function $g_{\mathcal{E},\boldsymbol{c}}$ will turn out to be the desired Lyapunov function.

Note that if $\mathcal{E}_1$ and $\mathcal{E}_2$ are two finite natural event-systems of the same dimension and if $\boldsymbol{c}$ is a positive strong $\mathcal{E}_1$-equilibrium point as well as a positive strong $\mathcal{E}_2$-equilibrium point, then the functions $g_{\mathcal{E}_1,\boldsymbol{c}}$ and $g_{\mathcal{E}_2,\boldsymbol{c}}$ are identical.

Lemma 2.5.3. *Let $\mathcal{E} = \{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2 - \tau_2 N_2, \ldots, \sigma_m M_m - \tau_m N_m\}$ be a finite, natural event-system of dimension n with positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c}$, such that for all $j = 1$ to m, $\sigma_j, \tau_j > 0$ and $M_j \prec N_j$. Then for all $\boldsymbol{x} \in \mathbb{R}^n_{>0}$,*

$$\nabla g_{\mathcal{E},c}(\boldsymbol{x}) \cdot \boldsymbol{P}_{\mathcal{E}}(\boldsymbol{x}) = \sum_{j=1}^{m} \left(\sigma_j M_j(\boldsymbol{x}) - \tau_j N_j(\boldsymbol{x})\right) \ln\left(\frac{\tau_j N_j(\boldsymbol{x})}{\sigma_j M_j(\boldsymbol{x})}\right)$$

Proof. Let $g = g_{\mathcal{E},c}$. Let $\boldsymbol{x} = \langle x_1, x_2, \ldots, x_n\rangle \in \mathbb{R}^n_{>0}$. Let $\boldsymbol{P} = \boldsymbol{P}_{\mathcal{E}}$.

$$\begin{aligned}
\nabla g(\boldsymbol{x}) \cdot \boldsymbol{P}(\boldsymbol{x}) &= \sum_{i=1}^{n} \left(\frac{\partial g}{\partial x_i}(\boldsymbol{x}) \cdot P_i(\boldsymbol{x})\right) \\
&= \sum_{i=1}^{n} \ln\left(\frac{x_i}{c_i}\right) \left(\sum_{j=1}^{m} \gamma_{j,i}\left(\sigma_j M_j(\boldsymbol{x}) - \tau_j N_j(\boldsymbol{x})\right)\right) \\
&= \sum_{j=1}^{m} \left(\sigma_j M_j(\boldsymbol{x}) - \tau_j N_j(\boldsymbol{x})\right) \sum_{i=1}^{n} \ln\left(\left(\frac{x_i}{c_i}\right)^{\gamma_{j,i}}\right) \\
&= \sum_{j=1}^{m} \left(\sigma_j M_j(\boldsymbol{x}) - \tau_j N_j(\boldsymbol{x})\right) \ln\left(\prod_{i=1}^{n} \left(\frac{x_i}{c_i}\right)^{\gamma_{j,i}}\right) \\
&= \sum_{j=1}^{m} \left(\sigma_j M_j(\boldsymbol{x}) - \tau_j N_j(\boldsymbol{x})\right) \ln\left(\frac{\tau_j N_j(\boldsymbol{x})}{\sigma_j M_j(\boldsymbol{x})}\right)
\end{aligned}$$

The last equality follows from the definition of $\Gamma_{\mathcal{E}}$ and the fact that $\boldsymbol{c}$ is a strong-equilibrium point. □

Lemma 2.5.4. *For all $x \in \mathbb{R}_{>0}$, $(1 - x)\ln(x) \leq 0$ with equality iff $x = 1$.*

Proof. If $0 < x < 1$ then $1 - x > 0$ and $\ln(x) < 0$. If $x > 1$ then $1 - x < 0$ and $\ln(x) > 0$. In either case, the product is strictly negative. If $x = 1$ then $(1 - x) \ln(x) = 0$ □

Theorem 2.5.5. *Let $\mathcal{E}$ be a finite, natural event-system of dimension n with positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c}$. Then for all $\boldsymbol{x} \in \mathbb{R}^n_{>0}$, $\nabla g_{\mathcal{E},\boldsymbol{c}}(\boldsymbol{x}) \cdot \boldsymbol{P}_{\mathcal{E}}(\boldsymbol{x}) \leq 0$ with equality iff $\boldsymbol{x}$ is a strong $\mathcal{E}$-equilibrium point.*

Proof. Let $\mathcal{E} = \{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2 - \tau_2 N_2, \ldots, \sigma_m M_m - \tau_m N_m\}$ be a finite, natural event-system of dimension n with positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c}$, such that for all $j = 1$ to m, $\sigma_j, \tau_j > 0$ and $M_j \prec N_j$. Let $\boldsymbol{P} = \boldsymbol{P}_{\mathcal{E}}$ and let $g = g_{\mathcal{E},c}$. By Lemma 2.5.3, for all $\boldsymbol{x} \in \mathbb{R}^n_{>0}$,

$$\nabla g(\boldsymbol{x}) \cdot \boldsymbol{P}(\boldsymbol{x}) = \sum_{j=1}^{m} (\sigma_j M_j(\boldsymbol{x}) - \tau_j N_j(\boldsymbol{x})) \ln\left(\frac{\tau_j N_j(\boldsymbol{x})}{\sigma_j M_j(\boldsymbol{x})}\right)$$

From Lemma 2.5.4 and the observation that for $j = 1, 2, \ldots, m$, $M_j(\boldsymbol{x}), N_j(\boldsymbol{x}) > 0$ when $\boldsymbol{x} \in \mathbb{R}^n_{>0}$ and by assumption $\sigma_j, \tau_j > 0$, we have,

$$\nabla g(\boldsymbol{x}) \cdot \boldsymbol{P}(\boldsymbol{x}) \leq 0$$

with equality iff for all $j = 1, 2, \ldots, m$, $\sigma_j M_j(\boldsymbol{x}) = \tau_j N_j(\boldsymbol{x})$. This occurs iff $\boldsymbol{x}$ is a strong $\mathcal{E}$-equilibrium point. □

Recall that a function g is a Lyapunov function at a point $\boldsymbol{p}$ for a vector field $\boldsymbol{v}$ iff g is smooth, positive definite at $\boldsymbol{p}$ and $L_{\boldsymbol{v}} g$ is negative semi-definite at $\boldsymbol{p}$ [18, p. 131]. For a finite natural event-system $\mathcal{E}$, $\boldsymbol{P}_{\mathcal{E}}$ induces a vector field on $\mathbb{R}^n$. We will show that, if

$\boldsymbol{c}$ is a positive strong $\mathcal{E}$-equilibrium point, then $g_{\mathcal{E},\boldsymbol{c}}$ is a Lyapunov function at $\boldsymbol{c}$ for the vector field induced by $\boldsymbol{P}_{\mathcal{E}}$.

Theorem 2.5.6 (Existence of Lyapunov Function)**.** *Let $\mathcal{E}$ be a finite, natural event-system of dimension n with positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c}$. Then $g_{\mathcal{E},\boldsymbol{c}}$ is a Lyapunov function for the vector field induced by $\boldsymbol{P}_{\mathcal{E}}$ at $\boldsymbol{c}$.*

Proof. Let $g = g_{\mathcal{E},\boldsymbol{c}}$. For $i = 1, 2, \ldots, n$:

$$\frac{\partial g}{\partial x_i} = \ln\left(\frac{x_i}{c_i}\right)$$

which are all in $\mathcal{C}^\infty$ as functions on $\mathbb{R}^n_{>0}$, hence g is in $\mathcal{C}^\infty$.

$$\frac{\partial g}{\partial x_i}(\boldsymbol{c}) = \ln\left(\frac{c_i}{c_i}\right) = 0$$

establishes that $\nabla g(\boldsymbol{c}) = \boldsymbol{0}$. For $i = 1, 2, \ldots, n$, for $k = 1, 2, \ldots, n$:

$$\frac{\partial^2 g}{\partial x_k \partial x_i} = \frac{\delta_{i,k}}{x_i}$$

where $\delta_{i,k}$ is the Kronecker delta function. Hence, for all $\boldsymbol{x} \in \mathbb{R}^n_{>0}$, the Hessian of g at $\boldsymbol{x}$ is positive definite. Therefore, g is strictly convex over $\mathbb{R}^n_{>0}$. Further, $g(\boldsymbol{c}) = 0$ and $\nabla g(\boldsymbol{c}) = \boldsymbol{0}$ and g is strictly convex together imply that g is positive definite at $\boldsymbol{c}$. To establish g as a Lyapunov function, it remains to show that the directional derivative $L_{\boldsymbol{P}}g$ of g in the direction of the vector field induced by $\boldsymbol{P} = \boldsymbol{P}_{\mathcal{E}}$ is negative semi-definite at $\boldsymbol{c}$. This follows from Theorem 2.5.5 since for all $\boldsymbol{x} \in \mathbb{R}^n_{>0}$, $L_{\boldsymbol{P}}g(\boldsymbol{x}) = \nabla g(\boldsymbol{x}) \cdot \boldsymbol{P}(\boldsymbol{x}) \leq 0$. $\square$

Henceforth, the function $g_{\mathcal{E},\boldsymbol{c}}$ will be called the Lyapunov function of $\mathcal{E}$ at $\boldsymbol{c}$. The next theorem shows that finite, natural event-systems satisfy a form of "detailed balance."

Theorem 2.5.7. *If $\mathcal{E}$ is a natural, finite event-system of dimension n then all positive $\mathcal{E}$-equilibrium points are strong $\mathcal{E}$-equilibrium points.*

Proof. Let $\boldsymbol{P} = \boldsymbol{P}_{\mathcal{E}}$. Let $\boldsymbol{c} \in \mathbb{R}^n_{>0}$ be a positive strong $\mathcal{E}$-equilibrium point. Let $\boldsymbol{x}$ be a positive $\mathcal{E}$-equilibrium point. That is, $\boldsymbol{P}(\boldsymbol{x}) = \boldsymbol{0}$. Hence, $\nabla g_{\mathcal{E},\boldsymbol{c}}(\boldsymbol{x}) \cdot \boldsymbol{P}_{\mathcal{E}}(\boldsymbol{x}) = 0$. By Theorem 2.5.5, $\boldsymbol{x}$ is a strong $\mathcal{E}$-equilibrium point. □

The following lemma was proved by Feinberg [12, Proposition B.1].

Lemma 2.5.8. *Let $n > 0$ be an integer. Let U be a linear subspace of $\mathbb{R}^n$, and let $\boldsymbol{a} = \langle a_1, a_2, \ldots, a_n\rangle$ and $\boldsymbol{b}$ be elements of $\mathbb{R}^n_{>0}$. There is a unique element $\boldsymbol{\mu} = \langle \mu_1, \mu_2, \cdots, \mu_n\rangle \in U^{\perp}$ such that $\langle a_1\mathrm{e}^{\mu_1}, a_2\mathrm{e}^{\mu_2}, \ldots, a_n\mathrm{e}^{\mu_n}\rangle - \boldsymbol{b}$ is an element of U.*

The next theorem follows from one proved by Horn and Jackson [17, Lemma 4B]. Our proof is derived from Feinberg's [12, Proposition 5.1].

Theorem 2.5.9. *Let $\mathcal{E}$ be a finite, natural event-system of dimension n. Let H be a positive conservation class of $\mathcal{E}$. Then H contains exactly one positive strong $\mathcal{E}$-equilibrium point.*

Proof. Let $\Gamma = \Gamma_{\mathcal{E}}$. Let $\boldsymbol{c}^* = \langle c_1^*, c_2^*, \ldots, c_n^*\rangle$ be a positive strong $\mathcal{E}$-equilibrium point. Let $\boldsymbol{p} \in H \cap \mathbb{R}^n_{>0}$. For all $\boldsymbol{c} \in \mathbb{R}^n_{>0}$,

(1) $\boldsymbol{c}$ is a strong $\mathcal{E}$-equilibrium point

$\Leftrightarrow \Gamma\langle \ln(c_1), \ln(c_2), \ldots, \ln(c_n)\rangle^T = \Gamma\langle \ln(c_1^*), \ln(c_2^*), \cdots, \ln(c_n^*)\rangle^T$. (Lemma 2.5.2)

$\Leftrightarrow \Gamma \left\langle \ln\left(\frac{c_1}{c_1^*}\right), \ln\left(\frac{c_2}{c_2^*}\right), \ldots, \ln\left(\frac{c_n}{c_n^*}\right)\right\rangle^T = 0$

$\Leftrightarrow$ There exists $\mu = \langle \mu_1, \mu_2, \ldots, \mu_n \rangle \in \ker \Gamma \cap \mathbb{R}^n$ such that

$\left\langle \ln\left(\frac{c_1}{c_1^*}\right), \ln\left(\frac{c_2}{c_2^*}\right), \ldots, \ln\left(\frac{c_n}{c_n^*}\right)\right\rangle^T = \boldsymbol{\mu}.$

$\Leftrightarrow$ There exists $\boldsymbol{\mu} = \langle \mu_1, \mu_2, \ldots, \mu_n \rangle \in \ker \Gamma \cap \mathbb{R}^n$ such that $c_i = c_i^* \mathrm{e}^{\mu_i}$ for $i = 1, 2, \ldots, n$.

