# Morphogenesis

**Abstract**

The purpose of this essay is to explain Morphogenesis, the biological process where patterns arise during growth, and also in mature adults when the body replaces old/damaged cell. I shall investigate the reaction and diffusion of chemicals under an initially uniform state, as suggested by Alan Turing in 1952, and hopefully gain an insight into how these chemicals alongside chemical processes such as diffusion encourage/diminish the process of Morphogenesis. In doing so, I shall discuss the non-linear evolution equations and their stability analysis for chemicals that react and diffuse in solution. When analysing the behaviour of these chemicals we shall need to do so under a variety of parameter values and in doing so this should help us comprehend how morphogenesis can be analysed in real life and how we may be able to best control the process. Through doing so I hope to draw conclusions on factors related to these chemicals that we can alter to potentially alter the rate of tumor growth.

## 1 Introduction

Morphogenesis is the biological process where patterns arise during growth, and a fundamental aspect of developmental biology (the study of the process by which animals and plants grow and develop). Cell divisions dictate multicellular morphogenesis, both cell division and morphogenesis occur when organisms grow and after reaching maturity morphogenesis occurs when cells divide to replace old/damaged cells. Healthy cells divide in a controlled manner, only when required of them, cancerous cells on the other hand divide uncontrollably pushing aside healthy cells and forming cancers/tumor. To be clear, morphogenesis takes place in mature organisms, in cell cultures and inside tumor cell masses. Morphogenesis is often described as the process by which many individual cells in a developing embryo diffuse in order to organise themselves in order to form the complex sturcutres (e.g. organs and systems) that make up a developed adult organism - but it is important to note that morphogenesis is not limited to embryology, thus as mentioned earlier it occurs in mature adults. Morphogenesis is stimulated by both chemical and mechanical factors, throughout this essay I aim to investigate the realtionship between characteristics of these chemicals (e.g. concentrations and diffusion rates) and the nature of the chemicals behaviour. From this I aim to gain an insight into how altering parameters affecting said chemicals (for instance promoting their presence or inhibiting them) in order to to see how the behaviour and characteristics (e.g. concentrations) of these chemicals are affected and how this affects the organism in which they are present. In particular I believe that by altering characteristics of the chemicals in models we will introduce, we can assess how changes such as this are likely to affect morphogenesis with respect to the development of cancerous/tumor tissue. Whilst our models will not necessarily mimick an in vivo environment, I believe the information gained from this and the trends we may identify may help to decide whether a morphogenesis model could accelerate cancer research and potentially save lives.

## 2 Cancers

### 2.1 The formation of Cancers

Cell division is an aspect of morphogenesis, and as mentioned in the introduction it occurs frequently in a controlled manner throughout the body, at least it is in a controlled manner when the cell dividing is healthy cell. It is the genes of the cell that are responsible for instructing the cell to divide, and the genes of cancer cells are often mutated. These mutations can often cause the cell to divide uncontrollably, causing cancerous/tumor tissue to grow rapidly. In order to have sufficient energy to continue growing the cancer requires a blood supply, the cancer

disperses chemical signals that draw blood vessels to it to fuel the cancers growth. These vessels allow cancer cells to diffuse and effectively spread to other parts of the body. Whilst some early cancers stop growing and never spread (referred to as benign tumors) many cancers are able invade their surrounding tissue in order to spread throughout the body (malignent cancers). The chemical signals dispersed by the cancerous cells are essential in the cell obtaining energy for growth, if we were able to ensure these chemical signals were not dispersed effectively we could potentially stop the growth of the cancer providing the cancer was identified early enough. We will later look into conditions which could potenitally reduce the impact of the chemical signal vastly, for instance we may see conditions which cause concentrations of particular chemicals to be lower. At some point we may need to assess whether it is feasible to replicate this conditions in an in vivo environment. Cancers often start off inside an organ in the body, its because of this

