Stationary Distributions for Asymmetrical Autocatalytic Reaction Networks with Discreteness-induced Transitions (DITs)

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Abstract

Stationary distributions for asymmetrical autocatalytic reaction networks with discreteness-induced transitions (DITs)

by

Cameron Gallinger

The phenomenon of discreteness-induced transitions is highly stochastic dependent dynamics observed in a family of autocatalytic chemical reaction networks including the acclaimed Togashi Kaneko model. These reaction networks describe the behaviour of several different species interacting with each other, and the counts of species concentrate in different extreme possible values, occasionally switching between them. This phenomenon is only observed under some regimes of rate parameters in the network, where stochastic effects of small counts of species takes effect.

The dynamics for networks in this family is ergodic with a unique stationary distribution. While an analytic expression for the stationary distribution in the special case of symmetric autocatalytic behaviour was derived by Bibbona, Kim, and Wiuf, not much is known about it in the general case. Here we provide a candidate distribution for reaction networks when the autocatalytic rates are different. It was inspired by a model in population genetics, the Moran model with genic selection, which shares many similar reaction dynamics to our autocatalytic networks. We show that this distribution is stationary when autocatalytic rates are equal, and that it is close to stationary when they are not equal.

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1 Introduction

Discreteness-induced transitions (DITs) are a phenomenon observed in a family of chemical reactions which appear when the number of molecules reacting is sufficiently small that the dynamics of the system are not governed by deterministic equations. Togashi and Kaneko investigated these DITs in a small system of autocatalytic reactions, now known as the Togashi-Kaneko (TK) network. Togashi and Kaneko showed through simulations of the network that when the total number of molecules was sufficiently small the process ran contrary to the deterministic process, when the total number of molecules is high, which is governed by a system of differential equations. They observed a switching pattern where the system would switch between two states while spending little time in between; the states were at extremes where two species of molecules would hold the vast majority of the total population while the other two species were nearly extinct, there would then be fast switching events where the two species which were nearly extinct would hold the majority of the total population and the other two were nearly extinct. It is also shown that as they increased the total population, by increasing the volume of the container, the process was again governed by the deterministic equations.

To analyze the behaviour of these types of reactions when the total population is low Bibbona, Kim and Wiuf provide a theoretical analysis of a family of autocatalytic reactions which includes the acclaimed TK model. Modeling the system stochastically as continuous time Markov chains, they prove positive recurrence and ergodicity for reactions in the family, which in turn proves the existence of a unique stationary distribution for each system. While it is very difficult to compute a closed form stationary distribution for many of these systems Bibbona *et al* show that for symmetric autocatalytic rates and equal outflow rates the networks have a Dirichlet-multinomial distribution. They also show that with classical volume scaling under mass-action dynamics, as the volume is increased to infinity the system converges to the classical deterministic system.

In this thesis, we will borrow a distribution from a model in population genetics, the Moran model with genic selection. This distribution is stationary for a system with similar dynamics to the autocatalytic networks, but includes asymmetrical autocatalyic-like reactions. This distribution can be thought of as a weighted Dirichlet-multinomial distribution, and when the rates are symmetric it reduces to the distribution given by Bibbona *et al*. The candidate distribution also shows the presence of DITs when the parameters are in certain regimes, as the Bibbona-Kim-Wiuf distribution does as well. To determine if this distribution is in fact stationary for the model, we must show it satisfies the global balance condition. Unfortunately the balance equation is not identically zero for this particular distribution, but under certain parameter regimes we can show that the balance equation is very close to zero. Using classical volume scaling, we show that the distribution agrees to the classical deterministic model when the volume is large. We also compare the distribution to exact simulations of the reaction network using the Gillespie algorithm, and it lines up with the

simulation results very nicely.

Before we get to the results, we will first discuss the tools needed to get there. First we will go over continuous time Markov chains, we will use them to describe how the populations of different species of molecules in chemical reaction networks evolve and there are several tools which we can use to describe the long term behaviour of our systems. We then will discuss the field of chemical reaction networks. We will look at both the deterministic model which describes the networks when the total population is very large, and the stochastic model which captures nuances which are washed out in the approximations of the deterministic model. We then draw a connection between the two models by looking into classical volume scaling under mass-action dynamics and show that as the volume gets very large the stochastic model converges to the deterministic model.

2 Preliminaries

2.1 Continuous time Markov Chains

We will be modelling our chemical reactions as continuous time Markov chains, so there are a number of theorems we must go over to describe the long term behaviour of these processes. We will see that under certain conditions, the stationary or limiting distribution of the process must satisfy certain conditions. The following definitions and theorems have been adapted from Grimmet and Stirzaker's *Probability and Random Processes* [9] and Norris' *Markov Chains* [14] to align with our notation.

Let $X = \big\{X(t) : t \geq 0\big\}$ be a family of Random variables in a countable state space S indexed by $t \in [0, \infty)$

Definition 2.1 (Markov Property)**.** *The process X satisfies the Markov property if*

$$\mathbb{P}\Big(X(t_n) = j | X(t_1) = i_1, \ldots, X(t_{n-1}) = i_{n-1}\Big) = \mathbb{P}\Big(X(t_{n-1}) = i_{n-1}\Big)$$

for all $j, i_1, \ldots, i_{n-1} \in I$ and any increasing sequence $t_1 < t_2 < \cdots < t_n$ of times.

Definition 2.2 (Right-Continuity)**.** *Let $X = \big\{X(t) : t \geq 0\big\}$ be a random process taking values in S a countable set. For a sample path $X(\cdot, \omega)$ corresponding to $\omega \in \Omega$ the sample space, we say $X(\cdot, \omega)$ is* **right-continuous** *if for $t \in [0, \infty)$ there exists an $\varepsilon_{t,\omega} > 0$ such that*

$$X(t, \omega) = X(t + u, \omega) \quad \text{for } 0 \leq u < \varepsilon_{t,\omega}$$

that is to say $X(\cdot, \omega)$ is constant on $[t, t + \varepsilon)$. X is called right-continuous if all its sample paths are right continuous.

Definition 2.3. *The process X is a continuous time Markov chain (CTMC) if it is right-continuous and satisfies the Markov property.*

Definition 2.4. *the* ***transition probability*** $p_{ij}(s,t)$ *is defined*

$$p_{ij}(s,t) = \mathbb{P}\big(X(t) = j | X(s) = i\big), \quad s \leq t \tag{2.1}$$

the CTMC is called ***homogeneous*** *if* $p_{ij}(s,t) = p_{ij}(0, t-s)$ *for all* $i, j, s \leq t$ *and we write* $p_{ij}(t-s)$ *for* $p_{ij}(s,t)$

Definition 2.5. *Let* $P(t)$ *be the* $|S| \times |S|$ *matrix with entries* $p_{ij}(t)$*. The family* $\{P(t) : t \geq 0\}$ *is called the* ***transition semigroup*** *of the CTMC* $X(t)$

Theorem 2.6. *The family* $\{P(t) : t \geq > 0\}$ *is a* ***stochastic semigroup****, i.e. it satisfies*

(i) $P(0) = I$ *the* $|S| \times |S|$ *identity matrix*

(ii) $P(t)$ *is a stochastic matrix, its entries are non-negative and rows sum to 1*

(iii) $P(t+s) = P(t)P(s)$ *for* $s, t \geq 0$ *(Chapman-Kolmogorov equations)*

Definition 2.7. *the* ***infinitesimal generator*** *of* $X(t)$ *is defined as the one-sided limit*

$$Q = \lim_{h \to 0^+} \frac{P(h) - I}{h} \tag{2.2}$$

and has the following properties:

(i) $\sum_j q_{ij} = 0$

(ii) $q_{ij} \geq 0$ *for* $i \neq j$

(iii) $\sum_{\jmath \neq i} qij = -q_{ii}$

Definition 2.8. *the* ***Kolmogorov forward equation*** *is given by* $P'(t) = P(t)Q$ *or*

$$p'_{ij}(t) = \sum_k p_{ik}(t) q_{kj}, \quad \forall i, j \in S \tag{2.3}$$

the ***Kolmogorov backward equation*** *is given by* $P'(t) = QP(t)$ *or*

$$p'_{ij}(t) = \sum_k q_{ik} p_{kj}(t), \quad \forall i, j \in S \tag{2.4}$$

Theorem 2.9. *Let* S *be a countable set and* Q *a generator on* S*. Let* X *be the Markov chain with generator* Q*.*

1. *the transition semigroup* $\big\{P(t) : t \geq 0\big\}$ *of* X *is the non-negative solution of the backward equation* $\frac{dP}{dt} = QP(t)$*, subject to* $P(0) = I$ *the identity matrix.*

2. *the semigroup* $\big\{P_t\big\}$ *is also the non-negative solution of the forward equation* $\frac{dP}{dt} = P(t)Q$*.*

Definition 2.10. *$X(t)$ is called **irreducible** if for any pair of states i, j we have $p_{ij}(t) > 0$ for some t*

Definition 2.11. *The state $i \in S$ is called **recurrent** if*

$$\mathbb{P}\big(\{t \geq 0 : X(t) = i\} \text{ is unbounded } \}\big) = 1 \tag{2.5}$$

*i is called **transient** if*

$$\mathbb{P}\big(\{t \geq 0 : X(t) = i\} \text{ is unbounded } \}\big) = 0 \tag{2.6}$$

Theorem 2.12. *the following dichotomy holds:*

(i) if $\sum_{j \neq i} q_{ij} = 0$ or $\mathbb{P}\big(\inf\{t : X(t) = i\} < \infty | X(0) = i\big) = 1$ then i is recurrent and $\int_0^\infty p_{ii}(t)dt = \infty$

(ii) if $\sum_{j \neq i} q_{ij} = 0$ and $\mathbb{P}\big(\inf\{t : X(t) = i\} < \infty\big) < 1$ then i is transient and $\int_0^\infty p_{ii}(t)dt < \infty$

Definition 2.13. *if $\sum_{j \neq i} q_{ij} = 0$ or the mean time to return to state i is finite, i.e. $\mathbb{E}\big[\inf\{t : X(t) = i\} | X(0) = i\big] < \infty$ the state i is called **positive recurrent***

Definition 2.14. *The CTMC $X(t)$ is called **non-explosive** if any of the following conditions hold*

(i) S is finite

(ii) $\sup_i \sum_j q_{ij} < \infty$

(iii) $X(0) = i$ where i is a recurrent state

Definition 2.15. *Suppose X is irreducible and non-explosive with transition semigroup $\Big\{P(t) : t \geq 0\Big\}$. The vector π is a **stationary measure** for X if $\pi = \pi P(t)$ for $t \geq 0$. If $\sum_i \pi_i = 1$ π is called a **stationary distribution**.*

Theorem 2.16. *Let X be an irreducible Markov chain with state space S.*

1. *if some $k \in S$ is positive recurrent, there exists a unique stationary distribution π which satisfies $\pi Q = 0$, and all states are positive recurrent.*
2. *if X is non-explosive and there exists a distribution π satisfying $\pi Q = 0$ then: i) all states are positive recurrent, ii) π is stationary, and iii) $\pi_k = 1/(m_k q_k) \forall k \in I$ where m_k is the expected return time to k*

*Note: the system of equations $Q\pi = 0$ is known as the **Global Balance equation***

Theorem 2.17 (Markov chain limit theorem)**.** *Let X be irreducible and non-explosive.*

1. *if the stationary distribution π exists, then it is unique and*

$$p_{ij}(t) \to \pi_j \text{ as } t \to \infty \quad \forall i, j$$

2. *if there is no stationary distribution, then*

$$p_{ij} \to 0 \text{ as } t \to \infty$$

2.1.1 Lumpability

Since the Markov Chains we will be working with have inflow and outflow reactions, that is the total population is changing in time as well as the individual populations of the species, we need a tool to help us separate the internal reactions from the inflow and outflow. We turn to the notion of **lumpability** which gives criteria for the construction of a new Markov chain on a partition of the state space, the following definitions and theorems for lumpability for CTMCs with countable state spaces are taken from [5]. Let $X(t)$ be a CTMC on a countable state space $S = \{e_1, e_2, \dots\}$ with semigroup $P(t) = \{p_{ij}(t)\}_{i,j\in S}$, and generator Q; without loss of generality we will take $S = \mathbb{N}$. Let $\mathcal{E} = \{E_1, E_2, \dots\}$ be some partition on $\mathbb{N}$, we define a function

$$\begin{aligned} &h : \mathbb{N} \to \mathbb{N} \\ &h(i) = j \iff i \in E_j \end{aligned} \tag{2.7}$$

we define $\bar{X}(t) = h\big(X(t)\big)$ to be the **lumped process** with respect to the partition $\mathcal{E}$

Definition 2.18. *let $v = (v_1, v_2, \dots)$ be an initial probability vector for the CTMC $X(t)$, we say*

*(i) $X(t)$ is **lumpable** with respect to $\mathcal{E}$ and v if $\bar{X}(t)$ is a CTMC given $X(t)$ has initial probability vector v*

*(ii) $X(t)$ is **strongly lumpable** with respect to $\mathcal{E}$ if it is lumpable for any initial probability vector v*

*(iii) $X(t)$ is **weakly lumpable** with respect to $\mathcal{E}$ if it is lumpable for at least one initial probability vector v*

Suppose $X(t)$ is weakly lumpable with respect to v, let $\hat{p}_{ij}$ be the transition probabilities for the lumped chain $\bar{X}(t)$ and $\hat{P}(t) = [\hat{p_{ij}}])$ the semigroup. For all $s \geq 0$

$$\begin{aligned} \hat{p}_{ij}(t) =& \mathbb{P}_v(X(t+s) \in E_j | X(s) \in E_i) \\ =& \frac{\sum_{k\in E_i} \mathbb{P}_v(X(s) = k)\mathbb{P}(X(t+s) \in E_j | X(s) = k)}{\sum_{k\in E_i} \mathbb{P}_v(X(s) = k)} \\ =& \frac{\sum_{k\in E_i} \mathbb{P}_v(X(s) = k)\mathbb{P}(X(t) \in E_j | X(0) = k)}{\sum_{k\in E_i} \mathbb{P}_v(X(s) = k)} \end{aligned}$$

where in the last line we use the fact that $X(t)$ is time homogeneous. Letting $s \to \infty$ we have

$$\hat{p}_{ij}(t) = \sum_{k\in E_i} \pi_k^{(i)} \sum_{l\in E_j} p_{kl}(t) \tag{2.8}$$

where

$$\pi_k^{(i)} = \frac{\pi_k}{\sum_{j\in E_i} \pi_j} \mathbb{1}_{k\in E_i}$$

Theorem 2.19. *The CTMC $X(t)$ on the state space $S = \{e_1, e_2, ...\}$ is strongly lumpable on the partition $\mathcal{E} = \{E_1, E_2, \dots\}$ provided*

(i) $X(t)$ *is irreducible, positive recurrent with stationary distribution* π

(ii) *every* E_i *is finite*

(iii) $\forall E_i, E_j \in \mathcal{E}$ *and* $\forall i, i' \in E_i$

$$\sum_{j \in E_j} q_{ij} = \sum_{j \in E_j} q_{i'j} = \bar{q}_{E_i E_j}$$

Where $\bar{q}_{E_i E_j}$ *are the transition rates of the lumped chain* $\bar{X}(t)$.

Since $\bar{X}(s) = E_i \iff X(s) \in E_i$

$$\mathbb{P}(\bar{X}(t) = j | X(s) = i, \bar{X}(s) = E_i) = \mathbb{P}(\bar{X}(t) = j | \bar{X}(s) = E_i) \tag{2.9}$$

That is, $\bar{X}(t)$ is independent of $X(s)$ given $\bar{X}(s)$. [6]

2.2 Chemical reaction networks (CRNs)

The following definitions and theorems on CRNs have been compiled from a survey [2] and textbook [3] by David F. Anderson and Thomas G. Kurtz as well as some unpublished lecture notes [1] by Anderson.

Definition 2.20. *A Chemical reaction network is described by the triple* $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ *where*

(i) $\mathcal{S} = \{S_1, \dots, S_d\}$ *is the set of species*

(ii) $\mathcal{C}$ *is the set of complexes, which consist of linear combinations of the species with non-negative integer coefficients*

(iii) $\mathcal{R}$ *the set of reactions, a binary relation on the complexes* y_k

an example of a CRN is given by the graph

$$A + B \to C \quad C + B \to B \quad \emptyset \to A \tag{2.10}$$

2.2.1 Mass-action kinetics

Consider a system with $\mathcal{S} = \{S_1, \dots, S_d\}$ and kth reaction $y_k \to y_k' \in \mathcal{R}$. We denote the rate of the reaction $\lambda_k(x)$ where $x \in \mathbb{R}^d_{\geq 0}$. For two vectors $u, v \in \mathbb{R}^d_{\geq 0}$ we define

$$u^v = \prod_{i=1}^{d} u_i^{v_i} \tag{2.11}$$

with $0^0 \equiv 1$. The kinetics of the reaction $y_r \to y_r'$ is called **mass-action kinetics** if for $x \in \mathbb{R}^d_{\geq 0}$

$$\lambda_r(x) = \kappa_r x^{y_r} \tag{2.12}$$

where $\kappa_r > 0$ is the **rate constant** for the rth reaction. Some examples of source complexes and their mass action rates:

$$\begin{array}{cc} S_1 \to * & \kappa x_1 \\ S_1 + S_2 \to * & \kappa x_1 x_2 \\ \emptyset \to * & \kappa \end{array}$$

2.2.2 Deterministic Model

Consider a chemical reaction network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ where the populations of the species are so high that a deterministic model accurately captures the dynamics of their concentrations. Let $x(t) \in \mathbb{R}^n_{\geq 0}$ be the vector where $x_i(t)$ models the concentration of species S_i at time t, then the deterministically modelled system is given by the Ordinary differential equation (ODE)

$$\dot{x}(t) = \sum_r \kappa_r x(t)^{y_r}(y'_r - y_r) \tag{2.13}$$

Where $y_r \to y'_r$ is the rth reaction with $y_r, y'_r \in \mathbb{Z}^d$. For example, the network:

$$S + I \to 2I \qquad I \to S \tag{2.14}$$

is governed by the deterministic system of ODEs

$$\begin{aligned} \dot{x}_S &= -\kappa_1 x_S x_I + \kappa_2 x_I \\ \dot{x}_I &= \kappa_1 x_S x_I - \kappa_2 x_I \end{aligned} \tag{2.15}$$

We can also represent equation (2.13) in integral form as

$$x(t) = x(0) + \sum_r \left(\int_0^t \kappa_r x(s)^{y_r} ds \right)(y'_r - y_r) \tag{2.16}$$

2.2.3 Stability of ODEs

Consider a system of ODEs in some domain $D \subset \mathbb{R}^d$

$$\dot{x}(t) = f((x(t)), \quad x(0) = x_0 \in D \tag{2.17}$$

We call a point c a **equilibrium point** or **fixed point** if $f(c) = 0$. At c the derivative with respect to time is 0, so the system is not changing at c, moreover if $x(0) = c$ then $x(t) = c$ for all t.