(2) $\boldsymbol{c} \in H \cap \mathbb{R}^n \Leftrightarrow \boldsymbol{c} - \boldsymbol{p} \in (\ker \Gamma)^\perp \cap \mathbb{R}^n$. (By Definition 2.3.6)

From (1) and (2), $\boldsymbol{c}$ is a positive strong $\mathcal{E}$-equilibrium point in H iff there exists $\boldsymbol{\mu} \in \ker \Gamma \cap \mathbb{R}^n$ such that $\boldsymbol{c} = \langle c_1^* \mathrm{e}^{\mu_1}, c_2^* \mathrm{e}^{\mu_2}, \ldots, c_n^* \mathrm{e}^{\mu_n} \rangle$ and $\langle c_1^* \mathrm{e}^{\mu_1}, c_2^* \mathrm{e}^{\mu_2}, \ldots, c_n^* \mathrm{e}^{\mu_n} \rangle - \boldsymbol{p} \in (\ker \Gamma)^\perp \cap \mathbb{R}^n$. Applying Lemma 2.5.8 with $\boldsymbol{a} = \boldsymbol{c}^*, \boldsymbol{b} = \boldsymbol{p}$ and $U = (\ker \Gamma)^\perp \cap \mathbb{R}^n$, it follows that there exists a unique $\boldsymbol{\mu}$ of the desired form. Hence, there exists a unique positive strong $\mathcal{E}$-equilibrium point in H given by $\boldsymbol{c} = \langle c_1^* \mathrm{e}^{\mu_1}, c_2^* \mathrm{e}^{\mu_2}, \ldots, c_n^* \mathrm{e}^{\mu_n} \rangle$. □

To prove the main theorem of this section (Theorem 2.5.15), we will first establish several technical lemmas.

Lemma 2.5.10 shows that an event that remains zero at all times along a process can be ignored.

Lemma 2.5.10. *Let $\mathcal{E}$ be a finite event-system of dimension n, let $\Omega \subseteq \mathbb{C}$ be non-empty, open and simply-connected, and let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω. Then either for all $t \in \Omega$, $\boldsymbol{f}(t)$ is a strong $\mathcal{E}$-equilibrium point or there exist a finite event-system $\hat{\mathcal{E}}$ of dimension $\hat{n} \leq n$, an $\hat{\mathcal{E}}$-process $\hat{\boldsymbol{f}} = \langle \hat{f}_1, \hat{f}_2, \ldots, \hat{f}_{\hat{n}} \rangle$ on Ω, and a permutation π on $\{1, 2, \ldots, n\}$ such that:*

1. If $\mathcal{E}$ is physical then $\hat{\mathcal{E}}$ is physical.

2. If $\mathcal{E}$ is natural then $\hat{\mathcal{E}}$ is natural.

3. If $\boldsymbol{c} = \langle c_1, c_2, \ldots, c_n \rangle$ is a positive strong $\mathcal{E}$-equilibrium point, then $\hat{\boldsymbol{c}} = \langle c_{\pi^{-1}(1)}, c_{\pi^{-1}(2)}, \ldots, c_{\pi^{-1}(\hat{n})} \rangle$ is a positive strong $\hat{\mathcal{E}}$-equilibrium point.

4. For all $e \in \hat{\mathcal{E}}$, there exists $t \in \Omega$ such that $e(\hat{\boldsymbol{f}}(t)) \neq 0$.

5. If $\hat{\mathcal{E}}$ is natural, $I \subseteq \Omega \cap \mathbb{R}_{\geq 0}$ is connected, $0 \in I$ and $\boldsymbol{f}(0)$ is a non-negative point then for all $t \in I \cap \mathbb{R}_{>0}$, $\hat{\boldsymbol{f}}(t)$ is a positive point.

6. For $i = 1, 2, \ldots, n$, if $\pi(i) \leq \hat{n}$ then for all $t \in \Omega$, $f_i(t) = \hat{f}_{\pi(i)}(t)$.

7. For $i = 1, 2, \ldots, n$, if $\pi(i) > \hat{n}$ then for all $t_1, t_2 \in \Omega$, $f_i(t_1) = f_i(t_2)$.

Proof. Let $m = |\mathcal{E}|$. Let $\mathcal{E}_1 = \{e \in \mathcal{E} \mid \text{there exists } t \in \Omega, e(\boldsymbol{f}(t)) \neq 0\}$. If $\mathcal{E}_1 = \varnothing$ then for all $t \in \Omega, e(\boldsymbol{f}(t)) = 0$, so $\boldsymbol{f}(t)$ is a strong $\mathcal{E}$-equilibrium point and the Lemma holds. Assume $\mathcal{E}_1 \neq \varnothing$ and let $\hat{m} = |\mathcal{E}_1|$. For $j = 1, 2, \ldots, m$, let $\sigma_j, \tau_j \in \mathbb{R}_{>0}$ and $M_j = \prod_{i=1}^{n} X_i^{a_{j,i}}, N_j = \prod_{i=1}^{n} X_i^{b_{j,i}} \in \mathbb{M}_\infty$ be such that $M_j \prec N_j$ and $\{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2 - \tau_2 N_2, \ldots, \sigma_{\hat{m}} M_{\hat{m}} - \tau_{\hat{m}} N_{\hat{m}}\} = \mathcal{E}_1$ and $\{\sigma_1 M_1 - \tau_1 N_1, \sigma_2 M_2 - \tau_2 N_2, \ldots, \sigma_m M_m - \tau_m N_m\} = \mathcal{E}$.

Let $C = \{i \mid \text{there exists } j \leq \hat{m} \text{ such that either } a_{j,i} \neq 0 \text{ or } b_{j,i} \neq 0\}$. Let $\hat{n} = |C|$. Let π be a permutation on $\{1, 2, \ldots, n\}$ such that $\pi(C) = \{1, 2, \ldots, \hat{n}\}$.

For $j = 1, 2, \ldots, \hat{m}$, let $e_{\pi,j} = \sigma_j \prod_{i=1}^{\hat{n}} X_i^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} X_i^{b_{j,\pi^{-1}(i)}}$. Let $\hat{\mathcal{E}} = \{e_{\pi,1}, e_{\pi,2}, \ldots, e_{\pi,\hat{m}}\}$.

It follows that $\hat{\mathcal{E}}$ is a finite event-system of dimension $\hat{n} \leq n$. For $i = 1, 2, \ldots, \hat{n}$, let $\hat{f}_i = f_{\pi^{-1}(i)}$. Let $\hat{\boldsymbol{f}} = \langle \hat{f}_1, \hat{f}_2, \ldots, \hat{f}_{\hat{n}} \rangle$.

Let $(\gamma_{j,i})_{m\times n} = \Gamma_{\mathcal{E}}$. Let $(\hat{\gamma}_{j,i})_{\hat{m}\times\hat{n}} = \Gamma_{\hat{\mathcal{E}}}$. It follows that for $j = 1, 2, \ldots, \hat{m}$, for $i = 1, 2, \ldots, \hat{n}$,

$$\hat{\gamma}_{j,i} = b_{j,\pi^{-1}(i)} - a_{j,\pi^{-1}(i)} = \gamma_{j,\pi^{-1}(i)}. \tag{2.15}$$

We claim that $\hat{\boldsymbol{f}}$ is an $\hat{\mathcal{E}}$-process on Ω. To see this, for $k = 1, 2, \ldots, \hat{n}$, for all $t \in \Omega :$

$\hat{f}'_k(t) = f'_{\pi^{-1}(k)}(t)$ [Definition of $\hat{f}_k$.]

$= \left[\left(\sum_{j=1}^{m} \gamma_{j,\pi^{-1}(k)} \left(\sigma_j \prod_{i=1}^{n} X_i^{a_{j,i}} - \tau_j \prod_{i=1}^{n} X_i^{b_{j,i}}\right)\right) \circ \boldsymbol{f}\right](t)$

[$\boldsymbol{f}$ is an $\mathcal{E}$-process on Ω.]

$= \left[\left(\sum_{j=1}^{\hat{m}} \gamma_{j,\pi^{-1}(k)} \left(\sigma_j \prod_{i=1}^{n} X_i^{a_{j,i}} - \tau_j \prod_{i=1}^{n} X_i^{b_{j,i}}\right)\right) \circ \boldsymbol{f}\right](t)$ [Definition of $\mathcal{E}_1$.]

$= \left[\left(\sum_{j=1}^{\hat{m}} \gamma_{j,\pi^{-1}(k)} \left(\sigma_j \prod_{i\in C} X_i^{a_{j,i}} - \tau_j \prod_{i\in C} X_i^{b_{j,i}}\right)\right) \circ \boldsymbol{f}\right](t)$

[Since $j \leq \hat{m}, i \notin C \Rightarrow a_{j,i} = b_{j,i} = 0$.]

$= \left[\left(\sum_{j=1}^{\hat{m}} \gamma_{j,\pi^{-1}(k)} \left(\sigma_j \prod_{i=1}^{\hat{n}} X_{\pi^{-1}(i)}^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} X_{\pi^{-1}(i)}^{b_{j,\pi^{-1}(i)}}\right)\right) \circ \boldsymbol{f}\right](t)$

[$\pi(C) = \{1, 2, \ldots, \hat{n}\}$.]

$= \sum_{j=1}^{\hat{m}} \gamma_{j,\pi^{-1}(k)} \left(\sigma_j \prod_{i=1}^{\hat{n}} (f_{\pi^{-1}(i)}(t))^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} (f_{\pi^{-1}(i)}(t))^{b_{j,\pi^{-1}(i)}}\right)$

[By composition.]

$= \sum_{j=1}^{\hat{m}} \hat{\gamma}_{j,k} \left(\sigma_j \prod_{i=1}^{\hat{n}} (f_{\pi^{-1}(i)}(t))^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} (f_{\pi^{-1}(i)}(t))^{b_{j,\pi^{-1}(i)}}\right)$

[From (2.15).]

$= \sum_{j=1}^{\hat{m}} \hat{\gamma}_{j,k} \left(\sigma_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{b_{j,\pi^{-1}(i)}}\right)$

[Definition of $\hat{f}_i$.]

$= \left[\left(\sum_{j=1}^{\hat{m}} \hat{\gamma}_{j,k} e_{\pi,j}\right) \circ \hat{\boldsymbol{f}}\right](t)$ [Definition of $e_{\pi,j}$.]

This establishes the claim.

With $\hat{\mathcal{E}}, \hat{n}, \hat{\boldsymbol{f}}$ and π as described, we will now establish (1) through (6).

(1) Follows from the definition of $\hat{\mathcal{E}}$.

(2) Follows from 3.

(3) Suppose $\mathcal{E}$ is natural. Hence, there exists a positive strong $\mathcal{E}$-equilibrium point $\langle c_1, c_2, \ldots, c_n \rangle$. For $j = 1, 2, \ldots, \hat{m}$:

$$
\begin{aligned}
& e_{\pi,j}\big(c_{\pi^{-1}(1)}, c_{\pi^{-1}(2)}, \ldots, c_{\pi^{-1}(\hat{n})}\big) \\
& = \sigma_j \prod_{i=1}^{\hat{n}} c_{\pi^{-1}(i)}^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} c_{\pi^{-1}(i)}^{b_{j,\pi^{-1}(i)}} \\
& = \sigma_j \prod_{i \in C} c_i^{a_{j,i}} - \tau_j \prod_{i \in C} c_i^{b_{j,i}} \qquad [j \leq \hat{m}, i \notin C \Rightarrow a_{j,i} = b_{j,i} = 0.] \\
& = e_j(c_1, c_2, \ldots, c_n) \\
& = 0
\end{aligned}
$$

Hence, $\hat{\boldsymbol{c}}$ is a positive strong $\hat{\mathcal{E}}$-equilibrium point.

(4) Suppose $j \leq \hat{m}$. Then for all $t \in \Omega$:

$$\begin{aligned}
e_{\pi,j}(\hat{\boldsymbol{f}}(t)) &= \sigma_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{b_{j,\pi^{-1}(i)}} \\
&= \sigma_j \prod_{i=1}^{\hat{n}} (f_{\pi^{-1}(i)}(t))^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} (f_{\pi^{-1}(i)}(t))^{b_{j,\pi^{-1}(i)}} \\
&= \sigma_j \prod_{i\in C} (f_i(t))^{a_{j,i}} - \tau_j \prod_{i\in C} (f_i(t))^{b_{j,i}} \\
&= \sigma_j \prod_{i=1}^{n} (f_i(t))^{a_{j,i}} - \tau_j \prod_{i=1}^{n} (f_i(t))^{b_{j,i}} \qquad [j \leq \hat{m}, i \notin C \Rightarrow a_{j,i} = b_{j,i} = 0.] \\
&= \left(\left(\sigma_j \prod_{i=1}^{n} X_i^{a_{j,i}} - \tau_j \prod_{i=1}^{n} X_i^{b_{j,i}}\right) \circ \boldsymbol{f}\right)(t) \\
&= e_j(\boldsymbol{f}(t))
\end{aligned}$$

Since $j \leq \hat{m}$, therefore $e_j \in \mathcal{E}_1$ and there exists $t \in \Omega$ such that $e_j(\boldsymbol{f}(t)) \neq 0$. Hence, for all $e_{\pi,j} \in \hat{\mathcal{E}}$, there exists $t \in \Omega$ such that $e_{\pi,j}(\hat{\boldsymbol{f}}(t)) \neq 0$.