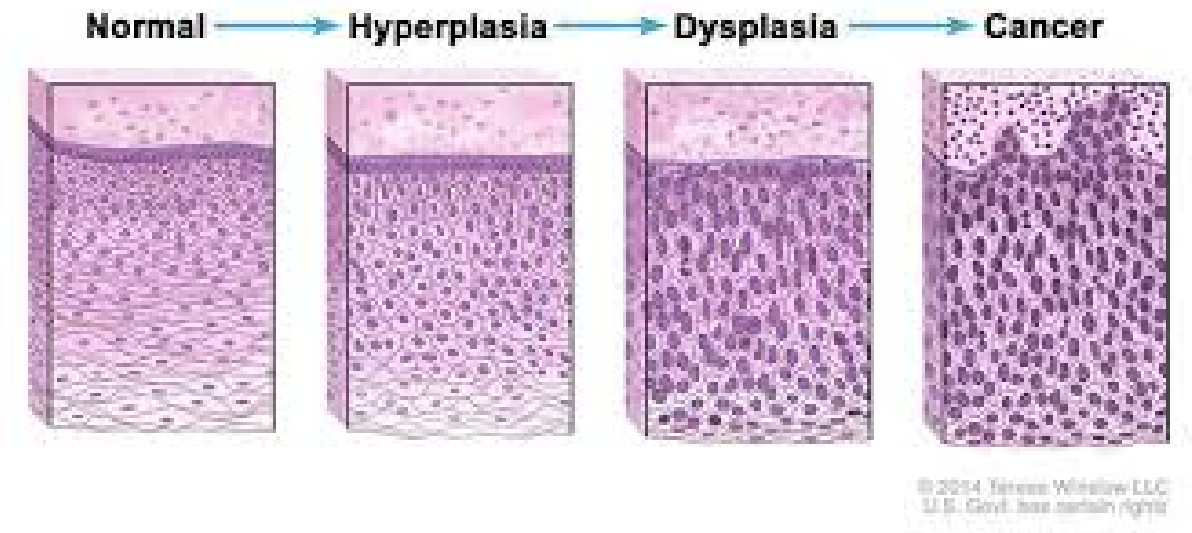


Figure 1: Patterns in cancer formation.

### 2.2 How does Cancer Spread?

reason that they often go unnoticed, at least before an individual begins to deplay symptoms. After developing the most dangerous thing a cancer can do is metastasis (the process by which a pathogenic agent spreads from an initiial or primary site to secondary sites within the host's body). As described (vaguely) earlier cancer cells are able to creep through the walls of blood vessels fusing them and from here they're in the blood stream and can diffuse around the body, spreading to other parts. Once the cancer has spread it is much harder to cure, so in over the course of the next sections we will gain an understanding of the processes occuring when morphogenesis occurs in order to consider this in the case when morphogenesis occurs producing cancerous cells. In the following research I aim to find if we can limit the production and spread of this cancer through analysing the nature of chemicals under different parameter values.

## 3 Diffusion

In this section we will discuss the diffusion of chemicals and cell matter, this is a process which takes place in and around tumor tissue, and as we will explain in the following subsection it aids in the facilitation of tumor invasion. Diffusion is simply the process by which small particles move randomly in their environment, diffusion occurs in a multitude of processes in the body and certainly occurs when cancerous cells are devloping - particularly when the cells disperse chemicals looking for an energy (blood) supply. We can model the process of diffusion

by the following equation:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2}$$

where $u$ in this case is the density of the material considered and $D$ is a parameter called the difffusion constant - the larger $D$ is the faster the rate of diffusion. Diffusion simply put is precisely what we do not want for pattern formation. However, the process reaction diffusion is where 2 or more different chemicals diffuse freely, but also interact with each other to affect their mutual concentrations.

### 3.1 Reaction-Diffusion Model of Tumor Invasion

On the microscopic scale population many interactions occur at the tumor-host interface, these processes strongly influence the clinically significant manifestations of invasive cancer. Despite their genetic instabilities we are able to encapsulate many of the common properties amongst tumors, and model these (although we shall not be modelling tumors within the essay). One consistent cellular dynamic is evolution of tumor populations away from the differentiated state of the tissue of origin, toward one that is more primitive and less ordered - this is a result of diffusion of cell matter, and can be described as morphogenesis. When a tumour cell is present, acid production is produced and the diffusion of that acid into surrounding healthy tissue creates a peritumoral microenvironment in which tumor cells survive and proliferate, whereas normal cells are unable to remain viable. This causes the following temporal sequence to ensue: high $H^+$ ion concentrations in tumors will extend, by chemical diffusion, as a gradient into adjacent normal tissue, exposing these normal cells to a tumor-like interstitial $pH$; normal cells immediately adjacent ot the tumor edge are then unable to survive in this chronically acidic environment; and the progressive loss of layers of normal cells at the tumor-host interface facilitates tumor invasion. The tumor-induced alteration of microenvironmental $pH$ described may provide a simple but complete mechanism for cancer invasion. Thus we shall investigate whether we are able to deter this alteration of $pH$ and maintain a $pH$ that does not facilitate tumor invasion. We will consider the high $H^+$ ion concentrations as one of $u$ and $v$ (as $u$ and $v$ represent concentrations of chemicals).
Continuing from our introduction, throughout this essay we shall consider the respective concentrations $u$ and $v$ of two chemicals and their behaviours with respect to parameters that we shall discuss later. Through understanding how the alteration of the values of said parameters correspond to the concentrations $(u, v)$ of the chemicals and how we can use this information to potentially alter the 'acidic environment' and analyse if altering the concentration appropriately could potentially inhibit 'tumour invasion'. We at least hope to justify whether or not this is a field worthy of channelling further research and investment in, in the hope that it could improve cancer treatment.