Definition 2.21. *The equilibrium point c is said to be **locally stable** if*

$$\exists \varepsilon > 0 \ni x(0) \in B_\varepsilon(c) \implies \lim_{t\to\infty} x(t) = c \tag{2.18}$$

*The equilibrium point c is said to be **globally stable** if*

$$\lim_{t\to\infty} x(t) = c \quad \forall x(0) \in D \tag{2.19}$$

A system may have multiple equilibrium points, unless it is globally stable, in which case there is only one equilibrium point. To prove local or global stability, we will use **Linear stability analysis** and **Lyapunov functions**.

Suppose c is a equilibrium point (i.e. f(c)=0), let us take a Taylor expansion around c of the right-hand side of (2.17)

$$\begin{aligned}\dot{x} =& f(c) + \frac{\partial f}{\partial x}\Big|_c (x-c) + \dots \\ =& \frac{\partial f}{\partial x}\Big|_c (x-c) + \dots\end{aligned} \tag{2.20}$$

$\frac{\partial f}{\partial x}$ is interpreted as the **Jacobian matrix**, J, given by:

$$J = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \dots & \frac{\partial f_1}{\partial x_n} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \dots & \frac{\partial f_2}{\partial x_n} \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \dots & \frac{\partial f_n}{\partial x_n} \end{bmatrix} \tag{2.21}$$

We now define $\delta x := x - c$, taking the derivative with respect to t we have $\dot{\delta x} = \dot{x}$ if $\delta x << 1$ then only the first term in our Taylor expansion is significant as the other terms involve higher powers of a small displacement from our point of interest c. we have

$$\dot{\delta x}(t) = J|_{x=c}\delta x \tag{2.22}$$

$J|_{x=c}$ is a constant matrix, so this is just a linear ODE, the solution of which can be written as a superposition of terms $e^{\lambda_i t}$, where λ_i are eigenvalues of the Jacobian. Let $\lambda_i = a_i + ib_i$ then our solution is a superposition of terms with

$$e^{\lambda_i t} = e^{a_i t}(\cos(b_i t) + i\sin(b_i t)) \tag{2.23}$$

The imaginary part of the eigenvalue gives an oscillatory component to the solution, while the real part is part of the exponential term in t. If $a_i > 0$ for some, i then the trajectories will move away from c.

Theorem 2.22. *A equilibrium point c of a system of ODEs as in (2.17) is called **linearly stable** if all the eigenvalues of the Jacobian evaluated at $x = c$ have negative real parts. The equilibrium point in unstable if at least one of the eigenvalues has a positive real part.*

Linear stability tells us how the system behaves near the equilibrium point, but gives us little information on what happens farther away. For a more global analysis of stability, we turn to the technique of Lyapunov functions. We consider again the system in (2.17) and assume there is a c which satisfies $f(c) = 0$. We also assume the existence of a continuous function $V : D \to \mathbb{R}_{\geq 0}$ which satisfies

(i) $V(x) \geq 0 \quad \forall x \in D$

(ii) $V(c) = 0$ and $V(x) > 0$ if $x \neq c$

(iii) The sublevel sets of V are bounded. That is, $\forall a$ the set

$$V_a := \{z \in D : V(z) \leq a\}$$

is bounded. This implies $V(x) \to \infty$ as $|x| \to \infty$

Theorem 2.23. *If for $a > 0$ we have*

$$\nabla V(x) \cdot f(x) < 0, \quad \forall x \in V_a \quad y \neq c \tag{2.24}$$

then c is locally stable.
If

$$\nabla V(x) \cdot f(x) < 0, \quad \forall x \in D \quad x \neq c \tag{2.25}$$

and $V(x) \to \infty$ so long as $x \to \partial D$ (The boundary or ∞), then we have global asymptotic stability.

2.2.4 Stochastic Model

When the populations of species in a CRN are not sufficiently large we cannot utilize the deterministic approach, instead we turn to a stochastic approach using continuous time Markov chains. We consider a CRN $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ with d species $S = \{S_1, \ldots, S_d\}$, state of the network is given by $X(t) \in \mathbb{Z}^d_{\geq 0}$, a vector giving counts of each of the species. $X(t)$ is a CTMC with transitions determined by the reactions. For the reaction, $y_r \to y'_r$, we assume an intensity function $\lambda_r(x)$ and define $\zeta_r = (y'_r - y_r)$. The transition rates are given by:

$$q_{x,y} = \sum_{r \in \mathcal{R}, \zeta_r = y - x} \lambda_r(x) \tag{2.26}$$

i.e. the transition rates are the sum of all the reaction rates whose reaction vectors take you from state x to state y. The Kolmogorov Forward equation $P'(t) = P(t)Q, \quad P(0) = I$ can be written component wise

$$p'_{ij}(t) = \sum_k q_{kj} p_{ik}(t), \quad p_{ij}(0) = \delta_{ij} \tag{2.27}$$

$$p'_{ij}(t) = \sum_{k, k \neq j} q_{kj} p_{ik}(t) - \Big(\sum_i q_{ji} \Big) p_{ij}(t), \quad p_{ij}(0) = \delta_{ij} \tag{2.28}$$

$$p'_{ij}(t) = \sum_{k, k \neq j} \sum_{r \in \mathcal{R}, \zeta_r = j - k} \lambda_r(k) p_{ik}(t) - \Big(\sum_{r \in \mathcal{R}} \lambda_r(j) \Big) p_{ij}(t), \quad p_{ij}(0) = \delta_{ij} \tag{2.29}$$

$$p'_{ij}(t) = \sum_{r \in \mathcal{R}} \lambda_r(j - \zeta_r) p_{i,(j - \zeta_r)}(t) - \Big(\sum_{r \in \mathcal{R}} \lambda_r(j) \Big) p_{ij}(t), \quad p_{ij}(0) = \delta_{ij} \tag{2.30}$$

This equation is called the **master equation**, the first term sums all reactions moving into j and the second term collects all the terms leaving j. Here p_{ij} is the transition probability function, defined as $p_{ij}(t) := \mathbb{P}(X(t + s) | X(s) = i)$. Recalling that if $X(t)$ is non-explosive and there exists a distribution π satisfying $\pi Q = 0$ then π is stationary, also if π exists then $p_{ij}(t) \to \pi_j$ as $t \to \infty$.

Definition 2.24. *the intensity function λ_r satisfies stochastic mass-action kinetics if there is a rate constant κ_r such that for $x \in \mathbb{Z}^d$*

$$\lambda_r(x) = \kappa_r \prod_{i=1}^{d} \frac{x_i!}{(x_i - y_i)!} I_{x_i \geq y_i}$$

and the system is said to satisfy mass-action kinetics if each reaction does.

Denote the filtration giving all the information up to time t as $\mathcal{F}_t$. we have

$$P(X(t+h) = X(t)|\mathcal{F}_t) = 1 - \sum_r \lambda_r\big(X(t)\big)h + o(h) \tag{2.31}$$

$$P(X(t+h) = X(t) + \zeta_r|\mathcal{F}_t) = \sum_{y_k \to y_k', \zeta_k = \zeta_r} \lambda_r\big(X(t)\big)h + o(h) \tag{2.32}$$

$$\tag{2.33}$$

in the case where the reaction vectors ζ_r are unique, we have

$$P(X(t+h) = X(t) + \zeta_r|\mathcal{F}_t) = \lambda_r\big(X(t)\big)h + o(h)$$

We define $N_r(t)$ to be the number of times the rth reaction has occurred by time t, and can write:

$$X(t) = X(0) + \sum_{r \in \mathcal{R}} N_r(t)\zeta_r \tag{2.34}$$

$$P(N_r(t+h) - N_r(t)|\mathcal{F}_t) = 1 - \lambda_r\big(X(t)\big)h + o(h) \tag{2.35}$$

$$P(N_r(t+h) - N_r(t)|\mathcal{F}_t) = 1 - \sum_{y_k \to y_k', \zeta_k = \zeta_r} \lambda_r\big(X(t)\big)h + o(h) \tag{2.36}$$

$$\tag{2.37}$$

The counting process $N_r(t)$ can be modelled via independent Poisson processes. We define $\{Y_1, \ldots, Y_R\}$ as independent unit-rate Poisson processes. If we let X be the solution of the equation:

$$X(t) = X(0) + \sum_r N_r(t)\zeta_r \tag{2.38}$$

with

$$N_r(t) = Y_r\left(\int_0^t \lambda_r(X(s))ds\right) \tag{2.39}$$

then $X(t)$ satisfies (2.31) and (2.35), that is the solution to the stochastic equation

$$X(t) = X(0) + \sum_r Y_r\left(\int_0^t \lambda_r(X(s))ds\right)\zeta_r \tag{2.40}$$

Is a realization of the stochastic CRN. Note also the similarity to equation (2.16) in the deterministic model. This representation was developed by Thomas G. Kurtz in [2, 11].

2.2.5 Scaling of rate constants

To connect the stochastic and deterministic models, we look at how they each represent the **abundance** of each molecule. In the stochastic model each species is represented by the number of its molecules, in the deterministic model the species are represented by their concentrations i.e. number of molecules per litre. To draw a connection we must take into account the volume, we do so by introducing a scaling parameter V which is proportional to the volume of the system. V typically is defined as the volume times Avogadro's number ($6.022 \times 10^2 3$), in any case we will simply refer to the parameter V as the volume and think of it as having some proportionality to the volume of the system. Let $X(t)$ be our process which gives the counts of the species, we define $\bar{X}(t) := X(t)/V$, which gives the concentration of the different species. The stochastic equation in (2.40) for our scaled process is given as:

$$\bar{X}(t) = \bar{X}(0) + \sum_r \frac{1}{V} Y_r \left(\int_0^t \lambda_r(V\bar{X}(s))ds \right) \zeta_r \tag{2.41}$$

under classical scaling the rate constants scale as such

$$\kappa_r = V^{-(\sum_i (y_r)_i - 1)} \kappa_r' \tag{2.42}$$

i.e. $\kappa_r = V^{-(\#\text{ of reactants}-1)}\kappa_r'$ to interpret $\lambda_r(V\bar{X}(s))$ we can look at some example reactions: for the reaction

$$\emptyset \to *$$

we have $\kappa_r = V\kappa_r'$ so $\lambda_r(Vx) = V\kappa_r'$ if we take $\lambda_r(x) = \kappa_r'$ then $\lambda_r(V\bar{X}(s)) = V\lambda_r(\bar{X}(s))$.

For the reaction

$$S_i \to *$$

we have $\kappa_r = \kappa_r'$ and again $\lambda_r(V\bar{X}(s)) = V\lambda_r(\bar{X}(s))$. For the reaction

$$S_1 + S_2 \to *$$

We have $\kappa_r = \kappa_r'/V$ and $\lambda_r(Vx) = \kappa_r'/V(Vx_1)(Vx_2) = V\lambda(x)$ again $\lambda_r(V\bar{X}(s)) = V\lambda_r(\bar{X}(s))$. For the reaction

$$2S_1 \to *$$

we have $\kappa_r = \kappa_r'/V$ and $\lambda_r(Vx) = \kappa_r'/V(Vx_1)(Vx_1 - 1) = V\kappa_r' x_1^2(1 - 1/V)$ this time $\lambda_r(V\bar{X}(s)) \neq V\lambda_r(\bar{X}(s))$, but as $V \to \infty$ $\lambda_r(V\bar{X}(s)) \approx V\lambda_r(\bar{X}(s))$

In general

$$\lambda_r(V\bar{X}(s)) \approx V\lambda_r(\bar{X}(s)) \tag{2.43}$$

Theorem 2.25. *Let $\bar{X}(t)$ be the volume scaled process as defined above, and $x(t)$ be the solution of the system of ODEs in 2.13. Let $T > 0$. If $\bar{X}(0) \xrightarrow{a.s.} x(0)$ as $V \to \infty$, then*

$$\sup_{t \le T} |\bar{X}(t) - x(t)| \xrightarrow{a.s.} 0 \quad \text{as } V \to \infty \tag{2.44}$$

Proof. because there is a conserved quantity, there is some $M > 0$ such that

$$\sup_t \leq T|\lambda_r(\bar{X}(t)| \leq M$$

$$\begin{aligned}\bar{X}(t) - x(t) =& \bar{X}(0) - x(0) + \sum_r \frac{1}{V}\left[Y_r\left(V\int_0^t \lambda_r(\bar{(}X)(s)ds\right) - V\int_0^t \lambda_r(\bar{X}(s))ds\right]\zeta_r \\ &+ \sum_r \left[\int_0^t \lambda_r(\bar{X}(s)ds - \int_0^t \lambda_r(x(s))ds\right]\zeta_r\end{aligned} \tag{2.45}$$

where $\sum_r \int_0^t \lambda_r(\bar{X}(s)ds\zeta_r$ has been added and subtracted. We have

$$\int_0^t \lambda_r(\bar{X}(s))ds \leq MT \quad t \leq T \tag{2.46}$$

by (2.43) and using theorem A.1 for a unit rate Poisson process Y with probability one we have

$$\lim_{n\to\infty} \sup_{u\leq u_0} \left|\frac{Y(nu)}{n} - u\right| \tag{2.47}$$

$$\lim_{V\to\infty} \sup_{t\leq} \left|\sum_r \frac{1}{V}\left[Y_r\left(V\int_0^t \lambda_r(\bar{(}X)(s)ds\right) - V\int_0^t \lambda_r(\bar{X}(s))ds\right]\zeta_r\right| = 0 \tag{2.48}$$

using our approximation $\lambda_r(\bar{X}(s)) \approx V\lambda_r(\bar{X}(s))$ and the fact the λ_r are Lipschitz there exists a $C > 0$ such that for every $u \leq T$

$$\begin{aligned}\sup_{t\leq u}\left|\sum_r \left[\int_0^t \lambda_r(\bar{X}(s)ds - \int_0^t \lambda_r(x(s))ds\right]\zeta_r\right| \leq& C\sup_{t\leq u}\int_0^t |\bar{X}(s) - x(s)|ds \\ \leq& \int_0^u \sup_{r\leq s}|\bar{X}(r) - x(r)|ds\end{aligned}$$

for $u \in [0, T]$ we define

$$g(u) = \sup_{r\leq u}|\bar{X}(r) - x(r)| \tag{2.49}$$

applying g to equation (2.45) we have

$$g(u) =\leq |\bar{X}(0) - x(0)| + C\int_0^t g(s)ds + \varepsilon^V \tag{2.50}$$

Using Gronwall's inequality (see Lemma A.8 [3]) we have

$$g(u) \leq \varepsilon^V e^C + |\bar{X}(0) - x(0)| \tag{2.51}$$

Taking the limit as $V \to \infty$ completes the proof.

We have connected the stochastic model to the deterministic model by scaling our stochastic process (CTMC) by the volume, and have shown under the limit as $V \to \infty$ the volume scaled process converges to the solution of the system of ODEs.

2.2.6 Positive recurrence and the Foster-Lyapunov criterion

Recall to prove the existence of a stationary distribution we must prove positive recurrence of the CTMC, we turn to the Foster-Lyanpunov criterion to aid us in proving positive recurrence for our chemical reaction networks.

Definition 2.26. *the **infinitesimal generator** for a Markov process is the operator Q acting on functions $f : \mathbb{Z}^d_{\geq 0} \to \mathbb{R}$ defined as:*

$$Qf(x) = \lim_{h \to 0} \frac{\mathbb{E}_x\big[f(X(h))\big] - f(x)}{h} \tag{2.52}$$

note that for countable state spaces this operator is the same as definition 2.7

for our models we have

$$\begin{aligned}
\mathbb{E}_x\big[f(X(h))\big] =& \bigg(\sum_{r \in \mathcal{R}} f(x + \zeta_r) P_x(X(h) = x + \zeta_r) \bigg) + f(x) P_x(X(h) = x) + o(h) \\
=& \bigg(\sum_{r \in \mathcal{R}} f(x + \zeta_r) \lambda_r(x) h + o(h) \bigg) + f(x) \bigg(1 - \sum_{r \in \mathcal{R}} \lambda_r(x) h + o(h) \bigg) + o(h) \\
=& \sum_{r \in \mathcal{R}} \lambda_r(x)(f(x + \zeta_r) - f(x))h + f(x) + o(h)
\end{aligned}$$

and

$$Qf(x) = \sum_{r \in \mathcal{R}} \lambda_r(x)(f(x + \zeta_r) - f(x)) \tag{2.53}$$

the following theorem from [12] as been slightly modified for countably infinite state spaces by Bibbona *et al* in [6].