(5) Suppose $\hat{\mathcal{E}}$ is natural, $I \subseteq \Omega \cap \mathbb{R}_{\geq 0}$ is connected, $0 \in I$ and $\boldsymbol{f}(0)$ is a non-negative point. It follows that $\hat{\boldsymbol{f}}(0)$ is a non-negative point and, from Theorem 2.4.5, for all $t \in I$, $\hat{\boldsymbol{f}}(t)$ is a non-negative point. Suppose, for the sake of contradiction, that there exist $i_0 \leq \hat{n}$ and $t_0 \in I \cap \mathbb{R}_{>0}$ such that $\hat{f}_{i_0}(t_0) = 0$. From Theorem 2.4.5 again, $\hat{f}_{i_0}(0) = 0$ and

for all $t \in I : \hat{f}_{i_0}(t) = 0$. Since I is an interval and $0, t_0 \in I$, I contains an accumulation point. Hence, since $\hat{f}_{i_0}$ is analytic on Ω and Ω is connected, for all $t \in \Omega$:

$$\hat{f}_{i_0}(t) = 0. \tag{2.16}$$

It follows that for all $t \in \Omega$:

$$0 = \hat{f}'_{i_0}(t) = \sum_{j=1}^{\hat{m}} \hat{\gamma}_{j,i_0} e_{\pi,j}(\hat{\boldsymbol{f}}(t)). \tag{2.17}$$

We claim that for $j = 1, 2, \ldots, \hat{m}$, for all $t \in \Omega : \hat{\gamma}_{j,i_0} e_{\pi,j}(\hat{\boldsymbol{f}}(t)) \geq 0$.

Case 1: Suppose $\hat{\gamma}_{j,i_0} = 0$. Then $\hat{\gamma}_{j,i_0} e_{\pi,j}(\hat{\boldsymbol{f}}(t)) = 0 \geq 0$.

Case 2: Suppose $\hat{\gamma}_{j,i_0} > 0$. Then $b_{j,\pi^{-1}(i_0)} > 0$. Hence,

$$\begin{aligned}
e_{\pi,j}(\hat{\boldsymbol{f}}(t)) &= \sigma_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{b_{j,\pi^{-1}(i)}} \\
&= \sigma_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{a_{j,\pi^{-1}(i)}} \qquad [\text{Since } b_{j,\pi^{-1}(i_0)} > 0 \text{ and from 2.16, } \hat{f}_{i_0}(t) = 0.] \\
&\geq 0 \qquad [\hat{\boldsymbol{f}}(t) \text{ is a non-negative point, by Theorem 2.4.5}]
\end{aligned}$$

Hence, $\hat{\gamma}_{j,i_0} e_{\pi,j}(\hat{\boldsymbol{f}}(t)) \geq 0$.

Case 3: Suppose $\hat{\gamma}_{j,i_0} < 0$. Then $a_{j,\pi^{-1}(i_0)} > 0$. Hence,

$$\begin{aligned} e_{\pi,j}(\hat{\boldsymbol{f}}(t)) &= \sigma_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{a_{j,\pi^{-1}(i)}} - \tau_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{b_{j,\pi^{-1}(i)}} \\ &= -\tau_j \prod_{i=1}^{\hat{n}} (\hat{f}_i(t))^{b_{j,\pi^{-1}(i)}} \qquad \text{[Since } a_{j,\pi^{-1}(i_0)} > 0 \text{ and from 2.16, } \hat{f}_{i_0}(t) = 0.] \\ &\leq 0 \qquad [\hat{\boldsymbol{f}}(t) \text{ is a non-negative point, by Theorem 2.4.5]} \end{aligned}$$

Hence, $\hat{\gamma}_{j,i_0} e_{\pi,j}(\hat{\boldsymbol{f}}(t)) \geq 0$. This completes the proof of the claim.

From 2.17 and the claim, it now follows that for $j = 1, 2, \ldots, \hat{m}$, for all $t \in \Omega$:

$$\hat{\gamma}_{j,i_0} e_{\pi,j}(\hat{\boldsymbol{f}}(t)) = 0 \tag{2.18}$$

Since $i_0 \leq \hat{n}$, there exists $j_0 \leq \hat{m}$ such that either $a_{j_0,i_0} \neq 0$ or $b_{j_0,i_0} \neq 0$. If $\hat{\gamma}_{j_0,i_0} \neq 0$ then, from 2.18, $e_{\pi,j_0}(\hat{\boldsymbol{f}}(t)) = 0$. If $\hat{\gamma}_{j_0,i_0} = 0$ then, since $\hat{\gamma}_{j_0,i_0} = b_{j_0,i_0} - a_{j_0,i_0}$, it follows that $a_{j_0,i_0} \neq 0$ and $b_{j_0,i_0} \neq 0$. Hence, X_{i_0} divides e_{π,j_0}. From 2.16, it follows that $e_{\pi,j_0}(\hat{\boldsymbol{f}}(t)) = 0$. Hence, irrespective of the value of $\hat{\gamma}_{j_0,i_0}$, for all $t \in \Omega : e_{\pi,j_0}(\hat{\boldsymbol{f}}(t)) = 0$. Since e_{π,j_0} is an element of $\hat{\mathcal{E}}$, this leads to a contradiction with Lemma 2.5.10.4. Hence, for all $i \leq \hat{n}$, for all $t \in I \cap \mathbb{R}_{>0} : \hat{f}_i(t) > 0$.

(6) Follows from the definition of $\hat{\boldsymbol{f}}$.

(7) For $i = 1, 2, \ldots, n$, if $\pi(i) > \hat{n}$ then $i \notin C$. That is, for $j = 1, 2, \ldots, m : \gamma_{j,i} =$

$b_{j,i} - a_{j,i} = 0 - 0 = 0$. Hence, for all $t \in \Omega : f_i'(t) = \sum_{j=1}^{m} \gamma_{j,i} e_j(\boldsymbol{f}(t)) = 0$. Hence, since f_i is analytic on Ω, and Ω is simply-connected, for all $t_1, t_2 \in \Omega : f_i(t_1) = f_i(t_2)$. $\square$

We have described, for finite, natural event-systems, Lyapunov functions on the positive orthant. We next extend the definition of these Lyapunov functions to admit values at non-negative points.

Definition 2.5.3. Let $\mathcal{E}$ be a finite, natural event-system of dimension n with positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c} = \langle c_1, c_2, \ldots, c_n \rangle$. For all $v \in \mathbb{R}_{>0}$, let $\overline{g_v} : \mathbb{R}_{\geq 0} \to \mathbb{R}$ be such that for all $x \in \mathbb{R}_{\geq 0}$

$$\overline{g_v}(x) = \begin{cases} x(\ln(x) - 1 - \ln(v)) + v, & \text{if } x > 0; \\ \\ v, & \text{otherwise.} \end{cases} \tag{2.19}$$

Then the *extended lyapunov function* $\overline{g_{\mathcal{E},\boldsymbol{c}}} : \mathbb{R}^n_{\geq 0} \to \mathbb{R}$ is

$$\overline{g_{\mathcal{E},\boldsymbol{c}}}(x_1, x_2, \ldots, x_n) = \sum_{i=1}^{n} \overline{g_{c_i}}(x_i) \tag{2.20}$$

The next lemma lists some properties of extended Lyapunov functions.

Lemma 2.5.11. *Let $\mathcal{E}$ be a finite, natural event-system of dimension n with positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c} = \langle c_1, c_2, \ldots, c_n \rangle$. Then:*

1. *$\overline{g_{\mathcal{E},\boldsymbol{c}}}$ is continuous on $\mathbb{R}^n_{\geq 0}$.*

2. *For all $x_1, x_2, \ldots, x_n \in \mathbb{R}_{\geq 0}$, $\overline{g_{\mathcal{E},\boldsymbol{c}}}(x_1, x_2, \ldots, x_n) \geq 0$ with equality iff $\langle x_1, x_2, \ldots, x_n \rangle = \boldsymbol{c}$.*

3. *For all $r \in \mathbb{R}_{\geq 0}$, the set $\{\boldsymbol{x} \in \mathbb{R}^n_{\geq 0} \mid \overline{g_{\mathcal{E},\boldsymbol{c}}}(\boldsymbol{x}) \leq r\}$ is bounded.*

4. *If $\Omega \subseteq \mathbb{C}$ is open, simply connected and such that $0 \in \Omega$, $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ is an $\mathcal{E}$-process on Ω such that $\boldsymbol{f}(0)$ is a non-negative point, and $I \subseteq \mathbb{R}_{\geq 0} \cap \Omega$ is an interval such that $0 \in I$ then $(\overline{g_{\mathcal{E},\boldsymbol{c}}} \circ \boldsymbol{f})$ is monotonically non-increasing on I.*

Proof. For $i = 1, 2, \ldots, n$, let $\overline{g_{c_i}}(x)$ be as defined in Equation 2.19.

1. For $i = 1, 2, \ldots, n, \overline{g_{c_i}}$ is continuous on $\mathbb{R}_{>0}$ and $\lim_{x \to 0^+} \overline{g_{c_i}}(x) = c_i = \overline{g_{c_i}}(0)$, so $\overline{g_{c_i}}$ is continuous on $\mathbb{R}_{\geq 0}$. Since $\overline{g_{\mathcal{E},\boldsymbol{c}}}$ is the finite sum of continuous functions on $\mathbb{R}_{\geq 0}$, $\overline{g_{\mathcal{E},\boldsymbol{c}}}$ is continuous on $\mathbb{R}^n_{\geq 0}$.

2. Let $j \in \{1, 2, \ldots, n\}$. Let $\overline{g} = \overline{g_{c_j}}$. For all $x \in \mathbb{R}_{>0}$, $\overline{g}\,'(x) = \ln\left(\dfrac{x}{c_j}\right)$. If $0 < x < c_j$ then, by substitution, $\overline{g}\,'(x) < 0$. Similarly, if $x > c_j$ then $\overline{g}\,'(x) > 0$. Hence, $\overline{g}$ is monotonically decreasing in $(0, c_j)$ and monotonically increasing in (c_j, ∞). From continuity of $\overline{g}$ in $\mathbb{R}_{\geq 0}$, it follows that

$$\text{For all } x \in \mathbb{R}_{\geq 0}, \overline{g}(x) \geq \overline{g}(c_j) = 0 \text{ with equality iff } x = c_j. \tag{2.21}$$

From Equations (2.20) and (2.21), the claim follows.

3. Observe that $\lim_{x \to +\infty} \overline{g}(x) = +\infty$. It follows that:

$$\text{For all } r \in \mathbb{R}_{\geq 0},\ \text{the set } \{x \in \mathbb{R}_{\geq 0} \mid \overline{g}(x) \leq r\} \text{ is bounded.} \tag{2.22}$$

If $x_1, x_2, \ldots, x_n \in \mathbb{R}_{\geq 0}$ are such that $\overline{g_{\mathcal{E},\boldsymbol{c}}}(x_1, x_2, \ldots, x_n) \leq r$, it follows from Equations (2.20) and (2.21) that for $i = 1, 2, \ldots, n : \overline{g_{c_i}}(x_i) \leq r$. The claim now follows from Equation (2.22).