### 3.2 Reaction Diffusion Equation

In the system we are interested in (for the above this could be an organisms body), molecules diffuse but also react chemically with each other in such a way that their concentration can vary. We will not consider a system of 2 chemicals with concentration $u$ and $v$ (as mentioend above) and with respective diffusion constants $D_u$ and $D_v$, we can have obeying the following general equation:

$$\begin{aligned}\frac{\partial u}{\partial t} &= f_1(u, v) + D_u\frac{\partial^2 u}{\partial x^2} \\ \frac{\partial v}{\partial t} &= f_2(u, v) + D_v\frac{\partial^2 v}{\partial x^2}\end{aligned} \tag{1}$$

where $f_1$ and $f_2$ are functions of the concentrations and aid in describing the interaction between the 2 chemicals. The system (1) describes the evolution of the two concentration fields $u(t,x)$ and $v(t,x)$ on the real line $-\infty < x < \infty$. The nonlinear functions $f_1$ and $f_2$ may be described as the reaction rates of the two chemicals while the $D_u$ and $D_v$ are the diffusion coefficients as earlier mentioned. The simplest possible model is obtained by assuming that there is no prior spatiotemporal structure(structure belonging to space and time), so that the functions and diffusion coefficients do not depend explicitly on time $t$ or on position $x$. Later, we will consider how this affects the legitimacy/accuracy of trends displayed by our model when related to chemicals surrounding tumor tissue. For further simplicity, we will assume that the diffusion coefficients are constants and so do not dpeend on the field values of $u(t,x)$ and $v(t,x)$ - these assumptions are considered reasonable for many experimental situations.
Since the system (1) does not incorporate any method of introducign more reactions into the system or removign products it is limited to describing a sustained equilbrium chemical system. Neglecting nonequilibrimum chemical systems is a major simplification of the system, as in order to introduce new reactants we must introduce complicated spatial structure.

One such model for the earlier mentioned functions $f_1$ and $f_2$ is the Brusselator model for which

$$\begin{aligned} f_1(u,v) &= a - (b+1)u + u^2 v \\ f_2(u,v) &= bu - u^2 v, \end{aligned} \tag{2}$$

where $a \geq 0$, $b \geq 0$.
The Brusselator (the system formed by (1) and (2)) does not describe any real system as such, but it is a simple example of a model which exhibits pattern formation. Real models can be much more complex but the Brusselator captures the important features of these models. The homogeneous stationary solutions of (2) are solutions which are independent of $x$ and $t$, thus $\frac{\partial u}{\partial t} = \frac{\partial v}{\partial t} = 0$ for the homogeneous solutions, let the homogeneous solutions be given by $u_0$ and $v_0$. Clearly as the solution are independent of both $x$ and $t$ we have $\frac{\partial^2 u}{\partial x^2} = \frac{\partial^2 v}{\partial x^2} = 0$ thus the solution requires that $f_1(u_0, v_0) = f_2(u_0, v_0) = 0$, and from this we can compute the special solutions to the Brusselator equation above. Q1
From 2 the above equation translates to the following:

$$v_0 u_0^2 - (b+1)u_0 + a = 0 \tag{3}$$

$$bu_0 - u_0^2 v_0 = 0 \tag{4}$$

From (3), we can use the quadratic formula to arrive at $u_0 = \frac{b+1 \pm \sqrt{(-(b+1))^2 - 4av_0}}{2v_0}$.
From (4), we can conclude that $v_0 = \frac{b}{u_0}$ and $u_0 = \frac{b}{v_0}$ provided that ($u_0 \neq 0$ and $v_0 \neq 0$).