Theorem 2.27 (Foster-Lyapunov Criterion)**.** *let $X(t)$ CTMC on a countable state space S. $X(t)$ is non-explosive, and positive recurrent if there exists a norm-like (Lyapunov) function V on S and positive constants $C, D > 0$ such that*

$$QV(x) \leq -CV(x) + D, \quad \forall x \in S \tag{2.54}$$

Moreover, $X(t)$ admits a unique stationary distribution π and $\exists B > 0$ and $\beta \in (0, 1)$ such that

$$\sup_A |P^t(x, A) - \pi(A)| \leq BV(x)\beta^t, \quad \forall x \in S \tag{2.55}$$

3 Models

3.1 Togashi-Kaneko Model

Togashi and Kaneko observed the appearance of unusual reaction dynamics in a small autocatalytic system when the total number of reacting molecules was made small. The Togashi-Kaneko (TK) model consists of 4 types of molecules

in a well stirred container with a reservoir that allows molecules to diffuse in and out of the container. The network is given graphically as

$$A_1 + A_2 \xrightarrow{\kappa} 2A_2 \qquad A_2 + A_3 \xrightarrow{\kappa} 2A_3 \qquad A_3 + A_4 \xrightarrow{\kappa} 2A_4 \qquad A_4 + A_1 \xrightarrow{\kappa} 2A_1$$
$$\emptyset \underset{\delta}{\overset{\lambda}{\rightleftharpoons}} A_i \tag{3.1}$$

Where κ is the rate of the autocatalytic reactions and, λ and δ are the diffusion into and out of the container. Classical volume scaling is utilized with $A_i = N_i/V$ where N_i is the number of i molecules and V is the volume of the container. The state of the system is given by the tuple $a = (a_1, a_2, a_3, a_4)$ and the transition rates are

$$q_{a,a-e_i+e_{i+1}} = \kappa a_i a_{i+1},\ i = 1, 2, 3 \qquad q_{a,a-e_4+e_1} = \kappa a_4 a_1$$
$$q_{a,a+e_i} = \lambda \qquad q_{a,a-e_i} = \delta a_i$$

under classical scaling, the rate constants are given by:

$$\kappa = \frac{\kappa'}{V} \qquad \delta = \delta' \qquad \lambda = \lambda' V$$

In [16] the authors linearly scale time to let $\kappa' = 1$, and they set $\delta' = \lambda' = D$. As discussed in section 2.2.2 when the populations of species are large enough the evolution of their concentrations can be described by a system of ODEs

$$\frac{da_i}{dt} = \kappa a_{i-1} a_i - \kappa a_i a_{i+1} + D s_i - D a_i \tag{3.2}$$

where s_i is the concentration of each molecule in the reservoir, the authors take $s_i = s$ for each species. The above system has a unique attractor at the equilibrium point $a_i = s$, and the Jacobian evaluated at the equilibrium point has a complex eigenvalue. The complex eigenvalue leads to oscillations around the equilibrium point with a frequency $\omega_p = \frac{\kappa s}{\pi}$. The authors then replace the deterministic reaction model with the Langevin equation by adding a noise term to (3.2), the concentrations again fluctuate around the equilibrium point with the dynamics of ω_p. As the strength of the noise term was increased, no decrease in the total number of molecules was observed. Through direct simulation of the reaction model it was observed that when D and V are large enough the results agreed with the Langevin equation with small fluctuations around its equilibrium, However as V was made small enough a behaviour not captured by the ODE approach was observed. As V decreased the authors noted two states, the first where N_1 and N_3 were large and $N_2, N_4 \approx 0$ and the second where N_2 and N_4 were large and $N_1, N_3 \approx 0$. The system would spend most of its time in these two states with rapid switches between the two, these switches were named discreetness induced transitions (DITs). The authors note that the switching states appear when $DV < 1$, but if V gets too small (e.g. $V < 4$) the system is destabilized by fluctuations. Although they only presented in their paper the case where the inflow rates, autocatalytic rates and diffusion rates were identical for all species, the authors confirm that DITs appear even when these rates are not identical.

3.2 Bibbona-Kim-Wiuf Model

Bibbona, Kim and Wiuf offer a theoretical analysis of the TK model as well as other similar autocatalytic reaction networks which exhibit DITs in [6]. The authors describe a general system as a continuous time Markov chain (CTMC) and prove the existence of stationary distribution. Their general d-dimensional network is given as:

$$A_i + A_j \xrightarrow{\kappa_{ij}} 2A_j \qquad \emptyset \underset{\delta_i}{\overset{\lambda_i}{\rightleftharpoons}} A_i \quad i,j = 1,2,\ldots,d \tag{3.3}$$

With associated Markov chain $[X(t)]_{n\geq 0}$ on the state space $E = \{a = (a_1,\ldots,a_d) \in \mathbb{N}^d\}$. For $\kappa_{ij} \geq 0, \lambda_i > 0, \delta_i > 0$ the authors prove that the CTMC associated with the system (3.3) is positive recurrent for any d, a unique stationary distribution exists, all moments are finite and convergence to the stationary distribution is exponentially fast (see Theorem 4.1 in [6]). While the existence of a stationary distribution is proven, computation of an analytic expression for the stationary distribution is difficult and an expression for the general system remains unsolved. Using the notion of lumpability (section (2.2) [6]) the state space can be partitioned into subsets $E_n = \{a \in \mathbb{N}^d | \sum_{i=1}^d = n\}$. If we let $\delta_i = \delta$ for every i the lumped process $\bar{X}(t)$ is a CTMC on E_n with associated transition rates

$$q_{n,n+1} = \sum_{i=1}^{d} \lambda_i \qquad q_{n,n-1} = n\delta \tag{3.4}$$

$\bar{X}(t)$ is a immigration-death process on $\mathbb{N}$ and admits a Poisson stationary distribution given by

$$\nu(n) = \frac{\mu^n}{n!} e^{-\mu}, \quad \mu = \frac{\sum_{i=1}^d \lambda_i}{\delta} \tag{3.5}$$

we can now condition the stationary distribution Π on the probability $\nu(n)$ of $\bar{X}(t)$ being in state n and write the stationary distribution as:

$$\Pi(a) = \pi(a|n)\nu(n) \tag{3.6}$$

Bibbona *et al* go on to show that under the assumptions $\kappa_{ij} = \kappa > 0$, $\delta_i = \delta > 0$, and $\lambda_i > 0$ $\pi(a|n)$ is given by a Dirichlet-multinomial distribution and the unique stationary distribution of the network shown in (3.3) is given by

$$\begin{aligned} &\Pi(a) = \pi(a|n)\nu(n) \\ &\text{where } \pi(a|n) = \binom{n}{a} \frac{\Gamma\big(\sum_{i=1}^d \alpha_i\big)}{\Gamma\big(n + \sum_{i=1}^d \alpha_i\big)} \prod_{i=1}^{d} \frac{\Gamma\big(a_i + \alpha_i\big)}{\Gamma\big(\alpha_i\big)} \\ &\qquad \text{with } \alpha_i = \frac{\delta\lambda_i}{\kappa \sum_{j=1}^d \lambda_j} \end{aligned} \tag{3.7}$$

Under classical volume scaling, the parameters are given as

$$\kappa = \frac{\kappa'}{V} \qquad \delta = \delta' \qquad \lambda = \lambda' V \qquad \alpha_i = \frac{\delta' \lambda_i'}{\kappa' \sum_{j=1}^{d} \lambda_j} V = \alpha_i' V \tag{3.8}$$

and the distribution $\pi(a|n)$ can be written as

$$\pi(a|n) = \binom{n}{a} \frac{\Gamma\big(V \sum_{i=1}^{d} \alpha_i'\big)}{\Gamma\big(n + V \sum_{i=1}^{d} \alpha_i'\big)} \prod_{i=1}^{d} \frac{\Gamma\big(a_i + V\alpha_i'\big)}{\Gamma\big(V\alpha_i\big)} \tag{3.9}$$

As the volume V gets large the mean vector of Π converges to $(\lambda_1'/\delta', \ldots, \lambda_d'/\delta')$, which is the equilibrium of the deterministic model, and the covariance matrix converges to the zero matrix. However, when $V \to 0$ the probability that all the molecules in the system are of one type approaches 1.

$$\begin{aligned} \lim_{V\to 0} \sum_{i=1}^{d} \pi(e_i|n) &= \lim_{V\to 0} \frac{\Gamma\big(V \sum_{i=1}^{d} \alpha_i'\big)}{\Gamma\big(n + V \sum_{i=1}^{d} \alpha_i'\big)} \sum_{i=1}^{d} \frac{\Gamma\big(a_i + V\alpha_i'\big)}{\Gamma\big(V\alpha_i\big)} \\ &= \lim_{V\to 0} \frac{1}{V \sum_{i=1}^{d} \alpha_i} \sum_{i=1}^{d} V\alpha_i = 1 \end{aligned} \tag{3.10}$$

This **corner configuration** alludes to the presence of $DITs$ where only one molecule type is present at a time. When the parameters are chosen as they were in [16] i.e.

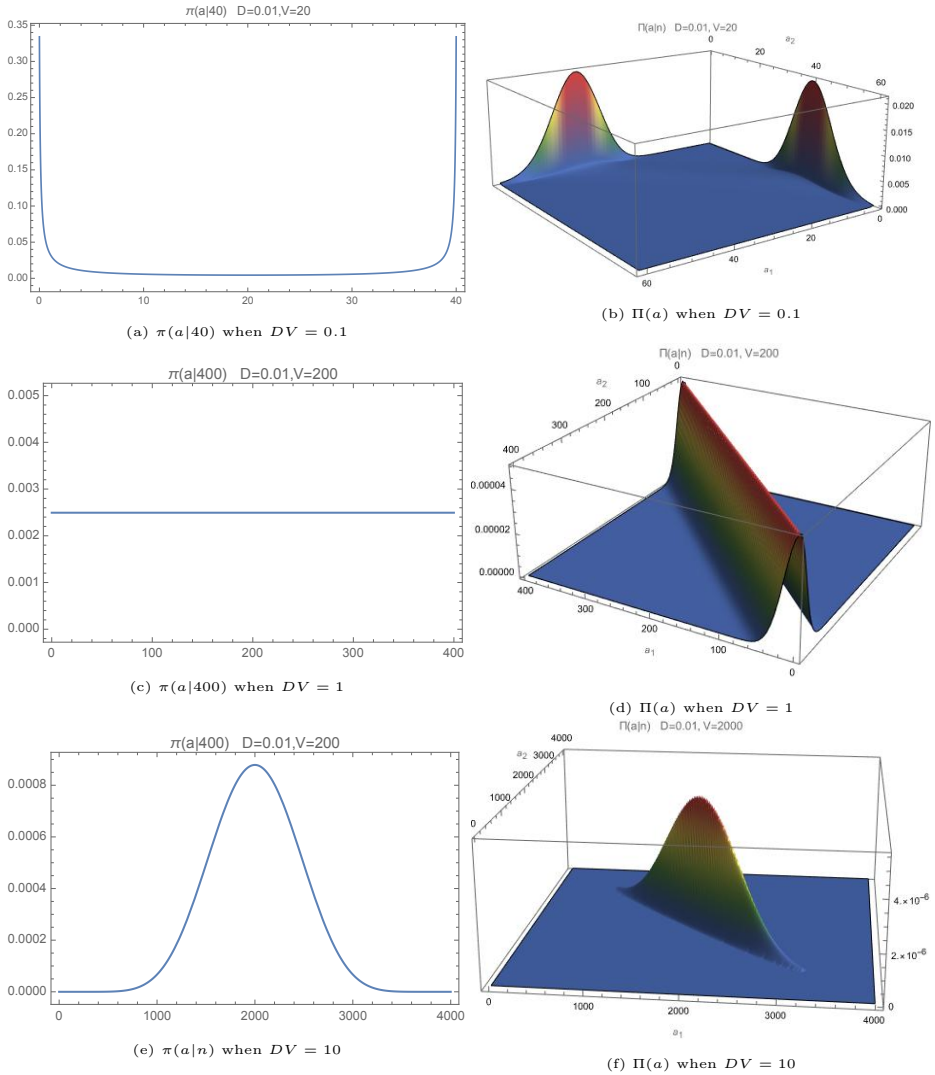
$$\kappa_i' = 1 \qquad \delta' = \lambda_i' = D, \quad i = 1, ...d \tag{3.11}$$

the parameters α_i are then given as

$$\alpha_i = \frac{DV}{d} \tag{3.12}$$

When $DV > d$ the density $\pi(a|n)$ is unimodal, when $DV = d$ the density is uniform, and when $DV < d$ the density becomes d-modal with the bulk of the mass on the boundaries; figure 1 shows the distribution $\pi(a|n)$ and the full distribution $\Pi(a)$ for the 3 regions of DV.

While the authors proved the existence of a unique stationary distribution for general systems, they only provide a closed form expression when the autocatalytic rates are the same. As mentioned previously Togashi and Kaneko noted that DITs occur when these rates are not identical, this coupled with the fact that the stationary distribution exists for systems with asymmetrical rates is the motivation for this thesis. To investigate the effect of asymmetric autocatalytic rates on the system ($\kappa_{ij} \neq \kappa \quad \forall i, j \in 1, ..., d$), we now move to a well known model from population genetics.



(a) $\pi(a|40)$ when $DV = 0.1$

(b) $\Pi(a)$ when $DV = 0.1$

(c) $\pi(a|400)$ when $DV = 1$

(d) $\Pi(a)$ when $DV = 1$

(e) $\pi(a|n)$ when $DV = 10$

(f) $\Pi(a)$ when $DV = 10$

Figure 1: The distribution $\pi(a|n)$ in two dimensions is shown for different values of V while D is held constant in (a),(c), and (e) and the corresponding plots of the full distribution is shown in (b),(d) and (f) . In (a) and (b) DV¡1 and the distribution is bimodal with most of the mass on the boundaries, (c) and (d) shows the critical case when DV=1 and the distribution is uniform, in (e) and (f) DV=10 and the distribution is unimodal with the mass centred when $a_1 = a_2$. The distribution was plotted in one dimension by letting $a_2 = n - a_1$ and the x-axis shows the number of a_1 molecules, n was taken as the mean of $\nu(n)$, which is 2V, for the 3 2D plots.

3.3 Moran Model with genic Selection

To aid in finding a stationary distribution for asymmetrical autocatalytic rates, we look to the Moran model with genic selection, which has similar reaction dynamics to our family of autocatalytic reactions. Etheridge and Griffiths, in

[7], provide a closed form stationary distribution for the Moran model with genic selection. In this Moran model, the population is equilibrium and consists of n individuals of d different types and $a_i(t)$ denotes the number of type i individuals at time t. An individual of type j gives birth at the rate $\kappa_j \geq 0$, and simultaneously an individual is chosen at random to die. This model also includes mutations where each type i individual changes to type j with a rate of νp_{ij}, where p_{ij} are the entries of a transition probability matrix P and $\nu \geq 0$. For our purposes, we assume parent-independent mutations, where $p_{ij} = p_j > 0$. The transition rate from a to $a - e_i + e_j$ is given as

$$q(a, a - e_i + e_j) = a_i \left[\frac{\kappa_j}{n} a_j + \nu p_j \right] \tag{3.13}$$

The system is represented graphically by:

$$A_i + A_j \xrightarrow{\kappa_j} 2A_j \qquad A_i \xrightarrow{\nu p_j} A_j \tag{3.14}$$

The process $\left[A(t)\right]_{t\geq 0}$ has a stationary distribution, $\pi(a)$ which is obtained by solving the balance equation:

$$\pi(a)q(a, a - e_i + e_j) = \pi(a - e_i + e_j)q(a - e_i + e_j, a) \tag{3.15}$$

which gives

$$\pi(a) \propto \kappa_1^{a_1} \cdots \kappa_d^{a_d} \binom{n}{a} \frac{\alpha_{1(a_1)} \cdots \alpha_{d(a_d)}}{|\alpha|_{(n)}} \tag{3.16}$$

Where

$$\alpha_i = \frac{n\nu p_i}{\kappa_i} \tag{3.17}$$

and $|\alpha| = \sum_{i=1}^{d} \alpha_i$. The normalizing constant for $\pi(a)$ is given as the partition function:

$$u(\alpha, \kappa, n) = \mathbb{E}\left[\left(\sum_{i=1}^{d} \kappa_i \xi_i \right)^n \right] \tag{3.18}$$

Where $\xi = (\xi_1, \xi_2, ..., \xi_d)$ has a Dirichlet$(\cdot, \alpha)$ distribution. $a_{(n)} = a(a+1)\cdots(a+n-1)$ denotes the rising factorial or Pochhammer function, which can be written in terms of Gamma functions as $a_{(n)} = \Gamma(a+n)/\Gamma(a)$.

$$\pi(a) \propto \prod_{i=1}^{d} \kappa_i^{a_i} \binom{n}{a} \frac{\Gamma(\sum_{i=1}^{d} \alpha_i)}{\Gamma(\sum_{i=1}^{d} \alpha_i + n)} \prod_{i=1}^{d} \frac{\Gamma(\alpha_i + a_i)}{\Gamma(\alpha_i)} \tag{3.19}$$

In the neutral model when $\kappa_i = \kappa$ for $i = 1, \ldots, d$ the partition function becomes $u(\alpha, \kappa, n) = \kappa^n \mathbb{E}\left[\left(\sum_{i=1}^{d} \xi_i \right)^n \right] = \kappa^n$ since $\sum_{i=1}^{d} \xi_i = 1$. The stationary distribution then reduces to the multinomial Dirichlet distribution.

$$\pi(a) = \binom{n}{a} \frac{\Gamma(\sum_{i=1}^{d} \alpha_i)}{\Gamma(\sum_{i=1}^{d} \alpha_i + n)} \prod_{i=1}^{d} \frac{\Gamma(\alpha_i + a_i)}{\Gamma(\alpha_i)} \tag{3.20}$$

The distribution in equation (3.20) is exactly the stationary distribution $\pi(a|n)$ derived by Bibbona *et al* in equation 3.7 with $\alpha_i = \frac{\delta\kappa_i}{\kappa \sum_{j=1}^{d} \kappa_j}$. This observation suggests that the stationary distribution from [7] is a good candidate for $\pi(a|n)$, as in [6], when the values of κ_{ij} are not all the same. The proposed distribution is:

$$\pi(a|n) = \frac{1}{u(\alpha, \kappa, n)} \left[\prod_{i=1}^{d} \kappa_i^{a_i} \right] \binom{n}{a} \frac{\Gamma(\sum_{i=1}^{d} \alpha_i)}{\Gamma(\sum_{i=1}^{d} \alpha_i + n)} \prod_{i=1}^{d} \frac{\Gamma(\alpha_i + a_i)}{\Gamma(\alpha_i)} \tag{3.21}$$

This does not exactly fit in the general case since the model which we are borrowing the distribution from requires parent independent mutations or $\kappa_{ij} = \kappa_j \quad \forall i \in 1, \ldots, d$.