4. Let $\Omega \subseteq \mathbb{C}$ be open, simply connected, and such that $0 \in \Omega$; let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω such that $\boldsymbol{f}(0)$ is a non-negative point; and let $I \subseteq \mathbb{R}_{\geq 0} \cap \Omega$ be an interval such that $0 \in I$. By Lemma 2.5.10 there exists $\hat{n}$, $\hat{\mathcal{E}}$, $\hat{\boldsymbol{f}}$, and π satisfying 2.5.10.1–2.5.10.7. Let $\hat{\boldsymbol{c}} = \langle \hat{c}_1, \hat{c}_2, \ldots, \hat{c}_{\hat{n}} \rangle = \langle c_{\pi^{-1}(1)}, c_{\pi^{-1}(2)}, \ldots, c_{\pi^{-1}(\hat{n})} \rangle$. By Lemma 2.5.10.2, $\hat{\boldsymbol{c}}$ is a positive strong equilibrium point of $\hat{\mathcal{E}}$. Then for all $t \in I$,

$$
\begin{aligned}
\left(\overline{g_{\mathcal{E},\boldsymbol{c}}} \circ \boldsymbol{f}\right)(t) &= \sum_{i=1}^{n} \overline{g_{c_i}}\left(f_i(t)\right) && \text{[Equation (2.20).]} \\
&= \sum_{i:\pi(i) \leq \hat{n}} \overline{g_{c_i}}\left(f_i(t)\right) + \sum_{i:\pi(i) > \hat{n}} \overline{g_{c_i}}\left(f_i(t)\right) \\
&= \sum_{i=1}^{\hat{n}} \overline{g_{c_{\pi^{-1}(i)}}}\left(f_{\pi^{-1}(i)}(t)\right) + \sum_{i:\pi(i) > \hat{n}} \overline{g_{c_i}}\left(f_i(t)\right) \\
&= \sum_{i=1}^{\hat{n}} \overline{g_{\hat{c}_i}}\left(\hat{f}_i(t)\right) + \sum_{i:\pi(i) > \hat{n}} \overline{g_{c_i}}\left(f_i(t)\right) \\
&\qquad \text{[Definition of } \hat{\boldsymbol{c}} \text{ and Lemma 2.5.10.6.]} \\
&= \left(\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}} \circ \hat{\boldsymbol{f}}\right)(t) + \sum_{i:\pi(i) > \hat{n}} \overline{g_{c_i}}\left(f_i(t)\right) && \text{[Equation (2.20).]} \\
&= \left(\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}} \circ \hat{\boldsymbol{f}}\right)(t) + \text{constant} && \text{[Lemma 2.5.10.7.]}
\end{aligned}
$$

By Definition 2.5.3, for all $\boldsymbol{x} \in \mathbb{R}^{\hat{n}}_{>0}$, $\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}}(\boldsymbol{x}) = g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}(\boldsymbol{x})$. By Lemma 2.5.10.5, for all $t \in I \cap \mathbb{R}_{>0}$, $\hat{\boldsymbol{f}}(t) \in \mathbb{R}^{\hat{n}}_{>0}$. So for all $t \in I \cap \mathbb{R}_{>0}$, $\left(\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}} \circ \hat{\boldsymbol{f}}\right)(t) = \left(g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}} \circ \hat{\boldsymbol{f}}\right)(t)$. Then, for all $t \in I \cap \mathbb{R}_{>0}$,

$$
\begin{aligned}
\left(\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}} \circ \hat{\boldsymbol{f}}\right)'(t) &= \left(g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}} \circ \hat{\boldsymbol{f}}\right)'(t) \\
&= \nabla g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}\left(\hat{\boldsymbol{f}}(t)\right) \cdot \hat{\boldsymbol{f}}'(t) && \text{[Chain rule.]} \\
&= \nabla g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}\left(\hat{\boldsymbol{f}}(t)\right) \cdot \boldsymbol{P}_{\hat{\mathcal{E}}}\left(\hat{\boldsymbol{f}}(t)\right) && \text{[Definition 2.3.3.]} \\
&\leq 0 && \text{[Theorem 2.5.5.]}
\end{aligned}
$$

Therefore $\left(\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}} \circ \hat{\boldsymbol{f}}\right)$ is non-increasing on $I \cap \mathbb{R}_{>0}$.

By Definition 2.3.3, $\hat{\boldsymbol{f}}$ is continuous on I; by Theorem 2.4.5, $\hat{\boldsymbol{f}}(I) \subseteq \mathbb{R}^{\hat{n}}_{\geq 0}$; and by Lemma 2.5.11.1, $\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}}$ is continuous on $\mathbb{R}^{\hat{n}}_{\geq 0}$; so $\left(\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}} \circ \hat{\boldsymbol{f}}\right)$ is continuous on I. Therefore $\left(\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}} \circ \hat{\boldsymbol{f}}\right)$ is non-increasing on I. Thus $(\overline{g_{\mathcal{E},\boldsymbol{c}}} \circ \boldsymbol{f})$ is a constant plus a monotonically non-increasing function on I, so $(\overline{g_{\mathcal{E},\boldsymbol{c}}} \circ \boldsymbol{f})$ is monotonically non-increasing on I. □

The next lemma makes use of properties of the extended Lyapunov function to show that $\mathcal{E}$-processes starting at non-negative points are uniformly bounded in forward real time.

Lemma 2.5.12. *Let $\mathcal{E}$ be a finite, natural event-system of dimension n. Let $\boldsymbol{\alpha} \in \mathbb{R}^n_{\geq 0}$. There exists $k \in \mathbb{R}_{\geq 0}$ such that for all $\Omega \subseteq \mathbb{C}$ open and simply connected and such that $0 \in \Omega$, for all $\mathcal{E}$-processes $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ on Ω such that $\boldsymbol{f}(0) = \boldsymbol{\alpha}$, for all intervals $I \subseteq \Omega \cap \mathbb{R}_{\geq 0}$ such that $0 \in I$, for all $t \in I$, for $i = 1, 2, \ldots, n$: $f_i(t) \in \mathbb{R}$ and $0 \leq f_i(t) < k$.*

Proof. Since $\mathcal{E}$ is natural, let $\boldsymbol{c} \in \mathbb{R}^n_{>0}$ be a positive strong $\mathcal{E}$-equilibrium point. Let $\overline{g} = \overline{g_{\mathcal{E},\boldsymbol{c}}}$.

Let $\ell = \overline{g}(\boldsymbol{\alpha})$. Let $S = \{\boldsymbol{x} \in \mathbb{R}^n_{\geq 0} \mid \overline{g}(\boldsymbol{x}) \leq \ell\}$. By Lemma 2.5.11.3, S is bounded. Hence, let k be such that for all $\boldsymbol{x} \in S : |\boldsymbol{x}|_\infty < k$.

Let $\Omega \subseteq \mathbb{C}$ be open, simply connected, and such that $0 \in \Omega$; let $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ be an $\mathcal{E}$-process on Ω such that $\boldsymbol{f}(0) = \boldsymbol{\alpha}$; and let $I \subseteq \mathbb{R}_{\geq 0} \cap \Omega$ be an interval such that $0 \in I$.

From Theorem 2.4.5, for all $t \in I$, for $i = 1, 2, \ldots, n : f_i(t) \in \mathbb{R}$ and $f_i(t) \geq 0$.

Consider the function:

$$\overline{g} \circ \boldsymbol{f}|_I : I \to \mathbb{R}$$

From Lemma 2.5.11.4, for all $t \in I$, $\overline{g} \circ \boldsymbol{f}|_I$ is monotonically non-increasing on I. That is, for all $t \in I$,

$$\overline{g}(\boldsymbol{f}(t)) \leq \ell \tag{2.23}$$

It follows from Equation 2.23 and the definition of S that $\boldsymbol{f}(I) \subseteq S$. By the definition of k, it follows that for all $t \in I$, for $i = 1, 2, \ldots, n$, $f_i(t) < k$. $\square$

The next lemma shows that, because $\mathcal{E}$-processes starting at non-negative points are uniformly bounded in real time, they can be continued forever along forward real time.

Lemma 2.5.13 (Existence and uniqueness of $\mathcal{E}$-process.)**.** *Let $\mathcal{E}$ be a finite, natural event-system of dimension n. Let $\boldsymbol{\alpha} \in \mathbb{R}^n_{\geq 0}$. There exist a simply-connected open set $\Omega \subseteq \mathbb{C}$, an $\mathcal{E}$-process $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ on Ω and $k \in \mathbb{R}_{\geq 0}$ such that:*

1. *$\mathbb{R}_{\geq 0} \subseteq \Omega$.*

2. $\boldsymbol{f}(0) = \boldsymbol{\alpha}$.

3. For all $t \in \mathbb{R}_{\geq 0}$*, for* $i = 1, 2, \ldots, n : f_i(t) \in \mathbb{R}$ *and* $0 \leq f_i(t) < k$.

4. For all simply-connected open sets $\widetilde{\Omega} \subseteq \mathbb{C}$*, for all* $\mathcal{E}$*-processes* $\tilde{\boldsymbol{f}}$ *on* $\widetilde{\Omega}$*, for all intervals* $I \subseteq \widetilde{\Omega} \cap \mathbb{R}_{\geq 0}$*, if* $0 \in I$ *and* $\tilde{\boldsymbol{f}}(0) = \alpha$*, then for all* $t \in I$*,* $\boldsymbol{f}(t) = \tilde{\boldsymbol{f}}(t)$.

Proof. Claim: There exists $k \in \mathbb{R}_{\geq 0}$ such that for all intervals $I \subseteq \mathbb{R}_{\geq 0}$ with $0 \in I$, for all real-$\mathcal{E}$-processes $\tilde{\boldsymbol{h}} = \langle \tilde{h}_1, \tilde{h}_2, \ldots, \tilde{h}_n \rangle$ on I with $\tilde{\boldsymbol{h}}(0) = \boldsymbol{\alpha}$, for all $t \in I$, for $i = 1, 2, \ldots, n$: $0 \leq \tilde{h}_i(t) \leq k$.

To see this, let $I \subseteq \mathbb{R}_{\geq 0}$ be an interval such that $0 \in I$. Let $\tilde{\boldsymbol{h}} = \langle \tilde{h}_1, \tilde{h}_2, \ldots, \tilde{h}_n \rangle$ be a real-$\mathcal{E}$-process on I such that $\tilde{\boldsymbol{h}}(0) = \boldsymbol{\alpha}$.

From Lemma 2.4.4, there exist an open, simply-connected $\widetilde{\Omega} \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\tilde{\boldsymbol{f}} = \langle \tilde{f}_1, \tilde{f}_2, \ldots, \tilde{f}_n \rangle$ on $\widetilde{\Omega}$ such that:

1. $I \subset \widetilde{\Omega}$
2. For all $t \in I : \tilde{\boldsymbol{f}}(t) = \tilde{\boldsymbol{h}}(t)$.

From Lemma 2.5.12, there exists $k \in \mathbb{R}_{\geq 0}$ such that for all $t \in I$, for $i = 1, 2, \ldots, n$: $\tilde{f}_i(t) \in \mathbb{R}$ and $0 \leq \tilde{f}_i(t) < k$. That is, for all $t \in I$, for $i = 1, 2, \ldots, n : 0 \leq \tilde{h}_i(t) < k$. This proves the claim.

Therefore, by [24, p. 397, Corollary], there exists $k \in \mathbb{R}_{\geq 0}$, there is a real-$\mathcal{E}$-process $\boldsymbol{h} = \langle h_1, h_2, \ldots, h_n \rangle$ on $\mathbb{R}_{\geq 0}$ such that $\boldsymbol{h}(0) = \boldsymbol{\alpha}$ and for all $t \in \mathbb{R}_{\geq 0}$,for $i = 1, 2, \ldots, n$: $0 \leq h_i(t) < k$.. By Lemma 2.4.4, there exist an open, simply-connected $\Omega \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\boldsymbol{f}$ on Ω such that $\mathbb{R}_{\geq 0} \subseteq \Omega$ and for all $t \in \mathbb{R}_{\geq 0}$, $\boldsymbol{f}(t) = \boldsymbol{h}(t)$. Therefore, for all $t \in \mathbb{R}_{\geq 0}$, for $i = 1, 2, \ldots, n : f_i(t) \in \mathbb{R}$ and $0 \leq f_i(t) < k$. Hence, Parts (1,2,3) are established. Part(4) follows from Lemma 2.4.2. ∎

The next lemma shows that the ω-limit points of $\mathcal{E}$-processes that start at non-negative points satisfy detailed balance.

Lemma 2.5.14. *Let $\mathcal{E}$ be a finite, natural event-system of dimension n, let $\Omega \subseteq \mathbb{C}$ be open and simply-connected, let $\boldsymbol{f}$ be an $\mathcal{E}$-process on Ω, and let $\boldsymbol{q} \in \mathbb{C}^n$. If $\mathbb{R}_{\geq 0} \subseteq \Omega$ and $\boldsymbol{f}(0)$ is a non-negative point and $\boldsymbol{q}$ is an ω-limit point of $\boldsymbol{f}$, then $\boldsymbol{q} \in \mathbb{R}^n_{\geq 0}$ and is a strong $\mathcal{E}$-equilibrium point.*

Proof. Suppose $\mathbb{R}_{\geq 0} \subseteq \Omega$, $\boldsymbol{f}(0)$ is a non-negative point, S is the set of ω-limit points of $\boldsymbol{f}$, and $\boldsymbol{q} \in S$. By Lemma 2.4.11 $\boldsymbol{q} \in \mathbb{R}^n_{\geq 0}$. By Lemma 2.5.13 there exists an open, simply-connected $\Omega_{\boldsymbol{q}} \subseteq \mathbb{C}$ such that $\mathbb{R}_{\geq 0} \subseteq \Omega_{\boldsymbol{q}}$ and an $\mathcal{E}$-process $\boldsymbol{h} = \langle h_1, h_2, \ldots, h_n \rangle$ on $\Omega_{\boldsymbol{q}}$ such that $\boldsymbol{h}(0) = \boldsymbol{q}$.

Let $\boldsymbol{c}$ be a positive strong $\mathcal{E}$-equilibrium point. By Lemma 2.5.11.2, $\overline{g_{\mathcal{E},\boldsymbol{c}}}(\boldsymbol{f}(t))$ is bounded below and, by Lemma 2.5.11.4, is monotonically non-increasing on $\mathbb{R}_{\geq 0}$. Therefore $\lim_{t\to\infty} \overline{g_{\mathcal{E},\boldsymbol{c}}}(\boldsymbol{f}(t))$ exists. Since $\overline{g_{\mathcal{E},\boldsymbol{c}}}$ is continuous, for all $\boldsymbol{\alpha} \in S$, $\overline{g_{\mathcal{E},\boldsymbol{c}}}(\boldsymbol{\alpha}) = \lim_{t\to\infty} \overline{g_{\mathcal{E},\boldsymbol{c}}}(\boldsymbol{f}(t))$. By Lemma 2.4.11, for all $t \in \mathbb{R}_{\geq 0}$, $\boldsymbol{h}(t) \in S$. Hence, $\overline{g_{\mathcal{E},\boldsymbol{c}}}(\boldsymbol{h}(t))$ is constant on $\mathbb{R}_{\geq 0}$.