Thus, from equating our two above equations the following is implied:

$$\begin{aligned}
&\implies \frac{b+1 \pm \sqrt{(-(b+1))^2 - 4av_0}}{2v_0} = \frac{b}{v_0} \\
&\implies b+1 \pm \sqrt{(-(b+1))^2 - 4av_0} = 2b \\
&\implies \pm\sqrt{(-(b+1))^2 - 4av_0} = b-1 \\
&\implies b^2 + 2b + 1 - 4av_0 = b^2 - 2b + 1 \\
&\implies 4b = 4av_0 \\
&\implies v_0 = \frac{b}{a} \text{ and } u_0 = \frac{b}{v_0} = \frac{b}{\frac{b}{a}} = a
\end{aligned}$$

provided $a \neq 0$ and $b \neq 0$.
We can confirm this by using our values for $u_0 = a$ and $v_0 = \frac{b}{a}$ in our original equations.
In (3) we have the following:

$$\begin{aligned}
v_0 u_0^2 - (b+1)u_0 + a &= 0 \\
\implies \frac{b}{a}a^2 - (b+1)a + a &= ab - ab - a + a \\
&= 0
\end{aligned}$$

In (4) we have the following:

$$\begin{aligned}
bu_0 - u_0^2 v_0 &= 0 \\
\implies ba - a^2\frac{b}{a} &= ab - ab \\
&= 0
\end{aligned}$$

This confirms the values $u_0 = a$ and $v_0 = \frac{b}{a}$ in fact satisfy the equations, thus they are the homogeneous solutions (or at least expressions for them).

## 4 Stability Analysis

Now that we have a simple solution for the above system we can now determine whether they are stable or not. Turing found that there are conditions under which the spatially uniform state is table in the absence of diffusion but can be come unstable to nonuniform perturbations precisely because of diffusion. Further, for many conditions the instability first occurs at a finite wave length and so a cellular pattern starts to appear. For simplicity, we will initially discuss this with respect the simple system we have formulated. As Turing did we question if we are to peturb the static solution by a small amount what does the solution do? Will it remain close tot he static solution, possibly returning back to the static solution after some time or does it move away from it, never returning? In order to study the stability problem for the system formed by (1) and (2) we can perform a linear stability analysis by assuming solutions of the form **Q2**

$$u = u_0 + \delta u(x,t) = a + \delta u(x,t) \tag{5}$$
$$v = v_0 + \delta v(x,t) = \frac{b}{a} + \delta v(x,t). \tag{6}$$

We can make use of (5) and (6) where $u_0 = a$ and $v_0 = \frac{b}{a}$ for our static solution, in the system formed by (1) and (2). For clarity and to remind ourselves, our Brusselator model is expressed by:

$$\frac{\partial u}{\partial t} = a - (b+1)u + u^2 v + D_u \frac{\partial^2 u}{\partial x^2} \tag{7}$$

$$\frac{\partial v}{\partial t} = bu - u^2 v + D_v \frac{\partial^2 v}{\partial x^2} \tag{8}$$

Using (5) and (6) in the (7) we have the following:

$$\frac{\partial}{\partial t}\left(a + \delta u(x,t)\right) = a - (b+1)\left(a + \delta u(x,t)\right) + \left(a + \delta u(x,t)\right)^2 \left(\frac{b}{a} + \delta v(x,t)\right) + D_u \frac{\partial^2}{\partial x^2}\left(a + \delta u(x,t)\right)$$

In the following derivation we will denote $u(x,t)$ as $u$ and $v(x,t)$ as $v$.

$$\begin{aligned}
\implies \frac{\partial \delta u}{\partial t} &= a - (a + ab + b\delta u + \delta u) + \\
&\quad \left((\delta u)^2 + 2a\delta u + a^2\right)\left(\frac{b}{a} + \delta v\right) + D_u \frac{\partial^2 \delta u}{\partial x^2} \\
&= -ab - b\delta u - \delta u + \frac{b}{a}(\delta u)^2 + 2b\delta u + ab + (\delta u)^2 \delta v + 2a\delta u \delta v + a^2 \delta v \\
&\quad + D_u \frac{\partial^2 \delta u}{\partial x^2} \\
&= -ab - b\delta u - \delta u + 2b\delta u + ab + 2a\delta u + a^2 \delta v + D_u \frac{\partial^2 \delta u}{\partial x^2} \\
&= (b-1)\delta u + a^2 \delta v + D_u \frac{\partial^2 \delta u}{\partial x^2}
\end{aligned}$$