3.4 Effective Model

The Moran model differs from the TK model in that it has a fixed population and lacks the inflow and outflow reactions. Nen Saito and Kunihiko Kaneko discuss a simplified version of the 2-dimensional TK model in [15], called the effective model. The model consists of autocatalytic reactions between two populations of molecules A_1 and A_2, but instead of inflow and outflow reactions, there are mutation reactions between the two types of molecules. The system is given as:

$$A_1 + A_2 \xrightarrow{\kappa_1} 2A_1 \qquad A_1 + A_2 \xrightarrow{\kappa_2} 2A_2 \qquad A_1 \underset{v_1}{\overset{v_2}{\rightleftharpoons}} A2 \tag{3.22}$$

with transition rates:

$$q(a, a - e_i + e_j) = a_i a_j \kappa_j + a_i v_j \tag{3.23}$$

We can show that the distribution:

$$\pi(a) = \frac{1}{u(\alpha, \kappa, n)} \kappa_1^{a_1} \kappa_2^{a_2} \binom{n}{a} \frac{\Gamma(\alpha_1 + \alpha_2)}{\Gamma(\alpha_1 + \alpha_2 + n)} \frac{\Gamma(\alpha_1 + a_1)\Gamma(\alpha_2 + a_2)}{\Gamma(\alpha_1)\Gamma(\alpha_2)} \tag{3.24}$$

with $\alpha_i = \frac{v_i}{\kappa_i}$, satisfies the global balance equation, and is the unique stationary distribution for this system.

$$\pi(a)q(a, a-e_1+e_2)+\pi(a)q(a, a+e_1-e_2) = \pi(a-e_1+e_2)q(a-e_1, +e_2, a)+\pi(a+e_1-e_2)q(a+e_1-e_2, a)$$

dividing both sides by $\pi(a)$ and looking at the right-hand side, we get

$$
\begin{aligned}
&\frac{\kappa_2}{\kappa_1}\frac{a_1}{a_2+1}\frac{\alpha_2+a_2}{\alpha_1+a_1-1}\big[(a_1-1)(a_2+1)\kappa_1+(a_2+1)v_1\big]\frac{\kappa_1}{\kappa_2}\frac{a_2}{a_1+1}\frac{\alpha_1+a_1}{\alpha_2+a_2-1}\big[(a_2-1)(a_1+1)\kappa_2+(a_1+1)v_2\\
=&\kappa_2 a_1\frac{\alpha_2+a_2}{\alpha_1+a_1-1}\big[(a_1-1)+\frac{v_1}{\kappa_1}\big]+\kappa_1 a_2\frac{\alpha_1+a_1}{\alpha_2+a_2-1}\big[(a_2-1)+\frac{v_2}{\kappa_2}\big]\\
=&\kappa_2 a_1\frac{\alpha_2+a_2}{\alpha_1+a_1-1}\big[(a_1-1)+\alpha_1\big]+\kappa_1 a_2\frac{\alpha_1+a_1}{\alpha_2+a_2-1}\big[(a_2-1)+\alpha_2\big]\\
=&\kappa_2 a_1(\alpha_2+a_2)+\kappa_1 a_2(\alpha_1+a_1)\\
=&a_1a_2\kappa_2+a_1\kappa_2\alpha_2+a_1a_2\kappa_1+a_2\kappa_1\alpha_1\\
=&(a_1a_2\kappa_2+a_1v_2)+(a_1a_2\kappa_1+a_2v_1)\\
=&q(a,a-e_1+e_2)+q(a,a+e_1-e_2)
\end{aligned}
$$

Which is the left-hand side divided by $\pi(a)$.

4 Results

The main goal of this thesis is to investigate the family of networks (3.3) described by Bibbona *et al* when the autocatalytic rates are asymmetrical. We will now investigate how well the distribution described in 3.19 fits in with our model.

4.1 The candidate distribution

The stationary distribution proved by Bibbona *et al* takes the form

$$
\begin{aligned}
\pi(a|n) &= \binom{n}{a}\frac{\Gamma\big(\sum_{i=1}^d \alpha_i\big)}{\Gamma\big(n+\sum_{i=1}^d \alpha_i\big)}\prod_{i=1}^d \frac{\Gamma\big(a_i+\alpha_i\big)}{\Gamma\big(\alpha_i\big)}\\
&\text{with } \alpha_i = \frac{\delta\lambda_i}{\kappa\sum_{j=1}^d \lambda_j}
\end{aligned}
\tag{4.1}
$$

the proposed stationary distribution is given as

$$
\pi(a|n) = \frac{1}{u(\alpha,\kappa,n)}\binom{n}{a}\left[\prod_{i=1}^d \kappa_i^{a_i}\right]\frac{\Gamma\big(\sum_{i=1}^d \alpha_i\big)}{\Gamma\big(n+\sum_{i=1}^d \alpha_i\big)}\prod_{i=1}^d \frac{\Gamma\big(a_i+\alpha_i\big)}{\Gamma\big(\alpha_i\big)} \tag{4.2}
$$

which suggests that

$$
\alpha_i = \frac{\delta\lambda_i}{\kappa_i\sum_{i=1}^d \lambda_i} \tag{4.3}
$$

Comparing these α parameters to the ones from the effective model would make $v_1 = \delta\lambda_1/(\lambda_1+\lambda_2)$ which would correspond to a birth of A_1 and simultaneous death of A_2 similarly $v_2 = \delta\lambda_2/(\lambda_1+\lambda_2)$ which corresponds to a birth of A_2 and

simultaneous death of A_1. If the system was such that only these simultaneous birth and death events occurred, keeping the total number of molecules fixed, this distribution would be the unique stationary distribution. To move from the fixed n case to the family of autocatalytic reactions described in [6] where n is changing due to the inflow and outflow reactions we must take special care in how this distribution changes for different values of n, specifically the partition function which depends on n.

4.2 Partition Function

The partition function is given as

$$u(\alpha, \kappa, n) = \mathbb{E}\Big[\Big(\sum_{i=1}^{d} \kappa_i \xi_i\Big)^n\Big] \tag{4.4}$$

By the multinomial theorem we can write rewrite the argument as

$$u(\alpha, \kappa, n) = \mathbb{E}\Big[\sum_{|l|=n} \binom{n}{l} \prod_{i=1}^{d} (\kappa_i \xi_i)^{l_i}\Big]$$

where $l = \big\{(l_1, \ldots, l_d)\big| l_i \geq 0\big\}$ l_i and $|l| = \sum_{i=1}^{d} l_i$. by the linearity of expectation, we can write

$$u(\alpha, \kappa, n) = \sum_{|l|=n} \binom{n}{l} \Big[\prod_{i=1}^{d} \kappa_i^{l_i}\Big] \mathbb{E}\Big[\prod_{i=1}^{d} \xi_i^{l_i}\Big]$$

since $\xi = (\xi_1, \ldots, \xi_d) \sim \mathrm{Dir}(\alpha)$ its product moments [4] can be expressed as :

$$\mathbb{E}\Big[\prod_{i=1}^{d} \xi_i^{l_i}\Big] = \frac{\Gamma(\sum_{i=1}^{d} \alpha_i)}{\Gamma(n + \sum_{i=1}^{d} \alpha_i)} \prod_{i=1}^{d} \frac{\Gamma(\alpha_i + l_i)}{\Gamma(\alpha_i)} \tag{4.5}$$

the partition function can now be written as:

$$u(\alpha, \kappa, n) = \sum_{|l|=n} \binom{n}{l} \Big[\prod_{i=1}^{d} \kappa_i^{l_i}\Big] \frac{\Gamma(\sum_{i=1}^{d} \alpha_i)}{\Gamma(n + \sum_{i=1}^{d} \alpha_i)} \prod_{i=1}^{d} \frac{\Gamma(\alpha_i + l_i)}{\Gamma(\alpha_i)} \tag{4.6}$$

The partition function can be seen here as summing the distribution over every possible $l = (l_1, l_2, \ldots, l_d)$ such that $\sum_{i=1}^{d} l_i = n$. In the two-dimensional case, the partition function becomes

$$u(\alpha, \kappa, n) = \sum_{|l|=n} \binom{n}{l} \kappa_1^{l_1} \kappa_2^{l_2} \frac{\Gamma(\alpha_1 + \alpha_2)}{\Gamma(n + \alpha_1 + \alpha_2)} \frac{\Gamma(\alpha_1 + l_1)}{\Gamma(\alpha_1)} \frac{\Gamma(\alpha_2 + l_2)}{\Gamma(\alpha_2)} \tag{4.7}$$

since $l_1 + l_2 = n$, if we let $l_1 = i$ and $l_2 = n - i$ the partition function can be written as

$$u(\alpha,\kappa,n)=\sum_{i=0}^{n}\binom{n}{i}\kappa_1^i\kappa_2^{n-i}\frac{\Gamma(\alpha_1+\alpha_2)}{\Gamma(n+\alpha_1+\alpha_2)}\frac{\Gamma(\alpha_1+i)}{\Gamma(\alpha_1)}\frac{\Gamma(\alpha_2+n-i)}{\Gamma(\alpha_2)}$$

$$u(\alpha,\kappa,n)=\frac{\Gamma(\alpha_1+\alpha_2)}{\Gamma(n+\alpha_1+\alpha_2)}\sum_{i=0}^{n}\binom{n}{i}\kappa_1^i\kappa_2^{n-i}\frac{\Gamma(\alpha_1+i)}{\Gamma(\alpha_1)}\frac{\Gamma(\alpha_2+n-i)}{\Gamma(\alpha_2)}\cdot\frac{\Gamma(\alpha_2+n)}{\Gamma(\alpha_2+n)}$$

$$u(\alpha,\kappa,n)=\frac{\Gamma(\alpha_1+\alpha_2)}{\Gamma(n+\alpha_1+\alpha_2)}\frac{\Gamma(\alpha_2+n)}{\Gamma(\alpha_2)}\kappa_2^n\sum_{i=0}^{n}\binom{n}{i}\frac{\Gamma(\alpha_1+i)}{\Gamma(\alpha_1)}\frac{\Gamma(\alpha_2+n-i)}{\Gamma(\alpha_2+n)}\left(\frac{\kappa_1}{\kappa_2}\right)^i$$

$$u(\alpha,\kappa,n)=\frac{\Gamma(\alpha_1+\alpha_2)}{\Gamma(n+\alpha_1+\alpha_2)}\frac{\Gamma(\alpha_2+n)}{\Gamma(\alpha_2)}\kappa_2^n\sum_{i=0}^{n}\binom{n}{i}(\alpha_1)_i\frac{1}{(\alpha_2+n-1)^{(i)}}\left(\frac{\kappa_1}{\kappa_2}\right)^i$$

$$u(\alpha,\kappa,n)=\frac{\Gamma(\alpha_1+\alpha_2)}{\Gamma(n+\alpha_1+\alpha_2)}\frac{\Gamma(\alpha_2+n)}{\Gamma(\alpha_2)}\kappa_2^n\sum_{i=0}^{n}\binom{n}{i}(\alpha_1)_i\frac{1}{(-1)^i(1-\alpha_2-n)_i}\left(\frac{\kappa_1}{\kappa_2}\right)^i$$

$$u(\alpha,\kappa,n)=\frac{\Gamma(\alpha_1+\alpha_2)}{\Gamma(n+\alpha_1+\alpha_2)}\frac{\Gamma(\alpha_2+n)}{\Gamma(\alpha_2)}\kappa_2^n\sum_{i=0}^{n}\binom{n}{i}(-1)^i\frac{(\alpha_1)_i}{(1-\alpha_2-n)_i}\left(\frac{\kappa_1}{\kappa_2}\right)^i$$

$$u(\alpha,\kappa,n)=\frac{\Gamma(\alpha_1+\alpha_2)}{\Gamma(n+\alpha_1+\alpha_2)}\frac{\Gamma(\alpha_2+n)}{\Gamma(\alpha_2)}\kappa_2^n\,{}_2F_1\big(-n,\alpha_1;1-\alpha_2-n;\frac{\kappa_1}{\kappa_2}\big)$$

where $(\cdot)_i$, and $(\cdot)^{(i)}$ are the falling and rising factorial functions and ${}_2F_1(\cdot,\cdot;\cdot;\cdot)$ is the Gauss hypergeometric function.

$$\pi(a|n)=\frac{1}{u(\alpha,\kappa,n)}\kappa_1^{a_1}\kappa_2^{a_2}\binom{n}{a}\frac{\Gamma(\alpha_1+\alpha_2)}{\Gamma(\alpha_1+\alpha_2+n)}\frac{\Gamma(\alpha_1+a_1)\Gamma(\alpha_2+a_2)}{\Gamma(\alpha_1)\Gamma(\alpha_2)}$$

$$\pi(a|n)=\frac{1}{{}_2F_1\big(-n,\alpha_1;1-\alpha_2-n;\frac{\kappa_1}{\kappa_2}\big)}\kappa_1^{a_1}\kappa_2^{a_2-n}\binom{n}{a}\frac{\Gamma(\alpha_1+a_1)\Gamma(\alpha_2+a_2)}{\Gamma(\alpha_1)\Gamma(\alpha_2+n)}$$

writing $a_1=a$ $a_2=n-a$ or $a=(a,n-a)$ we can reduce the distribution to 1 dimension

$$\pi(a|n)=\frac{1}{{}_2F_1\big(-n,\alpha_1;1-\alpha_2-n;\frac{\kappa_1}{\kappa_2}\big)}\left(\frac{\kappa_1}{\kappa_2}\right)^a\binom{n}{a}\frac{\Gamma(\alpha_1+a)\Gamma(\alpha_2+n-a)}{\Gamma(\alpha_1)\Gamma(\alpha_2+n)} \tag{4.8}$$

The Gauss hypergeometric function ${}_2F_1(a,b;c;z)$ is defined when c is not a non-positive integer, (i.e. $c\neq 0,-1,-2,\dots$) and (1) $|z|<1$ or (2) $|z|\leq 1$ when $c>a+b$. So in our case, we require $1-\alpha_2-n\neq 0,-1,-2\dots$ or $\alpha_2\neq 1-n,2-n,3-n\dots$. Since $\alpha_2=\frac{\delta\lambda_2}{\kappa_2(\lambda_1+\lambda_2)}$ and $\delta,\lambda_1,\lambda_2,\kappa_2>0$ ${}_2F_1\big(-n,\alpha_1;1-\alpha_2-n;\frac{\kappa_1}{\kappa_2}\big)$ is defined for $\frac{\kappa_1}{\kappa_2}\leq 1$. For simplicity of notation $F(a,b;c;z)$ will refer to ${}_2F_1(a,b;c;z)$ from now on. Note: to ensure that $\frac{\kappa_1}{\kappa_2}\leq 1$ we will set the larger of the two rates as κ_2, moreover we can always set $\kappa_1=1$ as was done by Togashi and Kaneko in [16].