By Lemma 2.5.10 either $\boldsymbol{q}$ is a strong $\mathcal{E}$-equilibrium or there exists a finite event-system $\hat{\mathcal{E}}$ of dimension $\hat{n} \leq n$, an $\hat{\mathcal{E}}$-process $\hat{\boldsymbol{h}} = \langle \hat{h}_1, \hat{h}_2, \ldots, \hat{h}_{\hat{n}} \rangle$ on $\Omega_{\boldsymbol{q}}$, and a permutation π on $\{1, 2, \ldots, n\}$ satisfying 1–7 of Lemma 2.5.10.

Assume $\boldsymbol{q}$ is not a strong $\mathcal{E}$-equilibrium point. By Lemma 2.5.10.6, for $i = 1, 2, \ldots, \hat{n}$, for all $t \in \Omega_{\boldsymbol{q}}$, $\hat{h}_i(t) = h_{\pi^{-1}(i)}(t)$. Let $\hat{\boldsymbol{c}} = \langle \hat{c}_1, \hat{c}_2, \ldots, \hat{c}_{\hat{n}} \rangle = \langle c_{\pi^{-1}(1)}, c_{\pi^{-1}(2)}, \ldots, c_{\pi^{-1}(\hat{n})} \rangle$. By Lemma 2.5.10.3, $\hat{\boldsymbol{c}}$ is an $\hat{\mathcal{E}}$-strong equilibrium point.

For all $v \in \mathbb{R}_{>0}$, let $\overline{g_v}$ be as defined in Equation 2.19 in Definition 2.5.3. Then for all $t \in \mathbb{R}_{\geq 0}$,

$$\begin{aligned}
\overline{g_{\mathcal{E},\boldsymbol{c}}}\left(\boldsymbol{h}\left(t\right)\right) - \overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right) &= \sum_{i=1}^{n} \overline{g_{c_i}}\left(h_i\left(t\right)\right) - \sum_{j=1}^{\hat{n}} \overline{g_{\hat{c}_j}}\left(\hat{h}_j\left(t\right)\right) \\
&= \sum_{i=1}^{n} \overline{g_{c_i}}\left(h_i\left(t\right)\right) - \sum_{j=1}^{\hat{n}} \overline{g_{c_{\pi^{-1}(j)}}}\left(h_{\pi^{-1}(j)}\left(t\right)\right) \\
&= \sum_{i=1}^{n} \overline{g_{c_{\pi^{-1}(i)}}}\left(h_{\pi^{-1}(i)}\left(t\right)\right) - \sum_{j=1}^{\hat{n}} \overline{g_{c_{\pi^{-1}(j)}}}\left(h_{\pi^{-1}(j)}\left(t\right)\right) \\
&= \sum_{i=\hat{n}+1}^{n} \overline{g_{c_{\pi^{-1}(i)}}}\left(h_{\pi^{-1}(i)}\left(t\right)\right)
\end{aligned}$$

But, by Lemma 2.5.10.7, if $\pi\left(i\right) > \hat{n}$ then $h_i\left(t\right)$ is constant. Hence, $\overline{g_{c_{\pi^{-1}(i)}}}\left(h_{\pi^{-1}(i)}\left(t\right)\right)$ is constant for $i = \hat{n}+1, \hat{n}+2, \ldots, n$, so $\overline{g_{\mathcal{E},\boldsymbol{c}}}\left(\boldsymbol{h}\left(t\right)\right) - \overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right)$ is constant. Since $\overline{g_{\mathcal{E},\boldsymbol{c}}}\left(\boldsymbol{h}\left(t\right)\right)$ and $\overline{g_{\mathcal{E},\boldsymbol{c}}}\left(\boldsymbol{h}\left(t\right)\right) - \overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right)$ are both constant, $\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right)$ must be constant. By Lemma 2.5.10.5, for all $t \in \mathbb{R}_{>0}$, $\hat{\boldsymbol{h}}\left(t\right)$ is a positive point, so by Definitions 2.5.2 and 2.5.3, $\overline{g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right) = g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right)$. Since $g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right)$ is constant, $\frac{d}{dt} g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right) = \nabla g_{\hat{\mathcal{E}},\hat{\boldsymbol{c}}}\left(\hat{\boldsymbol{h}}\left(t\right)\right) \cdot \boldsymbol{P}_{\mathcal{E}}\left(\hat{\boldsymbol{h}}\left(t\right)\right) = 0$. Then by Theorem 2.5.5 and continuity $\hat{\boldsymbol{h}}\left(0\right)$ must be a strong $\hat{\mathcal{E}}$-equilibrium point, so for all $e \in \hat{\mathcal{E}}$, for all $t \in \Omega_{\boldsymbol{q}}$, $e(\hat{\boldsymbol{h}}(t)) = 0$, which contradicts Lemma 2.5.10.4. Therefore $\boldsymbol{q}$ is a strong $\mathcal{E}$-equilibrium point. □

The next theorem consolidates our results concerning natural event-systems. It also establishes that positive strong equilibrium points are locally attractive relative to their conservation classes. Together with the existence of a Lyapunov function, this implies that positive strong equilibrium points are asymptotically stable relative to their conservation classes [18, Theorem 5.57].

Theorem 2.5.15. *Let $\mathcal{E}$ be a finite, natural event-system of dimension n. Let H be a positive conservation class of $\mathcal{E}$. Then:*

1. *For all $\boldsymbol{x} \in H \cap \mathbb{R}^n_{\geq 0}$, there exist $k \in \mathbb{R}_{\geq 0}$, an open, simply-connected $\Omega \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ on Ω such that:*

   (a) $\mathbb{R}_{\geq 0} \subseteq \Omega$.

   (b) $\boldsymbol{f}(0) = \boldsymbol{x}$.

   (c) *For all $t \in \mathbb{R}_{\geq 0}$, $\boldsymbol{f}(t) \in H \cap \mathbb{R}^n_{\geq 0}$.*

   (d) *For all $t \in \mathbb{R}_{\geq 0}$, for $i = 1, 2, \ldots, n$, $0 \leq f_i(t) \leq k$.*

   (e) *For all open, simply-connected $\widetilde{\Omega} \subseteq \mathbb{C}$, for all $\mathcal{E}$-processes $\tilde{\boldsymbol{f}}$ on $\widetilde{\Omega}$, if $0 \in \widetilde{\Omega}$ and $\tilde{\boldsymbol{f}}(0) = \boldsymbol{x}$ then for all intervals $I \subseteq \widetilde{\Omega} \cap \mathbb{R}_{\geq 0}$ such that $0 \in I$, for all $t \in I : \boldsymbol{f}(t) = \tilde{\boldsymbol{f}}(t)$.*

2. *There exists $\boldsymbol{c} \in H$ such that:*

   (a) *$\boldsymbol{c}$ is a positive strong $\mathcal{E}$-equilibrium point.*

   (b) *For all $\boldsymbol{d} \in H$, if $\boldsymbol{d}$ is a positive strong $\mathcal{E}$-equilibrium point, then $\boldsymbol{d} = \boldsymbol{c}$.*

   (c) *There exists $U \subseteq H \cap \mathbb{R}^n_{>0}$ such that*

      i. *U is open in $H \cap \mathbb{R}^n_{>0}$.*

      ii. $\boldsymbol{c} \in U$.

      iii. *For all $\boldsymbol{x} \in U$, there exist an open, simply-connected $\Omega \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\boldsymbol{f}$ on Ω such that*

         A. $\mathbb{R}_{\geq 0} \subseteq \Omega$.

         B. $\boldsymbol{f}(0) = \boldsymbol{x}$.

C. $\boldsymbol{f}(t) \to \boldsymbol{c}$ as $t \to \infty$ along the positive real line. (i.e. for all $\varepsilon \in \mathbb{R}_{>0}$, there exists $t_0 \in \mathbb{R}_{>0}$ such that for all $t \in \mathbb{R}_{>t_0}$: $||\boldsymbol{f}(t) - \boldsymbol{c}||_2 < \varepsilon$.)

Proof.

1. Follows from Lemma 2.5.13 and Theorem 2.3.3.

2.(a) and 2.(b) follow from Theorem 2.5.9.

2.(c) Let $\boldsymbol{c} \in H$ be a positive strong-$\mathcal{E}$-equilibrium point as in Theorem 2.5.15.2a. Let $g = g_{\mathcal{E},\boldsymbol{c}}$. Let $T = H \cap \mathbb{R}^n_{>0}$. For all $\boldsymbol{x} \in H \cap \mathbb{R}^n$, for all $r \in \mathbb{R}_{>0}$, let

$$B_r(\boldsymbol{x}) = \left\{\boldsymbol{y} \in H \cap \mathbb{R}^n \mid \|\boldsymbol{x} - \boldsymbol{y}\|_2 < r\right\}$$

$$S_r(\boldsymbol{x}) = \left\{\boldsymbol{y} \in H \cap \mathbb{R}^n \mid \|\boldsymbol{x} - \boldsymbol{y}\|_2 = r\right\}$$

$$\overline{B_r(\boldsymbol{x})} = \left\{\boldsymbol{y} \in H \cap \mathbb{R}^n \mid \|\boldsymbol{x} - \boldsymbol{y}\|_2 \leq r\right\}$$

Since $\mathbb{R}^n_{>0}$ is open in $\mathbb{R}^n$, it follows that T is open in $H \cap \mathbb{R}^n$. Therefore, there exists $\delta \in \mathbb{R}_{>0}$ such that $B_{2\delta}(\boldsymbol{c}) \subseteq T$. Let $\delta \in \mathbb{R}_{>0}$ be such that $B_{2\delta}(\boldsymbol{c}) \subseteq T$. It follows that $\overline{B_\delta(\boldsymbol{c})} \subseteq T$.

Since g is continuous and $S_\delta(\boldsymbol{c})$ is compact, let $\boldsymbol{x_0} \in S_\delta(\boldsymbol{c})$ be such that $g(\boldsymbol{x_0}) = \inf_{\boldsymbol{x} \in S_\delta(\boldsymbol{c})} g(\boldsymbol{x})$. Let $U = B_\delta(\boldsymbol{c}) \cap \{\boldsymbol{x} \in T \mid g(\boldsymbol{x}) < g(\boldsymbol{x_0})\}$. It follows that U is open in T. Since $\boldsymbol{x_0} \neq \boldsymbol{c}$, and by Lemma 2.5.11.2, $g(\boldsymbol{x_0}) = \overline{g_{\mathcal{E},\boldsymbol{c}}}(\boldsymbol{x_0}) > 0 = g(\boldsymbol{c})$. Hence, $\boldsymbol{c} \in U$.

Let $\boldsymbol{x} \in U$. From Lemma 2.5.13, there exist an open, simply-connected $\Omega \subset \mathbb{C}$ and an $\mathcal{E}$-process $\boldsymbol{f}$ on Ω such that $\mathbb{R}_{\geq 0} \subseteq \Omega$ and $\boldsymbol{f}(0) = \boldsymbol{x}$.

We claim that for all $t \in \mathbb{R}_{\geq 0}$, $\boldsymbol{f}(t) \in B_\delta(\boldsymbol{c})$. Suppose not. Then there exists $t_0 \in \mathbb{R}_{\geq 0}$ such that $\boldsymbol{f}(t_0) \in S_\delta(\boldsymbol{c})$. From the definition of $\boldsymbol{x_0}$, $g(\boldsymbol{x_0}) \leq g(\boldsymbol{f}(t_0))$. Since $\boldsymbol{f}(0) = \boldsymbol{x} \in U$, $g(\boldsymbol{f}(0)) < g(\boldsymbol{x_0})$. Hence, $g(\boldsymbol{f}(0)) < g(\boldsymbol{f}(t_0))$, contradicting Lemma 2.5.11.4.

To see that $\boldsymbol{f}(t) \to \boldsymbol{c}$ as $t \to \infty$ along the positive real line, suppose not. Then there exists $\varepsilon \in \mathbb{R}_{>0}$ such that $\varepsilon < \delta$ and there exists an increasing sequence of real numbers $\{t_i \in \mathbb{R}_{>0}\}_{i \in \mathbb{Z}_{>0}}$ such that $t_i \to \infty$ as $i \to \infty$ and for all i, $\boldsymbol{f}(t_i) \in \overline{B_\delta(\boldsymbol{c})} \setminus B_\varepsilon(\boldsymbol{c})$. Since $\overline{B_\delta(\boldsymbol{c})} \setminus B_\varepsilon(\boldsymbol{c})$ is compact, there exists a convergent subsequence. By Definition 2.4.5, the limit of this subsequence is an ω-limit point $\boldsymbol{q}$ of $\boldsymbol{f}$ such that $\boldsymbol{q} \in \overline{B_\delta(\boldsymbol{c})} \setminus B_\varepsilon(\boldsymbol{c})$. From Lemma 2.5.14, $\boldsymbol{q}$ is a strong-$\mathcal{E}$-equilibrium point. Since $\boldsymbol{q} \in \overline{B_\delta(\boldsymbol{c})}$, $\boldsymbol{q} \in T$. From Theorem 2.5.9, $\boldsymbol{q} = \boldsymbol{c}$. Hence, $\boldsymbol{c} \notin B_\varepsilon(\boldsymbol{c})$, a contradiction. □

We have established that positive strong equilibrium points are asymptotically stable relative to their conservation classes. A stronger result would be that if an $\mathcal{E}$-process starts at a positive point then it asymptotically tends to the positive strong equilibrium point in its conservation class. Such a result is related to the widely-held notion that, for systems of chemical reactions, concentrations approach equilibrium. We have been unable to prove this result. We will now state it as an open problem. This problem has a long history. It appears to have been first suggested in [17, Lemma 4C], where it was accompanied by an incorrect proof. The proof was retracted in [16].