4.3 Volume scaling

As in [6] under classical scaling the parameters are given as

$$\kappa_i = \frac{\kappa_i'}{V} \qquad \lambda_i = \lambda_i' V \qquad \delta = \delta' \qquad \alpha_i = V\alpha_i' \tag{4.9}$$

The volume scaled distribution is given as

$\Pi(a) = \nu(n)\pi(a|n)$

where

$$\begin{aligned}
\pi(a|n) &= \frac{1}{u(\alpha,\kappa,n)}\binom{n}{a}\left[\prod_{i=1}^{d}\kappa_i'^{a_i}\right]\frac{\Gamma\big(V\sum_{i=1}^{d}\alpha_i'\big)}{\Gamma\big(n+V\sum_{i=1}^{d}\alpha_i'\big)}\prod_{i=1}^{d}\frac{\Gamma\big(a_i+V\alpha_i'\big)}{\Gamma\big(V\alpha_i'\big)},\\
u(\alpha,\kappa,n) &= \frac{\Gamma\Big(\sum_{i=1}^{d}V\alpha_i'\Big)}{\Gamma\Big(n+V\sum_{i=1}^{d}\alpha_i'\Big)}\sum_{|l|=n}\binom{n}{l}\prod_{i=1}^{d}\kappa_i'^{l_i}\frac{\Gamma(V\alpha_i'+l_i)}{\Gamma(V\alpha_i')},\\
\nu(n) &= \frac{(V\mu')^n}{n!}\exp[-V\mu'], \quad \mu' = \frac{\sum_{i=1}^{d}\lambda_i'}{\delta'}
\end{aligned} \tag{4.10}$$

The κ_i' polynomial terms do not appear with a V since the V's are cancelled out by the partition function

$$\frac{\prod_{i=1}^{d}\frac{\kappa_i'^{a_i}}{V}}{\mathbb{E}\left[\Big(\sum_{i=1}^{d}\frac{\kappa_i'}{V}\xi_i\Big)^n\right]} = \frac{\frac{1}{V^n}\prod_{i=1}^{d}\kappa_i'^{a_i}}{\frac{1}{V^n}\mathbb{E}\left[\Big(\sum_{i=1}^{d}\kappa_i'\xi_i\Big)^n\right]} = \frac{\prod_{i=1}^{d}\kappa_i'^{a_i}}{\mathbb{E}\left[\Big(\sum_{i=1}^{d}\kappa_i'\xi_i\Big)^n\right]}$$

We look now at the two-dimensional model with two species of molecules interacting. Here, the vector $a = (a_1, a_2)$ represents the counts of the two species of molecules. The conditional distribution $\pi(a|n)$ is

$$\pi(a|n) = \frac{1}{u(\alpha,\kappa,n)}\binom{n}{a}\kappa_1'^{a_1}\kappa_2'^{a_2}\frac{\Gamma[V(\alpha_1'+\alpha_2')]}{\Gamma[V(\alpha_1'+\alpha_2')+n]}\frac{\Gamma(a_1+V\alpha_1')}{\Gamma(V\alpha_1')}\frac{\Gamma(a_2+V\alpha_2')}{\Gamma(V\alpha_2')} \tag{4.11}$$

We can also reduce the dimension to 1 by letting $a_1 = a, a_2 = n - a$ and write the distribution as a weighted Beta-binomial

$$\pi(a|n) = \frac{1}{u(\alpha,\kappa,n)}\kappa_1'^{a}\kappa_2'^{(n-a)}\binom{n}{a}\frac{B(a+V\alpha_1', n-a+V\alpha_2')}{B(V\alpha_1', V\alpha_2')} \tag{4.12}$$

We will set our parameters as was done in [6, 16] but instead of letting $\kappa_1' = \kappa_2' = 1$ we will set $\kappa_1' = 1$ and look at how different values of κ_2' influence the system. The rates are given as

$$\kappa_1' = 1 \qquad \delta' = \lambda_1' = \lambda_2' = D \tag{4.13}$$

and the α parameters are

$$\alpha_1 = \frac{DV}{2} \qquad \alpha_2 = \frac{DV}{2\kappa_2'} \tag{4.14}$$

Similar to the distribution in [6] the distribution behaves differently under different regimes of DV. When $DV < 2$ the α parameters are both less than 1 and the distribution is bimodal, however, the peak when $a_1 = 0$ and $a_2 = n$ is higher than when $a_2 = 0$ and $a_1 = n$. Small increases in κ_2 give the a_2 "corner" of the distribution large proportions of the mass, and when $\kappa_2 = 1.1$ almost the entire mass of the distribution is concentrated at $(a_1, a_2) = (0, 2V)$. (note here that 2V is the mean of $\nu(n)$) The peaks at the extreme values of a_1 and a_2 reflect the DITs in the system where most of the time is spent in the states $(0, n)$ and $(n, 0)$, and the quick switching between these states is shown by the lack of mass for states between these two peaks. As κ_2 is increased, we start to lose these DITs as the autocatalytic reaction $A_1 + A_2 \xrightarrow{\kappa_2} 2A_2$ overpowers the reaction in the opposite direction.

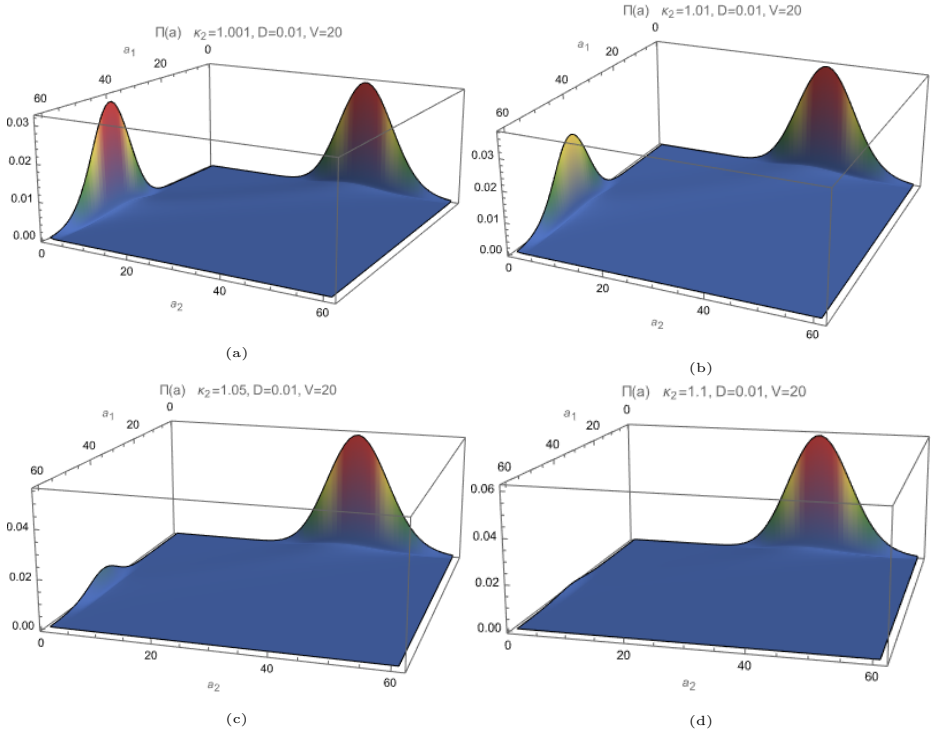
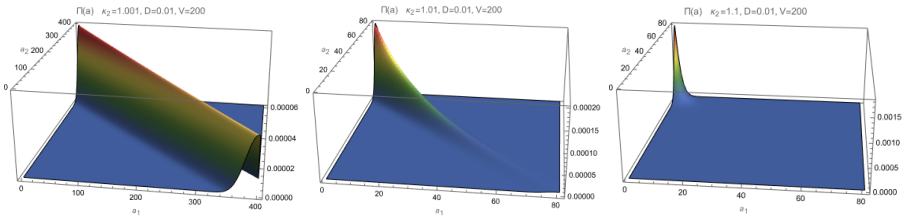


Figure 2: Plots of the full distribtion $\Pi(a)$ are shown when DV=0.2, the density is bimodal as $\alpha_1, \alpha_2 < 1$. κ_1' is fixed at 1 while κ_2' is increased, $\kappa_2 = 1.001, 1.01, 1.05$ and 1.1 for (a),(b),(c) and (d) respectively. In (a) the peaks at either extreme are almost equal, however only increasing κ_2' to 1.1 puts almost the entire mass of the distribution around $(a_1, a_2) = (0, 2V)$.

At the critical case where DV=2 we have $\alpha_1 = 1$ and $\alpha_2 = 1/\kappa_2$. When $\kappa_1 = \kappa_2 = 1$ we had a uniform density but as we increase κ_2 slightly, the density becomes skewed towards a_2 holding more mass, when $\kappa_2 = 1.1$ almost all the mass is at $(0, 2V)$. Figure 3 shows the behaviour of the distribution as we increase κ_2 while setting $DV = 2$ and holding κ_1 at 1.

When $\alpha_1, \alpha_2 > 1$, i.e. when $DV > 2$ we again have a unimodal distribution



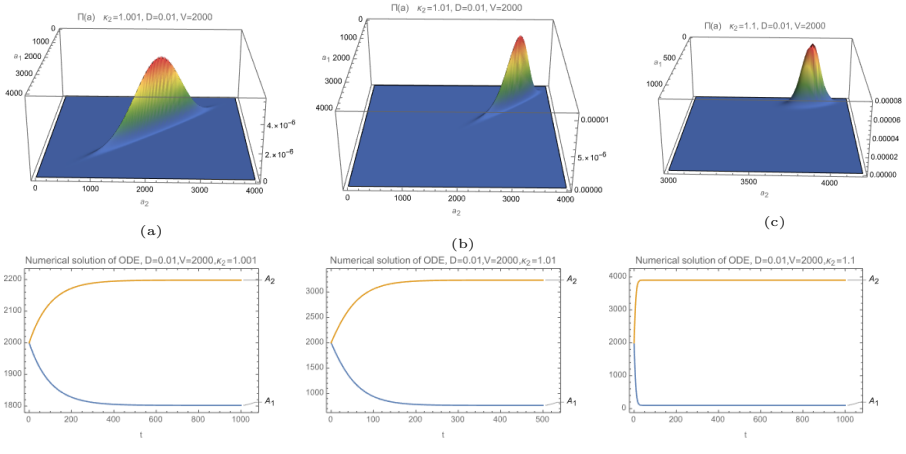
(a) (b) (c)

Figure 3: Plots of the full distribution $\Pi(a)$ at the critical case $DV = 2$, we have $\alpha_1 = 1$ and $\alpha_2 = 1/\kappa_2$. As κ_2 increases, we move from an almost uniform density in (a) to almost all the mass being in a_2 when $\kappa_2 = 1.1$ in (c)

concentrated near $(a_1, a_2) = (V, V)$, but as we κ_1 is fixed at 1, and we increase κ_2 the peak moves such that the distribution is concentrated at a higher proportion of a_2 molecules to a_1 molecules. As $V \to \infty$ the system should converge to the solution of the ODE

$$\begin{aligned} \dot{a_1}(t) &= (\kappa_1 - \kappa_2)a_1a_2 + \lambda_1 - \delta a_1 \\ \dot{a_2}(t) &= (\kappa_2 - \kappa_1)a_1a_2 + \lambda_2 - \delta a_2 \end{aligned} \tag{4.15}$$

When $\kappa_1 = \kappa_2$ equation (4.15) is a simple linear first order ODE with solution $A_1(t) = C_1e^{-\delta t} + \frac{\lambda_1}{\delta}$ and $A_2(t) = C_2e^{-\delta t} + \frac{\lambda_2}{\delta}$. When $\kappa_1 \neq \kappa_2$ unfortunately this system of ODEs is nonlinear and the solution is not simple to compute, however we can find a numerical solution for $A_1(t)$ and $A_2(t)$ which are shown in figure 4.



(a) (b) (c)

(d) (e) (f)

Figure 4: (a)-(c) shows $\Pi(a)$ for $\kappa_2 = 1.001, 1.01, 1.1$ with $D = 0.01, V = 2000$ and $\kappa_1 = 1$. The distributions are unimodal and concentrated around the deterministic equilibria which are shown in (d)-(f) as numerical solutions to the system of ODE's in equation (4.15) with equilibrium points $c_a = (1801.96, 2198.04)$, $c_b = (763.93, 3236.07)$, and, $c_c = (97.5, 3902.5)$. Note: range of the plot in (c) had to be changed due to computational issues.

4.4 Deterministic model

In theorem 2.25 we showed that as $V \to \infty$ the volume scaled process $\bar{X}(t) = X(t)/V$ converges to the deterministic solution of a system of ODEs $x(t)$. The system of ODEs for the 2D TK model is as previously mentioned

$$\begin{aligned} \dot{a_1}(t) &= (\kappa_1 - \kappa_2)a_1a_2 + \lambda_1 - \delta a_1 \\ \dot{a_2}(t) &= (\kappa_2 - \kappa_1)a_1a_2 + \lambda_2 - \delta a_2 \end{aligned} \tag{4.16}$$

In the case where $\kappa_1 = \kappa_2$ this system is linear, and the solution is trivial, but when the autocatalytic rates are not equal we have a non-linear term a_1a_2 and the solution is not easily computed. Even though we cannot directly compute the solution to our system, we can still analyze its equilibrium points and stability. We first check its linear stability. We have

$$\dot{x} = f(x) \tag{4.17}$$

with $x = [a_1(t), a_2(t)]$ and $f = [(\kappa_2-\kappa_1)a_1a_2-\delta a_1+\lambda_1, (\kappa_2-\kappa_1)a_1a_2-\delta a_2+\lambda_2]$, we find a equilibrium point $c = [c_1, c_2]$ by solving $f(c) = [0, 0]$ which gives only one solution with $a_1, a_2 \geq 0$ under the constraints $\lambda_1 > 0, \lambda_2 > 0, \delta > 0, \kappa_2 > \kappa_1 > 0$

$$\begin{aligned} c_1 =& \frac{1}{2\delta(\kappa_1 - \kappa_2)}\Big[\sqrt{(\delta^2 - (\kappa_1 - \kappa_2)(\lambda_1 + \lambda_2))^2 + 4\delta^2\lambda_1(\kappa_1 - \kappa_2)} - \delta^2 + (\lambda_1 + \lambda_2)(\kappa_1 - \kappa_2)\Big] \\ c_2 =& \frac{1}{2\delta(\kappa_1 - \kappa_2)}\Big[- \sqrt{(\delta^2 - (\kappa_1 - \kappa_2)(\lambda_1 + \lambda_2))^2 + 4\delta^2\lambda_1(\kappa_1 - \kappa_2)} + \delta^2 + (\lambda_1 + \lambda_2)(\kappa_1 - \kappa_2)\Big] \end{aligned}$$

the Jacobian is

$$J = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} \end{bmatrix} = \begin{bmatrix} a_2(\kappa_1 - \kappa_2) - \delta & a_1(\kappa_1 - \kappa_2) \\ a_2(\kappa_2 - \kappa_1) & a_1(\kappa_2 - \kappa_2) - \delta \end{bmatrix} \tag{4.18}$$

evaluating J at c we have

$$J_c = \begin{bmatrix} \frac{-\delta^2+(\lambda_1+\lambda_2)(\kappa_1-\kappa_2)-\gamma}{2\delta} & \frac{-\delta^2+(\lambda_1+\lambda_2)(\kappa_1-\kappa_2)+\gamma}{2\delta} \\ \frac{-\delta^2-(\lambda_1+\lambda_2)(\kappa_1-\kappa_2)+\gamma}{2\delta} & \frac{-\delta^2-(\lambda_1+\lambda_2)(\kappa_1-\kappa_2)-\gamma}{2\delta} \end{bmatrix} \tag{4.19}$$

where $\gamma = \sqrt{(\delta^2 - (\kappa_1 - \kappa_2)(\lambda_1 + \lambda_2))^2 + 4\delta^2\lambda_1(\kappa_1 - \kappa_2)}$. The eigenvalues of J_c are

$$\eta_1 = -\delta, \quad \eta_2 = -\frac{\gamma}{\delta} \tag{4.20}$$

note that $\gamma \in \mathbb{R}$ for all $\delta, \lambda_1, \lambda_2 > 0$ and $\kappa_2 > \kappa_1 > 0$. So we have two negative eigenvalues for any of our allowable parameters and by theorem 2.22 we have linear stability in a neighbourhood of c.

4.5 Corner configuration

It can be shown that the candidate distribution exhibits a corner configuration as the volume $V \to 0$. First we condition on the total population being n, or $a_1 + a_2 = n$ then we can write the conditional probability that all molecules are type i as

$$\pi(n \cdot e_i|n) = \frac{1}{u(\alpha,\kappa,n)} \kappa_i'^n \frac{\Gamma\left(V\sum_{i=1}^d \alpha_i'\right)}{\Gamma\left(n + V\sum_{i=1}^d \alpha_i'\right)} \frac{\Gamma(n + V\alpha_i')}{\Gamma(V\alpha_i')}$$

using the fact that $\Gamma(z) \approx 1/z$ as $z \to 0$ taking the limit as $V \to 0$

$$\begin{aligned}\lim_{V\to 0} \pi(n \cdot e_i|n) &= \lim_{V\to 0} \frac{1}{u(\alpha,\kappa,n)} \kappa_i'^n \frac{\Gamma(n + V\alpha_i')}{\Gamma\left(n + V\sum_{i=1}^d \alpha_i'\right)} \frac{V\alpha_i'}{V\sum_{i=1}^d \alpha_i'} \\ &= \frac{\kappa_i'^n \alpha_i'}{\sum_{i=1}^d \alpha_i'} \lim_{V\to 0} \frac{1}{u(\alpha,\kappa,n)}\end{aligned}$$

to look at the limit on the partition function, we first write it out as in (4.6)

$$\begin{aligned}\lim_{V\to 0} u(\alpha,\kappa,n) &= \sum_{|l|=n} \binom{n}{l} \frac{\Gamma\left(\sum_{i=1}^d V\alpha_i'\right)}{\Gamma\left(n + V\sum_{i=1}^d \alpha_i'\right)} \prod_{i=1}^d \kappa_i'^{l_i} \frac{\Gamma(V\alpha_i' + l_i)}{\Gamma(V\alpha_i')} \\ &= \lim_{V\to 0} \frac{1}{\Gamma(n)} \frac{1}{V\sum_{i=1}^d} \sum_{|l|=n} \binom{n}{l} \prod_{i=1}^d \kappa_i'^{l_i} \frac{\Gamma(V\alpha_i' + l_i)}{\Gamma(V\alpha_i')}\end{aligned}$$

Looking at the terms in the product if $l_i = 0$ then the term is 1 otherwise the term is $\kappa_i'^{l_i}\Gamma(l_i)V\alpha_i'$. So for each term in the sum if there is more than one $l_i > 0$ the term will have V to a power greater than 1, and as $V \to 0$ the term will also go to zero. If $l_i = n$ and $l_j = 0$ for $j \neq i$ then the term in the sum is given by $\kappa_i'^n\Gamma(n)V\alpha_i'$ so we can write

$$\begin{aligned}\lim_{V\to 0} u(\alpha,\kappa,n) &= \lim_{V\to 0} \frac{1}{\Gamma(n)V\sum_{i=1}^d \alpha_i'} \sum_{i=1}^d \kappa_i'^n \Gamma(n) V\alpha_i' \\ &= \frac{1}{\sum_{i=1}^d \alpha_i'} \sum_{i=1}^d \kappa_i'^n \alpha_i'\end{aligned}$$

and as $V \to 0$ the probability all the molecules are type i is given as

$$\lim_{V\to 0} \pi(n \cdot e_i|n) = \frac{\kappa_i'^n \alpha_i'}{\sum_{i=1}^d \kappa_i'^n \alpha_i'} \tag{4.21}$$

and the probability that all the molecules are of the same type and the rest

are extinct is given by

$$\lim_{V\to 0}\sum_{i=1}^{d}\pi(n\cdot e_i|n)=\sum_{i=1}^{d}\frac{\kappa_i'^n\alpha_i'}{\sum_{i=1}^{d}\kappa_i'^n\alpha_i'}=1 \tag{4.22}$$

Thus, as the volume gets very small the probability that the system is in a corner configuration approaches 1.

4.6 Global Balance Equation

To show the distribution $\Pi(a)=\nu(n)\pi(a|n)$ is stationary, it must satisfy the global balance equation

$$\Pi(a)\sum_{a'\in S}q(a,a')=\sum_{a'\in S}\Pi(a')q(a',a) \tag{4.23}$$

$\Pi(a)$ fulfills the global balance conditions when $\pi(a|n)$ satisfies the equation

$$R_n=L_{n-1}+L_n+L_{n+1} \tag{4.24}$$

where

$$R_n=[\lambda_1+\lambda_2+n\delta+(\kappa_1+\kappa_2)a_1a_2]\pi(a|n) \tag{4.25}$$

$$L_{n-1}=\frac{n\delta\lambda_1}{\lambda_1+\lambda_2}\pi(a-e_1|n-1)+\frac{n\delta\lambda_2}{\lambda_1+\lambda_2}\pi(a-e_2|n-1) \tag{4.26}$$

$$L_n=\kappa_2(a_1+1)(a_2-1)\pi(a+e_1-e_2|n)+\kappa_1(a_1-1)(a_2+1)\pi(a-e_1+e_2|n) \tag{4.27}$$

$$L_{n+1}=\frac{\lambda_1+\lambda_2}{n+1}(a_1+1)\pi(a+e_1|n+1)+\frac{\lambda_1+\lambda_2}{n+1}(a_2+1)\pi(a+e_2|n+1) \tag{4.28}$$

we have:

$$\frac{\pi(a-e_1|n-1)}{\pi(a|n)}=\frac{a_1}{n}\frac{n-1+\alpha_2}{a_1-1+\alpha_1}\frac{\kappa_2}{\kappa_1}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(1-n,\alpha_1,2-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}$$

$$\frac{\pi(a-e_2|n-1)}{\pi(a|n)}=\frac{a_2}{n}\frac{n-1+\alpha_2}{a_2-1+\alpha_2}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(1-n,\alpha_1,2-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}$$

$$\frac{\pi(a+e_1-e_2|n)}{\pi(a|n)}=\frac{a_2}{a_1+1}\frac{a_1+\alpha_1}{a_2-1+\alpha_2}\frac{\kappa_1}{\kappa_2}$$

$$\frac{\pi(a-e_1+e_2|n)}{\pi(a+e_1-e_2|n)}=\frac{a_1}{a_2+1}\frac{a_2+\alpha_2}{a_1-1+\alpha_1}\frac{\kappa_2}{\kappa_1}$$

$$\frac{\pi(a+e_1|n+1)}{\pi(a|n)}=\frac{n+1}{a_1+1}\frac{a_1+\alpha_1}{n+\alpha_2}\frac{\kappa_1}{\kappa_2}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}$$

$$\frac{\pi(a|n+1)}{\pi(a|n)}=\frac{n+1}{a_2+1}\frac{a_2+\alpha_2}{n+\alpha_2}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}$$

now dividing L_{n-1}, L_n and L_{n+1} by $\pi(a|n)$ we have:

$$\frac{L_{n-1}}{\pi(a|n)} = \frac{(n-1+\alpha_2)\delta}{\lambda_1+\lambda_2}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(1-n,\alpha_1,2-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}\Big[\frac{a_1\lambda_1}{a_1-1+\alpha_1}\frac{\kappa_2}{\kappa_1}+\frac{a_2\lambda_2}{a_2-1+\alpha_2}\Big]$$

$$\frac{L_n}{\pi(a|n)} = \kappa_1\frac{a_2-1}{a_2-1+\alpha_2}(a_1+\alpha_1)a_2+\kappa_2\frac{a_1-1}{a_1-1+\alpha_1}(a_2+\alpha_2)a_1$$

$$\frac{L_{n+1}}{\pi(a|n)} = \frac{\lambda_1+\lambda_2}{(n+\alpha_2)}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}\Big[\frac{\kappa_1}{\kappa_2}(a_1+\alpha_1)+(a_2+\alpha_2)\Big]$$

using the fact that $\alpha_i = \frac{\delta}{\lambda_1+\lambda_2}\frac{\lambda_i}{\kappa_i}$ we can manipulate the first equation such that

$$\frac{L_{n-1}}{\pi(a|n)} = (n-1+\alpha_2)\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(1-n,\alpha_1,2-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}\kappa_2\Big[\frac{a_1\alpha_1}{a_1-1+\alpha_1}+\frac{a_2\alpha_2}{a_2-1+\alpha_2}\Big]$$

$$
\begin{aligned}
\frac{L_n}{\pi(a|n)} =& \sum_{i=1}^{2}\sum_{j\neq i}\kappa_i(a_i+\alpha_i)\frac{a_j-1}{a_j-1+\alpha_j}a_j \\
=& \sum_{i=1}^{2}\sum_{j\neq i}\kappa_i(a_i+\alpha_i)\frac{a_j-1+\alpha_j}{a_j-1+\alpha_j}a_j - \sum_{i=1}^{2}\sum_{j\neq i}\frac{\kappa_i(a_i+\alpha_i)a_j\alpha_j}{a_j-1+\alpha_j} \\
=& \sum_{i=1}^{2}\sum_{j\neq i}\kappa_i(a_i+\alpha_i)a_j - \sum_{i=1}^{2}\sum_{j\neq i}\frac{\kappa_i(a_i+\alpha_i)a_j\alpha_j}{a_j-1+\alpha_j} \\
=&(\kappa_1+\kappa_2)a_1a_2 + \sum_{i=1}^{2}\sum_{j\neq i}\kappa_i\alpha_i a_j - \sum_{i=1}^{2}\sum_{j\neq i}\frac{\kappa_i(a_i+\alpha_i)a_j\alpha_j}{a_j-1+\alpha_j} \\
=&(\kappa_1+\kappa_2)a_1a_2 + \sum_{i=1}^{2}\sum_{j=1}^{2}\kappa_i\alpha_i a_j - \sum_{i=1}^{2}\kappa_i\alpha_i a_i \\
&- \sum_{i=1}^{2}\sum_{j=1}^{2}\frac{\kappa_j(a_j+\alpha_j)a_i\alpha_i}{a_i-1+\alpha_i} + \sum_{i=1}^{2}\frac{\kappa_i(a_i+\alpha_i)a_i\alpha_i}{a_i-1+\alpha_i} \\
=&(\kappa_1+\kappa_2)a_1a_2 + n\delta - \sum_{i=1}^{2}\kappa_i\alpha_i a_i \\
&- \sum_{i=1}^{2}\sum_{j=1}^{2}\frac{\kappa_j(a_j+\alpha_j)a_i\alpha_i}{a_i-1+\alpha_i} + \sum_{i=1}^{2}\frac{\kappa_i(a_i-1+\alpha_i)a_i\alpha_i}{a_i-1+\alpha_i} + \sum_{i=1}^{2}\frac{\kappa_i a_i\alpha_i}{a_i-1+\alpha_i} \\
=&(\kappa_1+\kappa_2)a_1a_2 + n\delta - \sum_{i=1}^{2}\kappa_i\alpha_i a_i \\
&- \sum_{i=1}^{2}\sum_{j=1}^{2}\frac{\kappa_j(a_j+\alpha_j)a_i\alpha_i}{a_i-1+\alpha_i} + \sum_{i=1}^{2}\kappa_i a_i\alpha_i + \sum_{i=1}^{2}\frac{\kappa_i a_i\alpha_i}{a_i-1+\alpha_i} \\
=&(\kappa_1+\kappa_2)a_1a_2 + n\delta - \sum_{i=1}^{2}\sum_{j=1}^{2}\frac{\kappa_j(a_j+\alpha_j)a_i\alpha_i}{a_i-1+\alpha_i} + \sum_{i=1}^{2}\frac{\kappa_i a_i\alpha_i}{a_i-1+\alpha_i} \\
=&(\kappa_1+\kappa_2)a_1a_2 + n\delta - \Big(\sum_{j=1}^{2}\kappa_j(a_j+\alpha_j)\Big)\sum_{i=1}^{2}\frac{a_i\alpha_i}{a_i-1+\alpha_i} + \sum_{i=1}^{2}\frac{\kappa_i a_i\alpha_i}{a_i-1+\alpha_i}
\end{aligned}
$$

The first two terms cancel out terms in R_n and looking at the remaining terms

we have:

$$
\begin{aligned}
&\sum_{i=1}^{2} \frac{\kappa_i a_i \alpha_i}{a_i - 1 + \alpha_i} - \Big(\sum_{j=1}^{2} \kappa_j (a_j + \alpha_j) \Big) \sum_{i=1}^{2} \frac{a_i \alpha_i}{a_i - 1 + \alpha_i} \\
=&\kappa_1 \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_1} + \kappa_2 \frac{a_2 \alpha_2}{a_2 - 1 + \alpha_2} \\
&- \kappa_1 (a_1 + \alpha_1) \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_1} - \kappa_2 (a_2 + \alpha_2) \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_1} \\
&- \kappa_1 (a_1 + \alpha_1) \frac{a_2 \alpha_2}{a_2 - 2 + \alpha_2} - \kappa_2 (a_2 + \alpha_2) \frac{a_2 \alpha_2}{a_2 - 1 + \alpha_2}
\end{aligned}
$$

under the assumption $\lambda_1 = \lambda_2$ we can use the fact that $\kappa_1 = \kappa_2(\alpha_2/\alpha_1)$

$$
\begin{aligned}
=&\kappa_2 \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_1} \Big[\frac{\alpha_2}{\alpha_1} - \frac{\alpha_2}{\alpha_1} (a_1 + \alpha_1) - (a_2 + \alpha_2) \Big] + \kappa_2 \frac{a_2 \alpha_2}{a_2 - 1 + \alpha_2} \Big[1 - \frac{\alpha_2}{\alpha_1} (a_1 + \alpha_1) - (a_2 + \alpha_2) \Big] \\
=&\kappa_2 \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_1} \Big[\frac{\alpha_2}{\alpha_1} - \frac{\alpha_2}{\alpha_1} a_1 - a_2 - 2\alpha_2 \Big] \\
&+ \kappa_2 \frac{a_2 \alpha_2}{a_2 - 1 + \alpha_2} \Big[1 - \frac{\alpha_2}{\alpha_1} a_1 - a_2 - 2\alpha_2 \Big] \\
=&- \kappa_2 (n - 1 + \alpha_2) \sum_{i=1}^{2} \frac{a_i \alpha_i}{a_i - 1 + \alpha_i} \\
&+ \kappa_2 \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_2} \Big[\frac{\alpha_2}{\alpha_1} + a_1 - \frac{\alpha_2}{\alpha_1} a_1 - 1 - \alpha_2 \Big] + \kappa_2 \frac{a_2 \alpha_2}{a_2 - 1 + \alpha_2} \Big[a_1 - \frac{\alpha_2}{\alpha_1} a_1 - \alpha_2 \Big] \\
=&- \kappa_2 (n - 1 + \alpha_2) \sum_{i=1}^{2} \frac{a_i \alpha_i}{a_i - 1 + \alpha_i} + \kappa_2 \sum_{i=1}^{2} \frac{a_i \alpha_i}{a_i - 1 + \alpha_i} \Big[a_1 \big(1 - \frac{\alpha_2}{\alpha_1} \big) - \alpha_2 \Big] + \kappa_2 \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_1} \Big[\frac{\alpha_2}{\alpha_1} - 1 \Big]
\end{aligned}
$$

again under the assumption that $\lambda_1 = \lambda_2$ we note that $\alpha_2/\alpha_1 = \kappa_1/\kappa_2$

$$
=- \kappa_2 (n - 1 + \alpha_2) \sum_{i=1}^{2} \frac{a_i \alpha_i}{a_i - 1 + \alpha_i} + \sum_{i=1}^{2} \frac{a_i \alpha_i}{a_i - 1 + \alpha_i} \Big[a_1 \big(\kappa_2 - \kappa_1 \big) - \kappa_2 \alpha_2 \Big] + \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_1} \Big[\kappa_1 - \kappa_2 \Big]
$$

L_n can now be written as

$$
\begin{aligned}
\frac{L_n}{\pi(a|n)} =&(\kappa_1 + \kappa_2) a_1 a_2 + n\delta - \kappa_2 (n - 1 + \alpha_2) \sum_{i=1}^{2} \frac{a_i \alpha_i}{a_i - 1 + \alpha_i} \\
&+ \sum_{i=1}^{2} \frac{a_i \alpha_i}{a_i - 1 + \alpha_i} \Big[a_1 \big(\kappa_2 - \kappa_1 \big) - \alpha_2 \Big] + \frac{a_1 \alpha_1}{a_1 - 1 + \alpha_1} \Big[\kappa_1 - \kappa_2 \Big]
\end{aligned} \tag{4.29}
$$

Again the first two terms in (4.29) cancel with terms in R_n, it is also important to note that the third term is the same as L_{n-1} apart from the ratio of Hypergeometric functions.

Looking at the equation for, L_{n+1} we can rewrite it as such:

$$\frac{L_{n+1}}{\pi(a|n)} = \frac{\lambda_1+\lambda_2}{n+\alpha_2}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}\Big[\frac{\kappa_1}{\kappa_2}(a_1+\alpha_1)+(a_2+\alpha_2)\Big]$$

we can write $a_2 = n - a_1$ and rearrange the terms in the square brackets

$$= \frac{\lambda_1+\lambda_2}{n+\alpha_2}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}\Big[(n+\alpha_2)+\frac{\kappa_1}{\kappa_2}(a_1+\alpha_1)-a_1\Big]$$

$$= (\lambda_1+\lambda_2)\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}$$

$$+ \frac{\lambda_1+\lambda_2}{n+\alpha_2}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}\Big[a_1\big(\frac{\kappa_1}{\kappa_2}-1\big)+\alpha_2\Big]$$

Writing out the balance equation as, $B = \frac{1}{\pi(a|n)}\big[R_n - (L_{n-1}+L_n+L_{n+1})\big]$ we can see how "in balance" the system is by seeing how close B is to zero.

$$\begin{aligned}
B =&(\lambda_1+\lambda_2)\left[1-\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}\right]\\
&-\kappa_2(n-1+\alpha_2)\sum_{i=1}^{2}\frac{a_i\alpha_i}{a_i-1+\alpha_i}\left[\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(1-n,\alpha_1,2-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}-1\right]\\
&-\sum_{i=1}^{2}\frac{a_i\alpha_i}{a_i-1+\alpha_i}\Big[a_1\big(\kappa_2-\kappa_1\big)-\kappa_2\alpha_2\Big]-\frac{a_1\alpha_1}{a_1-1+\alpha_1}\Big[\kappa_1-\kappa_2\Big]\\
&-\frac{\lambda_1+\lambda_2}{n+\alpha_2}\frac{F(-n,\alpha_1,1-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,\alpha_1,-\alpha_2-n,\frac{\kappa_1}{\kappa_2})}\Big[a_1\big(\frac{\kappa_1}{\kappa_2}-1\big)+\alpha_2\Big]
\end{aligned} \tag{4.30}$$

writing B in terms of our volume scaled parameters

$$\kappa_i = \frac{\kappa_i'}{V} \qquad \lambda_i = \lambda_i' V = DV \qquad \delta = \delta' = D$$

we have:

$$
\begin{aligned}
B =& 2DV\left[1-\frac{F(-n,V\alpha_1',1-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}{F(-1-n,V\alpha_1',-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}\right] \\
&-\frac{\kappa_2}{V}(n-1+V\alpha_2')\sum_{i=1}^{2}\frac{a_iV\alpha_i'}{a_i-1+V\alpha_i'}\left[\frac{F(-n,V\alpha_1',1-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}{F(1-n,V\alpha_1',2-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}-1\right] \\
&-\sum_{i=1}^{2}\frac{a_iV\alpha_i'}{a_i-1+VV\alpha_i''}\Big[a_1\big(\frac{\kappa_2}{V}-\frac{\kappa_1}{V}\big)-\frac{\kappa_2}{V}V\alpha_2'\Big]-\frac{a_1V\alpha_1'}{a_1-1+V\alpha_1'}\Big[\frac{\kappa_1}{V}-\frac{\kappa_2}{V}\Big] \\
&-\frac{\lambda_1+\lambda_2}{n+V\alpha_2'}\frac{F(-n,V\alpha_1',1-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}{F(-1-n,V\alpha_1',-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}\Big[a_1\big(\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}}-1\big)+V\alpha_2'\Big] \\
=& 2DV\left[1-\frac{F(-n,V\alpha_1',1-V\alpha_2'-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,V\alpha_1',-V\alpha_2'-n,\frac{\kappa_1}{\kappa_2})}\right] \\
&-\kappa_2(n-1+V\alpha_2')\sum_{i=1}^{2}\frac{a_i\alpha_i'}{a_i-1+V\alpha_i'}\left[\frac{F(-n,V\alpha_1',1-V\alpha_2'-n,\frac{\kappa_1}{\kappa_2})}{F(1-n,V\alpha_1',2-V\alpha_2'-n,\frac{\kappa_1}{\kappa_2})}-1\right] \\
&-\sum_{i=1}^{2}\frac{a_i\alpha_i'}{a_i-1+V\alpha_i'}\Big[a_1\big(\kappa_2-\kappa_1\big)-\kappa_2\alpha_2'\Big]-\frac{a_1\alpha_1'}{a_1-1+V\alpha_1'}\Big[\kappa_1-\kappa_2\Big] \\
&-\frac{2DV}{n+V\alpha_2'}\frac{F(-n,V\alpha_1',1-V\alpha_2'-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,V\alpha_1',-V\alpha_2'-n,\frac{\kappa_1}{\kappa_2})}\Big[a_1\big(\frac{\kappa_1}{\kappa_2}-1\big)+V\alpha_2'\Big] \\
=& 2DV\Bigg\{\left[1-\frac{F(-n,DV/2,1-DV/(2\kappa_2)-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,DV/2,-DV/(2\kappa_2)-n,\frac{\kappa_1}{\kappa_2})}\right] \\
&-\frac{1}{n+DV/(2\kappa_2)}\frac{F(-n,DV/2,1-DV/(2\kappa_2)-n,\frac{\kappa_1}{\kappa_2})}{F(-1-n,DV/2,-DV/(2\kappa_2)-n,\frac{\kappa_1}{\kappa_2})}\Big[a_1\big(\frac{\kappa_1}{\kappa_2}-1\big)+DV/(2\kappa_2)\Big]\Bigg\} \\
&-\kappa_2(n-1+DV/(2\kappa_2))\left[\frac{F(-n,DV/2,1-DV/(2\kappa_2)-n,\frac{\kappa_1}{\kappa_2})}{F(1-n,DV/2,2-DV/(2\kappa_2)-n,\frac{\kappa_1}{\kappa_2})}-1\right]\sum_{i=1}^{2}\frac{a_iDV/(2\kappa_i)}{a_i-1+DV/(2\kappa_i)} \\
&-\Big[a_1\big(\kappa_2-\kappa_1\big)-D/2\Big]\sum_{i=1}^{2}\frac{a_iD/(2\kappa_i)}{a_i-1+DV/(2\kappa_i)}-\frac{a_1D/2}{a_1-1+DV/2}\Big[\kappa_1-\kappa_2\Big]
\end{aligned}
$$

The ratios of hypergeometric functions are both close to 1 as seen in figure 5 so the two terms in the large square brackets are fairly small. Figure 6 shows values of B for different states $a = (a, n-a)$. B is fairly close to zero except when $n \approx 2V$, which is the mean of $\nu(n)$. B is the most non-zero when $a \approx (0, 2V), (1, 2V), (2V, 0)$ and $(2V, 1)$. Figure 7 shows B for different values of κ_2', as κ_2' gets closer to 1 the peaks get smaller.