Open 1. *Let $\mathcal{E}$ be a finite, natural event-system of dimension n. Let H be a positive conservation class of $\mathcal{E}$. Then*

1. *For all $\boldsymbol{x} \in H \cap \mathbb{R}^n_{\geq 0}$, there exist $k \in \mathbb{R}_{\geq 0}$, an open, simply-connected $\Omega \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\boldsymbol{f} = \langle f_1, f_2, \ldots, f_n \rangle$ on Ω such that:*

   (a) $\mathbb{R}_{\geq 0} \subseteq \Omega$.

   (b) $\boldsymbol{f}(0) = \boldsymbol{x}$.

   (c) For all $t \in \mathbb{R}_{\geq 0}$, $\boldsymbol{f}(t) \in H \cap \mathbb{R}^n_{\geq 0}$.

(d) *For all* $t \in \mathbb{R}_{\geq 0}$*, for* $i = 1, 2, \ldots, n$*,* $0 \leq f_i(t) < k$*.*

(e) *For all open, simply-connected* $\widetilde{\Omega} \subseteq \mathbb{C}$*, for all* $\mathcal{E}$*-processes* $\tilde{\boldsymbol{f}}$ *on* $\widetilde{\Omega}$*, if* $0 \in \widetilde{\Omega}$ *and* $\tilde{\boldsymbol{f}}(0) = \boldsymbol{x}$ *then for all intervals* $I \subseteq \widetilde{\Omega} \cap \mathbb{R}_{\geq 0}$*, if* $0 \in I$ *then for all* $t \in I$ *:* $\boldsymbol{f}(t) = \tilde{\boldsymbol{f}}(t)$*.*

2. *There exists* $\boldsymbol{c} \in H$ *such that:*

(a) $\boldsymbol{c}$ *is a positive strong* $\mathcal{E}$*-equilibrium point.*

(b) *For all* $\boldsymbol{d} \in H$*, if* $\boldsymbol{d}$ *is a positive strong* $\mathcal{E}$*-equilibrium point, then* $\boldsymbol{d} = \boldsymbol{c}$*.*

(c) *For all* $\boldsymbol{x} \in H \cap \mathbb{R}^n_{>0}$*, there exist an open, simply-connected* $\Omega \subseteq \mathbb{C}$ *and an* $\mathcal{E}$*-process* $\boldsymbol{f}$ *on* Ω *such that:*

i. $\mathbb{R}_{\geq 0} \subseteq \Omega$*.*

ii. $\boldsymbol{f}(0) = \boldsymbol{x}$*.*

iii. $\boldsymbol{f}(t) \to \boldsymbol{c}$ *as* $t \to \infty$ *along the positive real line. (i.e. for all* $\varepsilon \in \mathbb{R}_{>0}$*, there exists* $t_0 \in \mathbb{R}_{>0}$ *such that for all* $t \in \mathbb{R}_{>t_0} : ||\boldsymbol{f}(t) - \mathbf{c}||_2 < \varepsilon$*.)*

In light of Theorem 2.5.15, Open Problem 1 is equivalent to the following statement.

Open 2. *Let* $\mathcal{E}$ *be a finite, natural event-system of dimension* n*. Let* $\boldsymbol{x} \in \mathbb{R}^n_{>0}$*. Then there exists an open, simply-connected* $\Omega \subseteq \mathbb{C}$*, an* $\mathcal{E}$*-process* $\boldsymbol{f}$ *on* Ω *and a positive strong* $\mathcal{E}$*-equilibrium point* $\boldsymbol{c}$ *such that:*

1. $\mathbb{R}_{\geq 0} \subseteq \Omega$*.*

2. $\boldsymbol{f}(0) = \boldsymbol{x}$*.*

3. $\boldsymbol{f}(t) \to \boldsymbol{c}$ *as* $t \to \infty$ *along the positive real line. (i.e. for all* $\varepsilon \in \mathbb{R}_{>0}$*, there exists* $t_0 \in \mathbb{R}_{>0}$ *such that for all* $t \in \mathbb{R}_{>t_0} : ||\boldsymbol{f}(t) - \mathbf{c}||_2 < \varepsilon$*.)*

2.6 Finite Natural Atomic Event-systems

In this section, we settle Open 1 in the affirmative for the case of finite, natural, atomic event-systems. The atomic hypothesis appears to be a natural assumption to make concerning systems of chemical reactions. Therefore, our result may be considered a validation of the notion in chemistry that concentrations tend to equilibrium. We will prove the following theorem:

Theorem 2.6.1. *Let $\mathcal{E}$ be a finite, natural, atomic event-system of dimension n. Let $\boldsymbol{\alpha} \in \mathbb{R}^n_{>0}$. Then there exists an open, simply-connected $\Omega \subseteq \mathbb{C}$, an $\mathcal{E}$-process $\boldsymbol{f}$ on Ω, and a positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c}$ such that:*

1. $\mathbb{R}_{\geq 0} \subseteq \Omega$,
2. $\boldsymbol{f}(0) = \boldsymbol{\alpha}$, *and*
3. $\boldsymbol{f}(t) \to \boldsymbol{c}$ *as* $t \to \infty$ *along the positive real line (i.e. for all* $\varepsilon \in \mathbb{R}_{>0}$*, there exists* $t_0 \in \mathbb{R}_{>0}$ *such that for all* $t \in \mathbb{R}_{>t_0} : \|\boldsymbol{f}(t) - \boldsymbol{c}\|_2 < \varepsilon$*).*

It follows from Theorem 2.5.15 that the point $\boldsymbol{c}$ depends only on the conservation class of $\boldsymbol{\alpha}$ and not on $\boldsymbol{\alpha}$ itself. That is, two $\mathcal{E}$-processes starting at positive points in the same conservation class asymptotically converge to the same $\boldsymbol{c}$.

Implicit in the atomic hypothesis is the idea that atoms are neither created nor destroyed, but rather are conserved by chemical reactions. Our proof uses a formal analog of this idea. Recall from Definition 2.2.10 that if $\mathcal{E}$ is atomic then $C_{\mathcal{E}}(M)$ contains a unique monomial from $\mathbb{M}_{A_{\mathcal{E}}}$.

Definition 2.6.1. Let $\mathcal{E}$ be a finite, natural, atomic event-system of dimension n. The *atomic decomposition map* $\boldsymbol{D}_{\mathcal{E}} : \mathbb{M}_{\{X_1,X_2,\ldots,X_n\}} \to \mathbb{Z}^n_{\geq 0}$ is the function $M \mapsto \langle b_1, b_2, \ldots, b_n\rangle$ such that $X_1^{b_1}X_2^{b_2}\cdots X_n^{b_n} \in C_{\mathcal{E}}(M) \cap \mathbb{M}_{A_{\mathcal{E}}}$.

The next lemma lists some properties of the atomic decomposition map. Note that though the event-graph $G_{\mathcal{E}}$ is directed, if M and N are monomials and there exists a path in $G_{\mathcal{E}}$ from M to N then there also exists a path in $G_{\mathcal{E}}$ from N to M. Informally, this is because all events are "reversible."

Lemma 2.6.2. *Let $\mathcal{E}$ be a finite, natural, atomic event-system of dimension n and let $M, N \in \mathbb{M}_{\{X_1,X_2,\ldots,X_n\}}$. Then:*

1. $\boldsymbol{D}_{\mathcal{E}}(M) = \boldsymbol{D}_{\mathcal{E}}(N)$ *if and only if* $C_{\mathcal{E}}(M) = C_{\mathcal{E}}(N)$.

2. $\boldsymbol{D}_{\mathcal{E}}(MN) = \boldsymbol{D}_{\mathcal{E}}(M) + \boldsymbol{D}_{\mathcal{E}}(N)$.

Proof. Let $\boldsymbol{D} = \boldsymbol{D}_{\mathcal{E}}$.

(1) $\boldsymbol{D}(M) = \boldsymbol{D}(N) = \langle b_1, b_2, \ldots, b_n\rangle$ if and only if $X_1^{b_1}X_2^{b_2}\cdots X_n^{b_n} \in C_{\mathcal{E}}(M)$ and $X_1^{b_1}X_2^{b_2}\cdots X_n^{b_n} \in C_{\mathcal{E}}(N)$. Then $C_{\mathcal{E}}(M) = C_{\mathcal{E}}(N)$.

(2) Let $\boldsymbol{D}(M) = \langle b_1, b_2, \ldots, b_n\rangle$ and $\boldsymbol{D}(N) = \langle c_1, c_2, \ldots, c_n\rangle$. Then, in $G_{\mathcal{E}}$ there is a path from M to $X_1^{b_1}X_2^{b_2}\cdots X_n^{b_n} \in \mathbb{M}_{A_{\mathcal{E}}}$ and a path from N to $X_1^{c_1}X_2^{c_2}\cdots X_n^{c_n} \in \mathbb{M}_{A_{\mathcal{E}}}$. It follows that there is a path from MN to $X_1^{b_1+c_1}X_2^{b_2+c_2}\cdots X_n^{b_n+c_n} \in \mathbb{M}_{A_{\mathcal{E}}}$. Hence $\boldsymbol{D}(MN) = \langle b_1+c_1, b_2+c_2, \ldots, b_n+c_n\rangle = \boldsymbol{D}(M) + \boldsymbol{D}(N)$. □

Definition 2.6.2. Let $\mathcal{E}$ be a finite, natural, atomic event-system of dimension n. For all $i \in \{1, 2, \ldots, n\}$, for all $M \in \mathbb{M}_{\{X_1,X_2,\ldots,X_n\}}$, $D_{\mathcal{E},i}(M)$ is the i^{th} component of $\boldsymbol{D}_{\mathcal{E}}(M)$.

Definition 2.6.3. Let $\mathcal{E}$ be a finite, natural, atomic event-system of dimension n. For all $i \in \{1, 2, \ldots, n\}$ the function $\kappa_{\mathcal{E},i} : \mathbb{C}^n \to \mathbb{C}$ is given by

$$\langle z_1, z_2, \ldots, z_n \rangle \longmapsto \sum_{j=1}^{n} D_{\mathcal{E},i}(X_j) z_j.$$

Lemma 2.6.3. *Let $\mathcal{E}$ be a finite, natural, atomic event-system of dimension n. Then for all $i \in \{1, 2, \ldots, n\}$, the function $\kappa_{\mathcal{E},i}$ is a conservation law of $\mathcal{E}$.*

Proof. Let $m = |\mathcal{E}|$, and for $j = 1, 2, \ldots, m$, let $\sigma_j, \tau_j \in \mathbb{R}_{>0}$ and $M_j, N_j \in \mathbb{M}_\infty$ with $M_j \prec N_j$ be such that $\mathcal{E} = \{\sigma_1 M_1 - \tau_1 N_1, \ldots, \sigma_m M_m - \tau_m N_m\}$. For $i = 1, 2, \ldots, n$, let $a_{j,i}, b_{j,i} \in \mathbb{Z}_{>0}$ be such that $M_j = X_1^{a_{j,1}} X_2^{a_{j,2}} \cdots X_n^{a_{j,n}}$ and $N_j = X_1^{b_{j,1}} X_2^{b_{j,2}} \cdots X_n^{b_{j,n}}$. Let $(\gamma_{j,i})_{m \times n} = \Gamma_{\mathcal{E}}$.