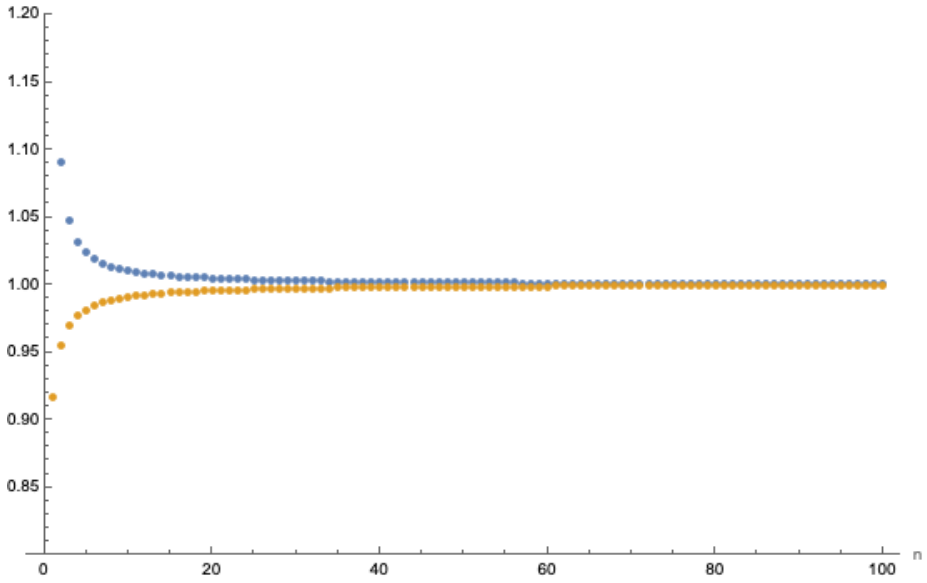


Figure 5: $\frac{F(-n,V\alpha_1',1-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}{F(1-n,V\alpha_1',2-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}$ and $\frac{F(-n,V\alpha_1',1-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}{F(-1-n,V\alpha_1',-V\alpha_2'-n,\frac{\frac{\kappa_1}{V}}{\frac{\kappa_2}{V}})}$ in blue and orange respectively. The functions were plotted for $\lambda_1' = \lambda_2' = \delta = 0.01, V = 20$ and $\kappa_2 = 1.001$ as a function of n

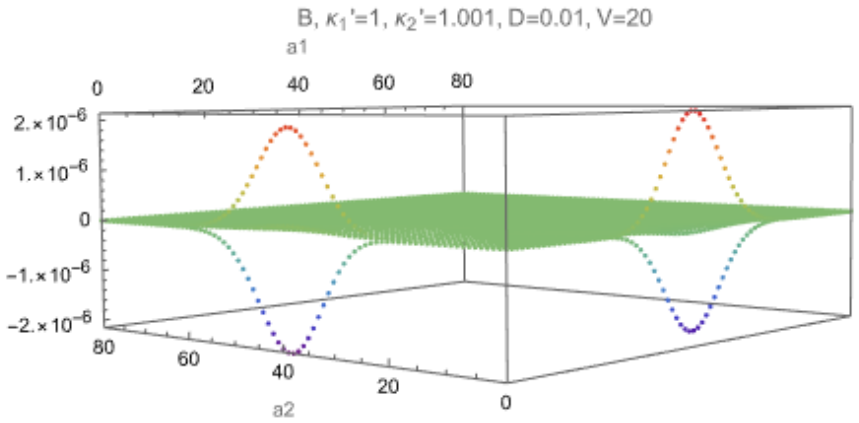


Figure 6: Values of B when $\lambda_1' = \lambda_2' = \delta' = 0.01, , \kappa_1' = 1, \kappa_2' = 1.001$ and $V = 20$

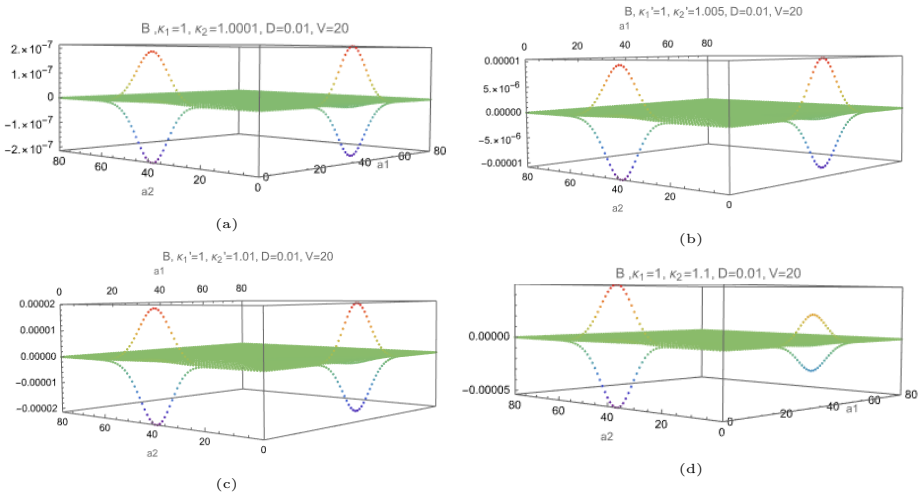


Figure 7: B plotted with $\kappa_1' = 1, \lambda_1' = \lambda_2' = \delta' = 0.01, V = 20$ and $\kappa_2' = 1.0001, 1.005, 1.01, 1.1$

4.7 Simulation

Simulation of the two-dimensional TK model was carried out using the Gillespie algorithm. The algorithm, formulated circa 1945 by Joseph L. Doob, and popularized by Dan Gillespie in a paper written in 1977 [8]. The Gillespie algorithm is a stochastic simulation algorithm based on the dynamic Monte Carlo method, it is used widely to simulate chemical and biological systems with great accuracy and efficiency. The algorithm is especially useful in our case since it can simulate a system with small numbers of reactants as every reaction is exactly simulated, the trajectory of a Gillespie simulation corresponds to an explicit sample from a distribution which satisfies the master equation of the system.

4.7.1 The Gillespie Algorithm

The following version of the Gillespie algorithm has been adapted from lecture notes by Paolo Milazzo [13]. Let $\mathcal{R} = \{R_1, R_2, \ldots, R_n\}$ be a set of reactions. We assume a reaction constant κ_μ for each reaction $R_\mu \in \mathcal{R}$ such that $c_\mu dt$ is the probability that the combination of reactants of R_μ react in an infinitesimal time step dt. The propensity of R_μ, a_μ, is computed as

$$a_\mu = h_\mu \kappa_\mu \tag{4.31}$$

where h_μ is the number of distinct reactant combinations for R_μ. i.e. if R_μ is given by:

$$k_1 S_1 + \cdots + k_n S_n \xrightarrow{\kappa} k_1' P_1 + \cdots + k_m' P_m \tag{4.32}$$

if the reaction is in a solution with A_i molecules of each reactant, S_i then h_μ is given as

$$h_\mu = \prod_{i=1}^{n} \binom{A_i}{k_i} \tag{4.33}$$

The time between occurrences of the reaction R_μ is a random variable with $Exp(a_\mu)$ distribution. We let

- $\{S_1, \ldots, S_n\}$ be a set of molecules
- $\{A_1, \ldots, A_n\}$ be the initial numbers of each molecule
- $\{R_1, \ldots, R_m\}$ a set of reactions of the molecules

the algorithm then proceeds as such:

1. set $t = 0$ and then initialize $A = [A_1, \ldots, A_2]$
2. the time $t + \tau$ at which the next reaction occurs is randomly chosen with $\tau \sim Exp\big[\sum_{i=1}^{m} a_i\big]$[1]
3. the reaction which occurs at time $t + \tau$ is randomly chosen, with the probability of choosing R_μ given by $\frac{a_\mu}{\sum_{i=1}^{m} a_i}$ [2]
4. $A = [A_1 \ldots, A_2]$ is updated by adding the products and subtracting the reactants of R_μ
5. steps 2 and 3 are repeated until t has reached a chosen value

For our particular model, we provide an example of the algorithm:

$$\begin{aligned} &R_1 : A_1 + A_2 \xrightarrow{1/20} 2A_1 \quad R_2 : A_1 + A_2 \xrightarrow{1.01/20} 2A_2 \\ &R_3 : \emptyset \xrightarrow{.2} A_1 \quad R_4 : \emptyset \xrightarrow{0.2} A_2 \\ &R_5 : A_1 \xrightarrow{0.01} \emptyset \quad R_6 : A_2 \xrightarrow{0.01} \emptyset \end{aligned} \tag{4.34}$$

We choose an initial state $A = [30, 10]$, and propensities are computed:

$$a_1 = 30{\cdot}10{\cdot}1/20 \quad a_2 = 30{\cdot}10{\cdot}1.01/20 \quad a_3 = 0.2 \quad a_4 = 0.2 \quad a_5 = 30{\cdot}0.01 \quad a_6 = 10{\cdot}0.01$$

$a_0 = \sum_i a_i = 15 + 15.15 + 0.2 + 0.2 + 0.3 + 0.1 = 30.95$. We then draw τ from $Exp[30.95]$ lets say $\tau = 0.032$ and choose a reaction with probability a_i/a_0. We choose $R_2 : R_2 : A_1 + A_2 \xrightarrow{1.01/20} 2A_2$ so subtract an A_1 and A_2 and add $2A_2$'s and the state of the system is now $A = [29, 11]$ at time $t = \tau$. We continue to update the state of the system as such, keeping track of each state visited, until a predetermined time. After the simulation we can plot a histogram of the states visited, this histogram should coincide with our distribution $\Pi(a)$

[1] τ is chosen by generating a random number $r_1 \in [0, 1]$ and computing $\tau = \frac{1}{\sum_{i=1}^{m} a_i} \ln\left(\frac{1}{r_1}\right)$

[2] to choose a reaction R_μ we generate a random number $r_2 \sim Unif[0, 1)$ and choose μ as the smallest integer satisfying $\sum_{i=1}^{k} a_i > r_2 \sum_{i=1}^{m} a_i$

4.7.2 Simulations of 2D TK model

Let $A(t) = [A_1(t), A_2(t)]$ be the state of our simulation in the Gillespie algorithm. Let's assume at time t there are n A_1 molecules and m A_2 molecules or $A_1(t) = n$ and $A_2(t) = m$. Let $p_{n,m}(t)$ be the probability that there are $A(t) = [n, m]$, if we consider an infinitesimal time step dt chosen such that only one event occurs there are only seven possible ways that $A(t + dt) = [n, m]$ either $A(t) = [n, m]$ and no reaction occurs in $[t, dt)$, $A(t) = [n - 1, m]$ and an A_1 is added with rate λ_1, $A(t) = [n, m - 1]$ and an A_2 is added with rate λ_2, $A(t) = [n + 1, m]$ with an A_1 dying with rate δ, $A(t) = [n, m + 1]$ with an A_2 dying at rate δ, $A(t) = [n + 1, m - 1]$ and we have an auto catalytic reaction at rate κ_2 or $A(t) = [n-1, m+1]$ and we have an autocatalytic reaction with rate κ_2. So,

$$\begin{aligned} p_{n,m}(t + dt) =& p_{n-1,m}(t)\lambda_1 dt + p_{n,m-1}(t)\lambda_2 dt \\ &+ p_{n+1,m}(t)\delta(n + 1)dt + p_{n,m+1}(t)\delta(m + 1)dt \\ &+ p_{n+1,m-1}(t)\kappa_2(n + 1)(m - 1)dt + p_{n-1,m+1}(t)\kappa_1(n - 1)(m + 1)dt \\ &+ p_{n,m}(t)\big(1 - (\lambda_1 dt + \lambda_2 dt + \delta n dt + \delta m dt + \kappa_1 nm dt + \kappa_2 nm dt)\big) \end{aligned} \tag{4.35}$$

manipulating the equation, we can write

$$\begin{aligned} \frac{p_{n,m}(t + dt) - p_{n,m}(t)}{dt} =& p_{n-1,m}(t)\lambda_1 + p_{n,m-1}(t)\lambda_2 \\ &+ p_{n+1,m}(t)\delta(n + 1) + p_{n,m+1}(t)\delta(m + 1) \\ &+ p_{n+1,m-1}(t)\kappa_2(n + 1)(m - 1) + p_{n-1,m+1}(t)\kappa_1(n - 1)(m + 1) \\ &- p_{n,m}(t)\big(\lambda_1 + \lambda_2 + \delta n + \delta m + \kappa_1 nm + \kappa_2 nm\big) \end{aligned} \tag{4.36}$$

taking the limit as $dt \to 0$ we get

$$\begin{aligned} \frac{dp_{n,m}}{dt} =& p_{n-1,m}(t)\lambda_1 + p_{n,m-1}(t)\lambda_2 \\ &+ p_{n+1,m}(t)\delta(n + 1) + p_{n,m+1}(t)\delta(m + 1) \\ &+ p_{n+1,m-1}(t)\kappa_2(n + 1)(m - 1) + p_{n-1,m+1}(t)\kappa_1(n - 1)(m + 1) \\ &- p_{n,m}(t)\big(\lambda_1 + \lambda_2 + \delta n + \delta m + \kappa_1 nm + \kappa_2 nm\big) \end{aligned} \tag{4.37}$$

Which is the Master equation for our chemical reaction network. The Gillespie algorithm provides an unbiased and convergent estimate of the solution of the chemical master equation [10], so if the algorithm is run for a sufficiently long time, we should be able to extract this solution to the master equation by looking at the proportions of time spent in each statec. Since the existence of a unique stationary distribution was proved for the general model by Bibbona *et al* in [6], it is a solution to the master equation and moreover the Gillespie algorithm is sampling from it. To compare the proposed distribution to the

true stationary distribution the Gillespie algorithm was run for a long period of time and the proportion of time spent in each state was plotted on a histogram, figure 8 shows some of these plots for $DV = 0.2$ when DITs are active in the system. The histograms agree with the plots of the proposed distribution, $\Pi(a)$ including the behaviour as κ_2 is increased and κ_1 is held at 1. In figure 9 we keep $DV = 0.2$ but for a volume of 10 and 40, both plots agree with the simulated data. In figure 10 volume is fixed at 20 and D is increased, as D increases the inflow and outflow reactions increase in frequency, so the system spends less time on the boundaries. Autocatalytic reactions are still at play, so there are still peaks at the boundaries, but they are less pronounced.