Then for $j = 1, 2, \ldots, m$:

$$\begin{aligned}
& \sigma_j M_j - \tau_j N_j \in \mathcal{E} & \\
\Rightarrow\quad & M_j \in C_{\mathcal{E}}(N_j) & \text{[Definition 2.2.8]} \\
\Rightarrow\quad & \boldsymbol{D}_{\mathcal{E}}(M_j) = \boldsymbol{D}_{\mathcal{E}}(N_j) & \text{[Lemma 2.6.2]} \\
\Rightarrow\quad & \sum_{i=1}^{n} a_{j,i} \boldsymbol{D}_{\mathcal{E}}(X_i) = \sum_{i=1}^{n} b_{j,i} \boldsymbol{D}_{\mathcal{E}}(X_i) & \text{[Lemma 2.6.2]} \\
\Rightarrow\quad & \sum_{i=1}^{n} (b_{j,i} - a_{j,i}) \boldsymbol{D}_{\mathcal{E}}(X_i) = \mathbf{0} & \\
\Rightarrow\quad & \sum_{i=1}^{n} \gamma_{j,i} \boldsymbol{D}_{\mathcal{E}}(X_i) = \mathbf{0} & \text{[Definition 2.3.1]}
\end{aligned}$$

It follows that for all $j \in \{1, 2, \ldots, m\}$, for all $k \in \{1, 2, \ldots, n\}$,

$$\sum_{i=1}^{n} \gamma_{j,i} D_{\mathcal{E},k}(X_i) = 0$$

Therefore, for all $k \in \{1, 2, \ldots, n\}$, $\Gamma_{\mathcal{E}} \cdot \langle D_{\mathcal{E},k}(X_1), D_{\mathcal{E},k}(X_2), \ldots, D_{\mathcal{E},k}(X_n)\rangle^T = \mathbf{0}$. Since the vector $\langle D_{\mathcal{E},k}(X_1), D_{\mathcal{E},k}(X_2), \ldots, D_{\mathcal{E},k}(X_n)\rangle^T$ is in the kernel of $\Gamma_{\mathcal{E}}$, by Theorem 2.3.2, $\kappa_{\mathcal{E},k}$ is a conservation law of $\mathcal{E}$. $\square$

Lemma 2.6.4. *Let $\mathcal{E}$ be a finite, natural event-system of dimension n. Let $M, N \in \mathbb{M}_\infty$ and let $\boldsymbol{q} \in \mathbb{C}^n$. If $M \in C_{\mathcal{E}}(N)$ and $\boldsymbol{q}$ is a strong $\mathcal{E}$-equilibrium point and $M(\boldsymbol{q}) = 0$, then $N(\boldsymbol{q}) = 0$.*

Proof. Let $\langle v_0, v_1\rangle$ be an edge in $G_{\mathcal{E}}$. Then there exist $e \in \mathcal{E}$ and $\sigma, \tau \in \mathbb{R}_{>0}$ and $T, U, V \in \mathbb{M}_\infty$ such that $e = \sigma U - \tau V$ and $v_0 = TU$ and $v_1 = TV$.

Assume $v_0(\boldsymbol{q}) = 0$. Then either $T(\boldsymbol{q}) = 0$ or $U(\boldsymbol{q}) = 0$. If $T(\boldsymbol{q}) = 0$ then $v_1(\boldsymbol{q}) = 0$. If $U(\boldsymbol{q}) = 0$ and $\boldsymbol{q}$ is a strong $\mathcal{E}$-equilibrium point, then $e(\boldsymbol{q}) = \sigma U(\boldsymbol{q}) - \tau V(\boldsymbol{q}) = 0$, so $V(\boldsymbol{q}) = 0$. Therefore $v_1(\boldsymbol{q}) = 0$. The lemma follows by induction. $\square$

We are now ready to prove Theorem 2.6.1.

Proof of Theorem 2.6.1. Since $\boldsymbol{\alpha}$ is a positive point, it is in some positive conservation class H. By Theorem 2.5.15:

1. There exists exactly one positive strong $\mathcal{E}$-equilibrium point $\boldsymbol{c} \in H$.

2. There exist an open and simply-connected $\Omega \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\boldsymbol{f}$ on Ω such that $\mathbb{R}_{\geq 0} \subset \Omega$ and $\boldsymbol{f}(0) = \boldsymbol{\alpha}$.

3. For all $t \in \mathbb{R}_{\geq 0}$, $\boldsymbol{f}(t) \in H \cap \mathbb{R}^n_{\geq 0}$.

4. There exists $k \in \mathbb{R}_{\geq 0}$ such that for $i = 1, 2, \ldots, n$, for all $t \in \mathbb{R}_{\geq 0}$, $f_i(t) \in \mathbb{R}$ and $0 \leq f_i(t) \leq k$.

Let $\{t_j\}_{j \in \mathbb{Z}_{>0}}$ be an infinite sequence of non-negative reals such that $t_j \to \infty$ as $j \to \infty$. Then $\{\boldsymbol{f}(t_j)\}_{j \in \mathbb{Z}_{>0}}$ is an infinite sequence contained in a compact subset of $\mathbb{R}^n$, so it must have a convergent subsequence. Let $\boldsymbol{q} = \langle q_1, q_2, \ldots, q_n \rangle \in \mathbb{C}^n$ be the limit point of a convergent subsequence of $\{\boldsymbol{f}(t_j)\}_{j \in \mathbb{Z}_{>0}}$. H and $\mathbb{R}^n_{\geq 0}$ are both closed in $\mathbb{C}^n$, so $\boldsymbol{q} \in H \cap \mathbb{R}^n_{\geq 0}$. Since $\mathcal{E}$ is natural and $\boldsymbol{q}$ is an ω-limit of $\boldsymbol{f}$, $\boldsymbol{q}$ must be a strong $\mathcal{E}$-equilibrium point by Lemma 2.5.14.

Assume, for the sake of contradiction, that $\boldsymbol{q} \notin \mathbb{R}^n_{>0}$. Let $i \in \{1, 2, \ldots, n\}$ be such that $q_i = 0$. Let $N \in C_{\mathcal{E}}(X_i) \cap \mathbb{M}_{A_{\mathcal{E}}}$. Since $\mathcal{E}$ is atomic, a unique such N exists. It follows from the definition of event graph that $X_i \in C_{\mathcal{E}}(N)$. By Lemma 2.6.4, $N(\boldsymbol{q}) = X_i(\boldsymbol{q}) = q_i = 0$. It follows that $N \neq 1$. Hence, there exists $X_a \in A_{\mathcal{E}}$ such that X_a divides N and $X_a(\boldsymbol{q}) = 0$.

For all $j \in \{1, 2, \ldots, n\}$ such that $D_{\mathcal{E},a}(X_j) \neq 0$, let $M_j \in C_{\mathcal{E}}(X_j) \cap \mathbb{M}_{A_{\mathcal{E}}}$. Then X_a divides M_j, so $M_j(\boldsymbol{q}) = 0$. Again by Lemma 2.6.4, $X_j(\boldsymbol{q}) = M_j(\boldsymbol{q}) = 0$, so $q_j = 0$. It follows that for all $j \in \{1, 2, \ldots, n\}$ either $D_{\mathcal{E},a}(X_j) = 0$ or $q_j = 0$ so

$$\kappa_{\mathcal{E},a}(\boldsymbol{q}) = \sum_{j=1}^{n} D_{\mathcal{E},a}(X_j) q_j = 0.$$

Since $\kappa_{\mathcal{E},a}$ is a conservation law of $\mathcal{E}$ by Lemma 2.6.3 and $\boldsymbol{q}$ is an ω-limit point of $\boldsymbol{f}$, it follows that

$$\kappa_{\mathcal{E},a}(\boldsymbol{\alpha}) = 0. \tag{2.24}$$

For all j, $D_{\mathcal{E},a}(X_j)$ is nonnegative, and $\boldsymbol{\alpha}$ is a positive point, so for all $j \in \{1, 2, \ldots, n\}$, $D_{\mathcal{E},a}(X_j)\alpha_j \geq 0$. But $D_{\mathcal{E},a}(X_a) = 1$ and $\alpha_a > 0$ so $\kappa_{\mathcal{E},a}(\boldsymbol{\alpha}) > 0$, contradicting equation (2.24). Therefore $\boldsymbol{q} \in \mathbb{R}^n_{>0}$. Since $\boldsymbol{c}$ is the unique positive strong $\mathcal{E}$-equilibrium point in H, $\boldsymbol{c} = \boldsymbol{q}$.

Let $U \subseteq H \cap \mathbb{R}^n_{>0}$ be the open set stated to exist in Theorem 2.5.15.2c. Since $\boldsymbol{c}$ is an ω-limit point of $\boldsymbol{f}$, there exists $t_0 \in \mathbb{R}_{>0}$ such that $\boldsymbol{f}(t_0) \in U$. Again by Theorem 2.5.15, there exist $\widetilde{\Omega} \subseteq \mathbb{C}$ and an $\mathcal{E}$-process $\tilde{\boldsymbol{f}}$ on $\widetilde{\Omega}$ such that $\mathbb{R}_{\geq 0} \subseteq \widetilde{\Omega}$ and $\tilde{\boldsymbol{f}}(0) = \boldsymbol{f}(t_0)$ and $\tilde{\boldsymbol{f}}(t) \to \boldsymbol{c}$ as $t \to \infty$. By Lemma 2.4.3, for all $t \in \mathbb{R}_{\geq 0}$, $\boldsymbol{f}(t + t_0) = \tilde{\boldsymbol{f}}(t)$. Therefore, $\boldsymbol{f}(t) \to \boldsymbol{c}$ as $t \to \infty$. □

2.7 Conclusion

We have endeavored to place the kinetic theory of chemical reactions on a firm mathematical foundation and to make the law of mass action available for purely mathematical consideration.

With regard to chemistry, we have proven that many of the expectations acquired through empirical study are warranted. In particular:

1. For finite event-systems, the stoichiometric coefficients determine conservation laws that processes must obey (Theorem 2.3.3). In fact, we can show (manuscript in preparation):

    (a) For finite, physical event-systems, the stoichiometric coefficients determine all linear conservation laws;

(b) For finite, natural event-systems, the stoichiometric coefficients determine *all* conservation laws.

2. For finite, physical event-systems, a process begun with positive (non-negative) concentrations will retain positive (non-negative) concentrations through forward real time where it is defined (Theorem 2.4.5). For finite, natural event-systems, a process begun with positive (non-negative) concentrations will retain positive (non-negative) concentrations through *all* forward real time (Theorem 2.5.15) — that is, it will be defined through all forward real time.

3. Finite, natural event-systems must obey the "second law of thermodynamics" (Theorem 2.5.6). In addition, the flow of energy is very restrictive — finite, natural event-systems can contain no energy cycles (Theorem 2.5.1).

4. For finite, natural event-systems, every positive conservation class contains exactly one positive equilibrium point. This point is a strong equilibrium point and is asymptotically stable relative to its conservation class (Theorem 2.5.15).

Unfortunately, we, like our predecessors, are unable to settle the problem of whether a process begun with positive concentrations must approach equilibrium. We consider this the fundamental open problem in the field (Open Problem 1). For finite, natural event-systems that obey a mathematical analogue of the atomic hypothesis, we settle Open Problem 1 in the affirmative (Theorem 2.6.1). In particular, we show that for finite, natural, atomic event-systems, every positive conservation class contains exactly one non-negative equilibrium point. This point is a positive strong equilibrium point and is globally stable relative to the intersection of its conservation class with the positive orthant.

In terms of expanding the mathematical aspects of our theory, there are several potentially fruitful avenues including:

1. **Complex-analytic aspects of event-systems.** While we exploit some of the complex-analytic properties of processes in this paper, we believe that a deeper investigation along these lines is warranted. For example, if we do not restrict the domain of a process to be simply-connected, then each component of a process becomes a complete analytic function in the sense of Weierstrass.

2. **Infinite event-systems.** Issues of convergence arise when considering infinite event-systems. To obtain a satisfactory theory, some constraints may be necessary. For example, a bound on the maximum degree of events may be worth considering. It may also be possible to generalize the notion of an atomic event-system to the infinite-dimensional case in such a way that each atom has an associated conservation law. One might then restrict initial concentrations to those for which each conservation law has a finite value. Additional constraints are likely to be needed as well.

3. **Algebraic-geometric aspects of event-systems.** Every finite event-system that generates a prime ideal has a corresponding affine toric variety (as defined in [11, p. 15]). The closed points of this variety are the strong equilibria of the event-system. Further, every affine toric variety is isomorphic to an affine toric variety whose ideal is generated by a finite event system. One could generalize event-systems to allow

irreversible reactions. In that case, it appears that the prime ideals generated by such event-systems are exactly the ideals corresponding to affine toric varieties.

We can show (proof not provided) that finite, natural, atomic event-systems generate prime ideals. We are working towards settling Open Problem 1 in the affirmative for every finite, natural event-system that generates a prime ideal.

2.8 Acknowledgements

This work benefitted from discussions with many people, named here in alphabetical order: Yuliy Baryshnikov, Yuriy Brun, Qi Cheng, Ed Coffman, Ashish Goel, Jack Hale, Lila Kari, David Kempe, Eric Klavins, John Reif, Paul Rothemund, Robert Sacker, Rolfe Schmidt, Bilal Shaw, David Soloveichik, Hal Wasserman, Erik Winfree.

Chapter 3

Experiments in DNA Self-Assembly

See plastic Nature working to this end,
The single atoms each to other tend,
Attract, attracted to, the next in place
Form'd and impell'd its neighbour to embrace.
—Alexander Pope, *An Essay on Man*.

Nickolas Chelyapov, Yuriy Brun, Dustin Reishus, Bilal Shaw, Leonard Adleman and I have used DNA self-assembly to form triangles and hexagonal tilings. In Section 3.1, I present a jointly-authored article [8] describing this research.

In Section 3.2, I present cylinders and Möbius strips self-assembled from DNA. This work was done in collaboration with Leonard Adleman and Nikhil Gopalkrishnan.

3.1 DNA Triangles and Self-Assembled Hexagonal Tilings

3.1.1 Abstract

We have designed and constructed DNA complexes in the form of triangles. We have created hexagonal planar tilings from these triangles via self-assembly. Unlike previously reported structures self-assembled from DNA, our structures appear to involve bending of double helices. Bending helices may be a useful design option in the creation of self-assembled DNA structures. It has been suggested that DNA self-assembly may lead to novel materials and efficient computational devices.