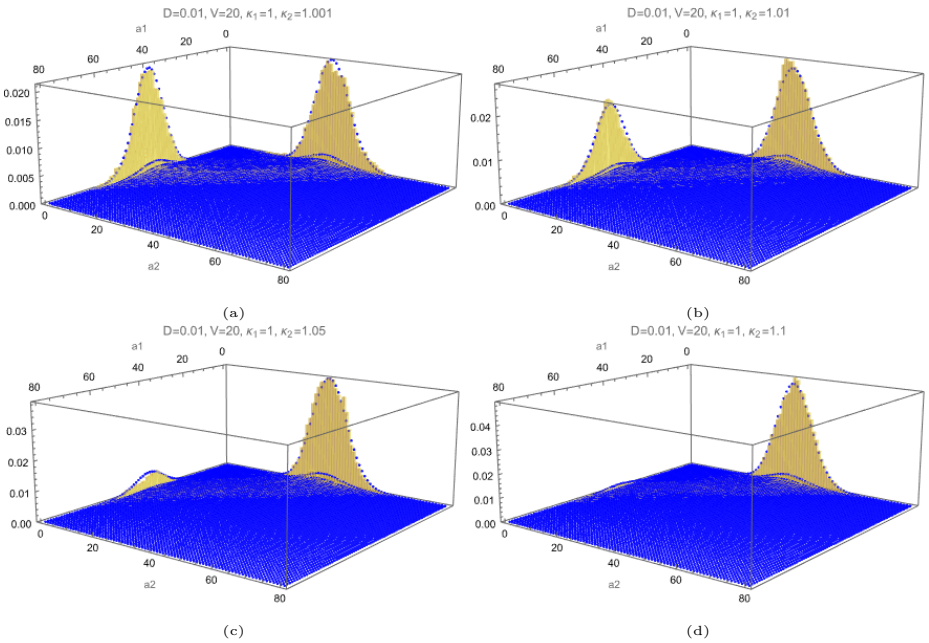


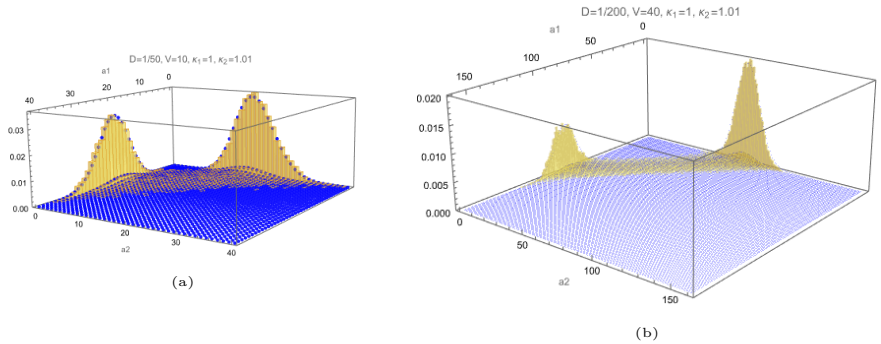
Figure 8: Histograms for simulations of 2D TK network with asymmetric autocatalytic rates are shown in yellow with $\Pi(a)$ overlaid in blue. Volume scaled rates are $\kappa_1' = 1, \lambda_1' = \lambda_2' = \delta' = D = 0.01$ with volume $V = 20$ for all 4 plots, $\kappa_2' = 1.001, 1.01, 1.05, 1.1$ for (a),(b),(c), and (d) respectively.

4.8 Discussion

In this thesis we have studied a family of autocatalytic reactions

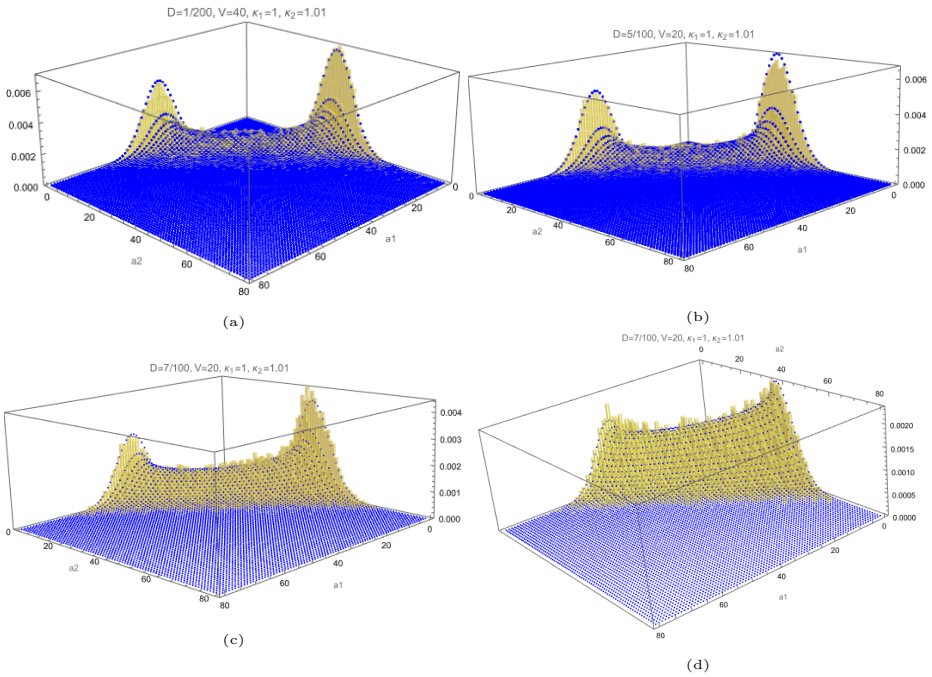
$$A_i + A_j \xrightarrow{\kappa_{ij}} 2A_j \qquad A_i \underset{\lambda_i}{\overset{\delta_i}{\rightleftharpoons}} \emptyset \tag{4.38}$$

Modelling the counts of each species as a continuous time Markov chain Bibbona *et al* proved the existence of a stationary distribution for a general system in this family, they also show a under the condition where all catalytic reaction



(a) (b)

Figure 9: Histograms for simulations of 2D TK network with asymmetric autocatalytic rates are shown in yellow, with $\Pi(a)$ overlaid in blue. Volume and D were varied while keeping $DV = 0.2$ Volume scaled rates are $\kappa_1' = 1, \kappa_2' = 1.01, \lambda_1' = \lambda_2' = D$ with volume $V = 10$ and $D = 1/50$ in (a), $V = 40$ and $D = 1/200$



(a) (b) (c) (d)

Figure 10: Histograms for simulations of 2D TK network with asymmetric autocatalytic rates are shown in yellow with $\Pi(a)$ overlaid in blue. D was varied while keeping the volume fixed at $V = 20$. Volume scaled rates are $\kappa_1' = 1, \kappa_2 = 1.01\lambda_1' = \lambda_2' = D$ with and $D = 2/100, 5/100, 7/100, 9/100$ in (a), (b), (c), and (d) respectively.

rates $\kappa_{ij} = \kappa$ that the stationary distribution conditional on the total population being n takes the form of a Dirichlet-multinomial distribution. To investigate the case when the autocatalytic rates are not identical, we have tested a distribution which is stationary for a model which similar dynamics. The distribution is a

Dirichlet-multinomial distribution but weighted on the autocatalytic rates, it should also be noted that it does not hold for general autocatalytic rates κ_{ij} but only when $\kappa_{ij} = \kappa_j$ for all i. When the outflow rates δ_i are identical the lumped process $\bar{X}(t)$, which is the count of the total population of the system at time t, is a CTMC with stationary distribution

$$\nu(n) = \frac{\mu^n}{n!} \exp(-\mu), \quad \mu = \frac{\sum_i \lambda_i}{\delta} \tag{4.39}$$

Conditioning on the stationary probability, $\nu(n)$, of $\bar{X}(t)$ being in the state $n = \sum_i a_i$ the stationary distribution of $X(t)$ can be factorized as $\Pi(a) = \nu(n)\pi(a|n)$. We looked at the two-dimensional model

$$A_1 + A_2 \xrightarrow{\kappa_1} 2A_1 \qquad A_1 + A_2 \xrightarrow{\kappa_2} 2A_2 \qquad A_i \underset{\lambda_i}{\overset{\delta_i}{\rightleftharpoons}} \emptyset \tag{4.40}$$

and analyzed the distribution

$$\pi(a_1, a_1|n) = \frac{1}{u(\alpha, \kappa, n)} \binom{n}{a_1, a_2} \kappa_1^{a_1} \kappa_2^{a_2} \frac{\Gamma(\alpha_1 + \alpha_2)}{\Gamma(\alpha_1 + \alpha_2 + n)} \frac{\Gamma(a_1 + \alpha_1)}{\Gamma(\alpha_1)} \frac{\Gamma(a_2 + \alpha_2)}{\Gamma(\alpha_2)} \tag{4.41}$$

Under classical volume scaling of the rate parameters we showed that $\pi(a|n)$ exhibits DITs in the low volume regime, and when the volume is large the distribution was unimodal and centred around the equilibrium point of the deterministic system of ODEs:

$$\begin{aligned} \dot{a_1}(t) &= (\kappa_1 - \kappa_2) a_1 a_2 + \lambda_1 - \delta a_1 \\ \dot{a_2}(t) &= (\kappa_2 - \kappa_1) a_1 a_2 + \lambda_2 - \delta a_2 \end{aligned} \tag{4.42}$$

We also used the Gillespie algorithm to simulate the process and compared the simulations to our distribution $\Pi(a) = \nu(n)\pi(a|n)$. The histograms of our simulations resembled our distribution; particularly, both the simulation results and the candidate distribution show that when κ_1 is held at 1 and κ_2 is increased, most of the mass of the distribution is moved towards the states where the population of the system is entirely in A_1 and A_2 is extinct. When $\kappa_2 = 1.1$ almost all the mass of the distribution is in the states where A_2 holds the entire population.

To determine if the distribution $\Pi(a)$ is indeed stationary, we analyzed the global balance condition $\Pi Q = 0$. Unfortunately, for our distribution the global balance condition was not satisfied, although it was shown to be very close to zero. The global balance equates, at equilibrium, the probability flux leaving each state i and the probability flux entering each state i. The probability flux in this case means the expected number of transitions per unit time. Since our distribution does not satisfy global balance, it means there is extra probability flux not accounted for by our distribution, which would not be there if it were the unique stationary distribution. Since it seems like the distribution is more "out of balance" near the boundaries when $n \approx 2V$, the mean of $\nu(n)$, (i.e.

when $a \approx (0, 2V), (2V, 0), (1, 2V)$, and $(2V, 1)$). It is not clear why the balance equation is farthest from zero at these points, it could be due to computational error since these are the points at which the distribution has its largest values and is very small elsewhere. Why this was not an issue when $\kappa_1 = \kappa_2$ is mysterious, especially since this distribution reduces to the exact stationary distribution when κ's are equal. What exactly this means as to how "close" our candidate distribution is to the true stationary distribution quantitatively is not clear however; qualitatively, from the simulations it does appear to be very similar to the true distribution.

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A Appendix

A.1 Theorems and Lemmas

The following is theorem 1.2 in [2]

Theorem A.1. *If Y is a Poisson process, then for each $u_0 > 0$,*

$$\lim_{n\to\infty} \sup_{u\le u_0} \left| \frac{Y(nu)}{n} - u \right| = 0 \quad a.s. \tag{A.1}$$

proof. Let $\varepsilon > 0$ and let $\{u_i\}$ be a discretization of $[0, u_0]$ so that

$$|u_{i+1} - u_i| \le \varepsilon/2$$

Let N be large enough such that for $n \ge N$ we have

$$\left| \frac{Y(nu_i)}{n} - u_i \right| \le \varepsilon/2 \tag{A.2}$$

for each i. Let $u \in [0, u_0]$ and j be such that $u_j \le u \le u_{j+1}$. For $n \ge N$ we have

$$\frac{Y(nu)}{n} - u \le \frac{Y(nu_{j+1})}{n} - u_{j+1} + (u_{j+1} - u) \le \varepsilon/2 + \varepsilon/2 = \varepsilon$$

and

$$\frac{Y(nu)}{n} - u \ge \frac{Y(nu_j)}{n} - u_j + (u_j - u) \ge -\varepsilon/2 - \varepsilon/2 = -\varepsilon$$

so

$$\sup_{u\le u_0} \left| \frac{Y(nu)}{n} - u \right| \le \varepsilon$$

□

the following is Gronwall's inequality, the proof is taken from [3].

Lemma A.1.1. *Suppose that A is non-negative, cadlag, and non-decreasing. Furthe supposed X is cadlag, and*

$$0 \le X(t) \le \varepsilon + \int_0^t X(s-)dA(s)$$

then

$$X(t) \le \varepsilon e^{A(t)}$$

proof.

$$\begin{aligned} X(t) &\le \varepsilon + \int_0^t X(s-)dA(s) \\ &\le \varepsilon + \varepsilon A(t) + \int_0^t \int_0^{s-} X(u-)dA(u)dA(s) \\ &\le \varepsilon + \varepsilon A(t) + \varepsilon \int_0^t A(s-)dA(s) + \int_0^t \int_0^{s-} \int_0^{u-} X(r-)dA(r)dA(u)dA(s) \end{aligned}$$

Since A is finite variation, making $[A]_t^c \equiv 0$. Ito's formula yields

$$\begin{aligned}
e^{A(t)} &= 1 + \int_0^t e^{A(s-)} dA(s) + \sum_{s \le t} (e^{A(s) - e^{A(s-)} - e^{A(s-)}} \Delta A(s) \\
&\ge 1 + \int_0^t e^{A(s-)} dA(s) \\
&\ge 1 + A(t) + \int_0^t \int_0^{s-} e^{A(u-)} dA(u) dA(s) \\
&\ge 1 + A(t) + \int_0^t A(s-) dA(s) + \int_0^t \int_0^{s-} \int_0^{u-} e^{A(r-)} dA(r) dA(u) dA(s)
\end{aligned}$$

continuing the iteration we get $X(t) \le \varepsilon e^{A(t)}$
□

A.2 Foster-Lyapunov Criterion for Bibbona-Kim-Wiuf model

Let $X(t)$ be the associated Markov Chain for a general network described by (3.3). Let $V(x) = e^{\|x\|_1}$, where $\|x\|_1 = \sum_{i=1}^d |x_i|$. We will show that theorem 2.27 holds for some C and D.

$$\begin{aligned}
QV(x) =& \sum_{i,j} \kappa_{ij} x_i x_j (V(x - e_i + e_j) - V(x)) \\
&+ \sum_{i=1}^d \delta_i x_i (V(x - e_i) - V(x)) + \sum_{i=1}^d \lambda_i (V(x + e_i) - V(x)) \\
=& \sum_{i=1}^d \delta_i x_i (V(x - e_i) - V(x)) + \sum_{i=1}^d \lambda_i (V(x + e_i) - V(x)
\end{aligned}$$

let $K_n = \{x \in \mathbb{N}^d : x_i \ge n, \quad \forall i\}$. For $x \in K_n$

$$\begin{aligned}
QV(x) =& V(x) \left(\sum_{i=1}^d \delta_i x_i (e^{-1} - 1) + \sum_{i=1}^d \lambda_i (e_i - 1) \right) \\
&\le \left((\min_i \delta_i)(e^{-1} - 1) dn + \sum_{i=1}^d \lambda_i (e - 1) \right) V(x)
\end{aligned}$$

we choose N such that

$$C = -\left((\min_i \delta_i)(e^{-1} - 1) dN + \sum_{i=1}^d \lambda_i (e - 1) \right) > 0$$

then theorem 2.27 holds with $D = 2C \max_{x \in K_N} V(x)$, which implies $X(t)$ is non-explosive, positive recurrent and exponentially ergodic, moreover it implies the existence of a unique stationary distribution π.

A.3 Gillespie Algorithm

Mathematica code was modified, from a Mathematica stack exchange post by Istvan Zachar [17], to work with our chemical reaction network. The code used is shown in figure 11.

```
GillespieSSA[res : {__Rule}, in_Association,
  rateconst_?VectorQ, influx_Association: <||>,
  {mint_?NumberQ, maxt_?NumberQ, dstep_Integer: 1}] := Module[
  {vars, reactant, product, balance, propensities, initialValues,
   fluxRates, symRates, rep, stepList, iterations = 10^7, step,
   compiled, times, rest},
(* Pre-generating a list is much faster than iteratively calling one-by-one. *)
  stepList = N@RandomVariate[ExponentialDistribution@1, iterations + 1];
   {vars, initialValues} = {Keys@in, Values@in};
  {reactant, product} =
   Outer[Coefficient[#1, #2] &, #, vars, 1] & /@
    Transpose@(List @@@ res);
  balance = product - reactant;
  propensities =
   Inner[Binomial[#2, #1] &, reactant, vars, Times]*
    PadRight[rateconst, Length@res, 1];
  fluxRates = If[influx === <||>, 0 & /@ vars, vars /. influx];
   Block[{count},
   rep = Thread[vars → Table[Indexed[count, i], {i, Length@vars}]];
   symRates = propensities /. rep;
   compiled = ReleaseHold[
     Hold@Compile[{
         {init, _Integer, 1}, {flux, _Integer, 1}, {bal, _Integer, 2},
         {dtList, _Real, 1}, {min, _Real}, {max, _Real},
         {iter, _Integer}, {resol, _Integer}},
        Module[{
          count = init, rates, i = 1, c = 1, t = min, dt, ff, f, range,
          r, fReal = 0. & /@ flux, rateSum, data = Internal`Bag[]},
         rates = "SymbolicRates";
         rateSum = N@Total@rates;
         range = Range@Length@rates;
         Internal`StuffBag[data, Internal`Bag[Join[{t}, N@count]]];
             While[Total@count > 0. && rateSum > 0. && t ≤ max && i ≤ iter,
          i++;
          dt = dtList[[i]]/rateSum;
          t = t + dt;
          r = RandomChoice[rates → range];
          (* Fractional part is carried over to minimize undersampling error *)
          ff = (flux*dt) + fReal;
          f = IntegerPart@ff;
          fReal = ff - f;
          (* `count` is maintained as an integer not to loose precision. *)
          count = Max[0, #] & /@ (count + bal[[r]] + f);
          If[Mod[i, resol] == 0, c++;
           Internal`StuffBag[data, Internal`Bag[Join[{t}, N@count]]];];
         rates = "SymbolicRates";
         rateSum = N@Total@rates;
         ];
        If[t < max && i < iter, c++;
         Internal`StuffBag[data, Internal`Bag[Join[{max}, N@count]]]];
        Table[Internal`BagPart[Internal`BagPart[data, j], All], {j, c}]
        ],
       Parallelization → True , RuntimeAttributes → Listable,
       RuntimeOptions → "Speed",
       CompilationOptions → {"InlineExternalDefinitions" → True,
         "InlineCompiledFunctions" → True}
       ] /. "SymbolicRates" → symRates];
        {times, rest} = {First@#, Rest@#} &@Transpose@compiled[
      Round@initialValues, N@fluxRates, Round@balance,
      N@stepList, N@mint, N@maxt, Round@iterations, dstep];
   Interpolation[Transpose@{Join[times,{times[[Length[times]]+10^-4}],Join[{#[[1]]},#]},InterpolationOrder→0] & /@ rest
   ]];
```

Figure 11: Mathematica code for Gillespie Algorithm