3.1.2 Main Paper

There are exactly three regular tilings of the plane: one composed of triangles, one of squares, and one of hexagons. We have constructed DNA complexes in the form of triangles that self-assemble into planar structures in the form of regular hexagonal tilings.

To date, only a small number of DNA complexes have been demonstrated to self-assemble into orderly structures. For example, Seeman et al.[30] created double-crossover complexes and Winfree et al.[35] showed that they self-assemble into planar structures in the form of rectangular tilings. LaBean et al.[20] extended the double-crossover motif to create triple-crossover complexes that also assemble into structures of this form. Quadruple-crossover complexes that assemble into structures of this form have also been reported.[7] Yan et al.[38] created 4 by 4 complexes that assemble into planar structures in the form of square tilings, and Liu et al.[23] created triangular complexes that can assemble into orderly structures of several different forms. Recently, Ding et al.[9] also

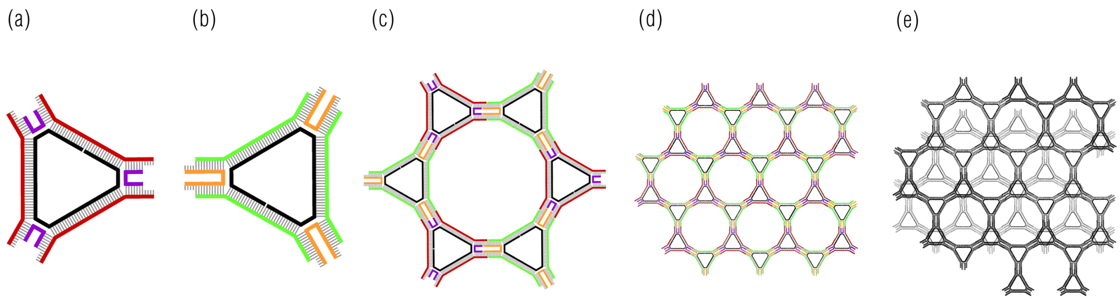
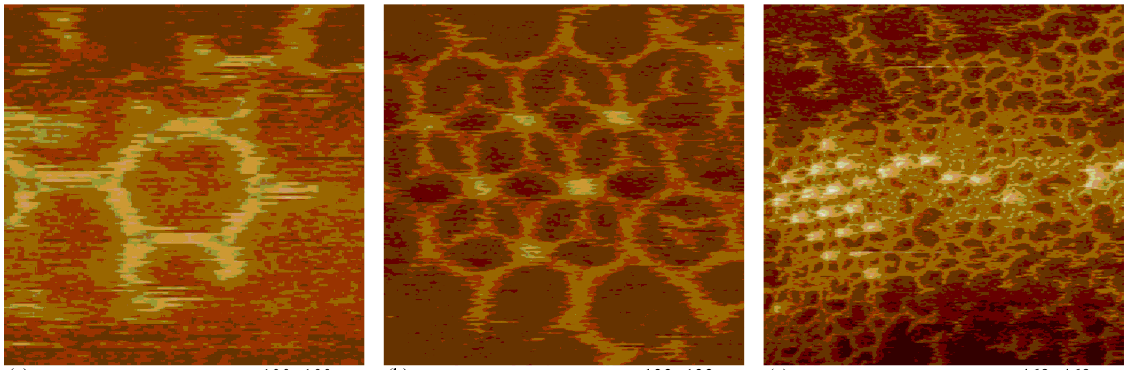


Figure 3.1: Schematics. (a) Type-a triangular complex. Core strand (black), side strands (red), horseshoe strands (purple), Watson-Crick pairing (gray). (b) Type-b triangular complex. Core strand (black), side strands (green), horseshoe strands (orange), Watson-Crick pairing (gray). (c) Hexagonal structure composed of six triangular complexes. (d) Hexagonal tiling composed of hexagonal structures. (e) A pair of overlapping hexagonal tilings. Top layer shown gray; bottom layer shown black. (see also Figure 3.2b).

demonstrated the creation of hexagonal structures from triangular complexes using an approach different from the one presented here.

We were inspired to explore triangular complexes by Yang et al.[39], who used them as markers on structures formed from double-crossover complexes. We created free-standing triangular complexes composed of seven strands of DNA. We designed two such complexes that stick to one another at their vertices. The type-a complex, Figure 1a, has a 90-mer core strand (the same length as the core strand used by Yang et al.), three 52-mer side strands with identical sequences, and three 14-mer horseshoe strands with identical sequences. The type-b complex, Figure 1b, has a 90-mer core strand with sequence identical to that used in the type-a complex, three 52-mer side strands with identical sequences, and three 30-mer horseshoe strands with identical sequences. The unpaired bases at the ends of the side strands in the type-a complex are complementary to the unpaired bases at the ends of the horseshoe strands in the type-b complex, allowing



(a) 100×100 nm (b) 133×133 nm (c) 469×469 nm

Figure 3.2: Atomic force micrograph images of self-assembled structures. Height information sensed by the AFM is encoded in pixel amplitude. (a) Hexagonal structure composed of six triangular complexes. (b) A pair of overlapping hexagonal tilings (see also Figure 1e). (c) Structures composed of hexagonal and non-hexagonal rings.

triangles to connect at these sticky ends. In theory, such triangles can form a hexagon, as shown in Figure 1c, and hexagons can form a tiling, as shown in Figure 1d.

The two types of triangular complexes were assembled in separate tubes by annealing. The complexes were then combined at room temperature. Atomic force microscope images of the resulting structures are shown in Figure 2.

Figure 2a shows six triangular complexes assembled into a single hexagonal structure. The distance between opposing sides is approximately 35 nm, which is in good agreement with expectations based on number of base pairs in the structure. Figure 2b (see also Figure 1e) shows two hexagonal tilings, one lying on top of the other. One-half of the triangles of the top tiling lie in the centers of the hexagons of the bottom tiling. The remaining triangles of the top tiling lie directly on top of the triangles of the bottom tiling. Where triangles overlap the structure has greater height, as revealed by bright spots in Figure 2b. In our experience, tilings layered in this way are common. Layering of tilings also occurs in the hexagonal lattices of Ding et al.,[9] where the hexagons on successive layers appear to have centers that coincide.

We designed our complexes to form equilateral triangles and to stick to each other but not to themselves. Figure 2a suggests that they do have this form and stick in this way. However, sticking in this way is also consistent with the formation of ring structures containing any even number of triangular complexes. Such structures are perhaps energetically less favorable than a hexagonal structure; nonetheless, they do form. Figure 2c shows a broad view of structures consisting of hexagons together with ring structures with more or fewer than six vertices. It seems likely that the number of such non-hexagonal ring structures could be reduced by using more than two types of triangular complexes.

Occasionally, rings with an odd number of triangles also form. These may result from our use of the same core strand in the two types of triangular complexes. A common core strand allows for the creation of chimeric triangular complexes containing side strands from complexes of different types. It seems likely that the number of such rings could be reduced by using distinct strands in triangular complexes of different types.

In many published works on DNA self-assembly, the assembled structures are planar and composed of double helices running in parallel[30, 35, 20, 22, 21, 13]. While our structures are planar, they do not have this form. In the case of hexagons as shown in Figure 1c, helices run parallel where sticky ends come together, but meet at angles of 150 or 60 where no sticky ends are present. It appears that some helices in our structures are bent. The use of long side strands with a 30-mer complementarity to the core strand in our triangular complexes may be critical in allowing bending to occur. In fact, when triangular complexes employing shorter side strands with only a 21-mer complementarity to a 63-mer core strand were attempted, AFM imaging revealed no structures (data not shown). While existing DNA self-assembled structures use helices as linear elements, bending may allow for the use of helices as curvilinear elements, thus providing greater freedom in the design of future self-assembled DNA structures.

The 4 by 4 complexes of Yan et al.[38] produce planar structures with helices intersecting at 90 angles. The helices in the 4 by 4 complex have unpaired stretches of polyT. Images show that helices make right-angle turns, presumably at these sites[38]. Thus, unlike our structures, where helices apparently bend, helices in structures created with the 4 by 4 complex apparently hinge.

Liu et al.[23] also described structures with nonparallel helices. However, these structures are not planar, and helices are allowed to cross each other without bending. Like our structures, these structures are created from triangular complexes designed to stick to one another at vertices. While the triangular complexes of Liu et al. stick to one another via one helix, our complexes stick via two. This may provide greater integrity. In addition, our structures may be useful when planarity is desired.

Ding et al.[9] have recently created pseudohexagonal structures from triangles. They appear to have avoided the problem of nonhexagonal ring formation by using triangles with sides composed of double crossovers,1 which may provide greater rigidity than the single-helical sides used in our triangles.

Using the design concepts described here, it seems possible, in principle, to create complexes with arbitrary polygonal shapes. Of immediate interest would be the creation of squares, pentagons, and non-equilateral triangles.

3.1.3 Acknowledgment.

This research has been supported by grants from the NSF, DARPA, and NASA/JPL.

3.1.4 DNA Sequences

Type-a triangular complex

black: ttcgtccagtgagcatcctgtagttgcggattcgtccagtgagcatcctgtagttgcggattcgtccagt gagcatc-ctgtagttgcgga

red: ggatagcgccatgctcactggacgaatccgcaactacaggaacgaacactcc

purple: tgttcgttggcgct

Type-b triangular complex black is the same as in type-a triangular complex

green: gactgagcccatgctcactggacgaatccgcaactacaggaactactcatcc

orange: atccggatgagtagttgggctcagtcggag

Purple and orange sequences were derived from those found in [38].

3.1.5 Materials and Methods

DNA strands were synthesized and PAGE purified by Integrated DNA Technologies (IDT). Type-a triangular complexes were created in a solution consisting of 0.2 M black strand, 0.6 M red strand, and 0.6 M purple strand in TAE/Mg2+ buffer (40mM Tris-HCl, pH 8.0; 1 mM EDTA; 12.5 mM MgOAc). The solution was heated to 90 C for 2 minutes, then cooled to 40 C at 2 C/min, then to 25 C at 1 C/min. Type-b complexes were created similarly.

3.1.6 AFM Sample Preparation and Imaging

Equal volumes of solutions containing type-a and type-b triangular complexes were combined and incubated at room temperature for several hours. A 5 l aliquot was spotted onto freshly cleaved mica (Ted Pella), left for 30 seconds and then topped with 25 l of TAE/Mg2+ buffer. Imaging was performed on a Multimode Nanoscope IIIa atomic force microscope (Digital Instruments) in tapping mode, using a fluid cell, J scanner and 200 m cantilevers with Si3N4 tips.

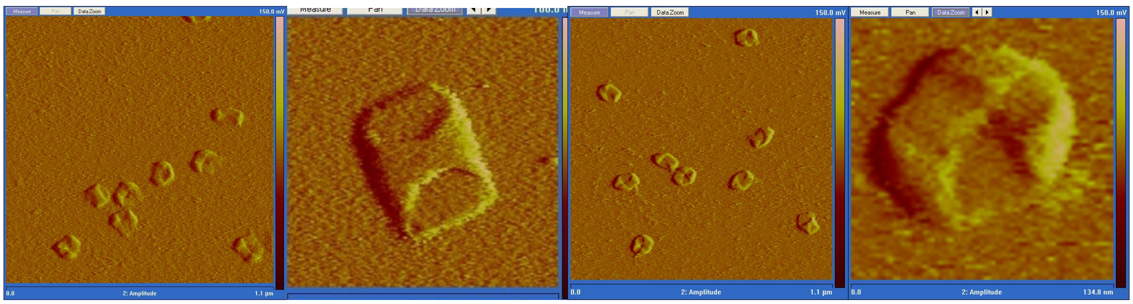
3.2 Cylinders and Möbius strips from DNA origami

We report the self-assembly of two novel DNA complexes. Using the technique of DNA origami [26], we have assembled DNA complexes in the shape of cylinders (Figures 3.3a,3.3b) and in the shape of Möbius strips (Figures 3.3c,3.3d). We believe this is the first demonstration of Möbius strips at the nanoscale.

Rothemund's origami square, our cylinder and our Möbius strip employ nearly the same set of oligonucleotides. If cut open, both the cylinder and the Möbius strip would form squares of approximately 100 nm a side.

The structures of Rothemund [26] and the origami nanotubes of Douglas et al. [10] were designed to enforce specific angles between adjacent double helices. We nonetheless suspected that the Rothemund square would have sufficient residual flexibility to absorb the stress induced by twisting into a Möbius strip or a cylinder. Our results confirm that this is the case.

Möbius strips are known to be chiral in Euclidean 3-space. They may be clockwise or counterclockwise. Atomic force micrographs suggest that there may be a preference for our DNA self-assembly to produce counterclockwise Möbius strips. If this is so, then DNA self-assembled structures might ultimately be useful as a basis for the creation of asymmetric catalysts for the enantioselective synthesis of chiral compounds.



(a) 1.1 $\mu m \times 1.1$ μm (b) 175.8 $nm \times 175.8$ nm (c) 1.1 $\mu m \times 1.1$ μm (d) 134.8 $nm \times 134.8$ nm

Figure 3.3: Atomic force microscope scans of cylinders (a,b) and Möbius strips (c,d).

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