Similarly using (5) and (6) in (8) we have the following:

$$\frac{\partial}{\partial t}\left(\frac{b}{a} + \delta v(x,t)\right) = b(a + \delta u(x,t)) - \left(a + \delta u(x,t)\right)^2 \left(\frac{b}{a} + \delta v(x,t)\right) + D_v \frac{\partial^2}{\partial x^2}\left(\frac{b}{a} + \delta v(x,t)\right)$$

We will again denote $u(x,t)$ as $u$ and $v(x,t)$ as $v$ to be concise.

$$\begin{aligned}
\implies \frac{\partial \delta v}{\partial t} &= ab + b\delta u - \left((\delta u)^2 + 2a\delta u + a^2\right)\left(\frac{b}{a} + \delta v\right) + D_v \frac{\partial^2 \delta v}{\partial x^2} \\
&= ab + b\delta u - \left(\frac{b}{a}(\delta u)^2 + 2b\delta u + ab + (\delta u)^2 \delta v + 2a\delta u \delta v + a^2 \delta v\right) + D_v \frac{\partial^2 \delta v}{\partial x^2} \\
&= ab + b\delta u - \frac{b}{a}(\delta u)^2 - 2b\delta u - ab - (\delta u)^2 \delta v - 2a\delta u \delta v - a^2 \delta v + D_v \frac{\partial^2 \delta v}{\partial x^2} \\
&= -b\delta u - a^2 \delta v + D_v \frac{\partial^2 \delta v}{\partial x^2}
\end{aligned}$$

Note in the above we disregard any term of the form $\delta u^p \delta v^q$ with $p + q > 1$, this is due to the fact we are only considering small perturbation and term $\delta u^p \delta v^q$ with $p + q > 1$ are negligible - this also simplifies the equations significantly. This gives us the following two equations:

$$\frac{\partial \delta u}{\partial t} = (b-1)\delta u + a^2 \delta v + D_u \frac{\partial^2 \delta u}{\partial x^2}$$

$$\frac{\partial \delta v}{\partial t} = -b\delta u - a^2 \delta v + D_v \frac{\partial^2 \delta v}{\partial x^2}$$

which we may write as

$$\frac{\partial \mathbf{u}}{\partial t} = \mathbf{A}\delta\mathbf{u} + \mathbf{D}\frac{\partial^2 \delta\mathbf{u}}{\partial \mathbf{x^2}} \tag{9}$$

where $\delta\mathbf{u} = \begin{pmatrix}\delta u \\ \delta v\end{pmatrix}$, $\mathbf{A} = \begin{pmatrix} b-1 & a^2 \\ -b & -a^2\end{pmatrix}$ and $\mathbf{D} = \begin{pmatrix} D_u & 0 \\ 0 & D_v\end{pmatrix}$.

Here we have derived a matrix representation for the Brusselator model (at least for the homogeneous case we have simplified it to), and we can use this to further aid our stability analysis. To continue with our task of studying the stability of the homogeneous solutions to our brusselator mode, we must compute the solutions for 9. Again as we are considering the homogeneous case in which the solutions are independent of $x$ and $t$ we may reduce the problem to the following differential equation (whilst remaining in matrix form):

$$\frac{\partial \delta\mathbf{u}}{\partial t} = \mathbf{A}\delta\mathbf{u}. \tag{10}$$

As we see that the partial derivative of this equation is equal to a 'multiple' of itself we may wish to consider exponential solutions, in fact we solve this equation by considering solutions of the form

$$\delta\mathbf{u} = \mathbf{w}exp(\sigma t) \tag{11}$$

where $\mathbf{w}$ is a constant vector of arbitrary amplitude and $\sigma \in \mathbb{C}$ a constant that we must determine. As $\mathbf{w}$ defines a specific direction, its length is arbitrary as (9) is linear, and we can impose $|\mathbf{w}| = \mathbf{1}$. Thus substuting (11) into (9) provides us with the following condition

$$\mathbf{A}\mathbf{w} = \sigma\mathbf{w} \tag{12}$$

clearly this displays that $\sigma$ is an eigenvalue of the matrix $\mathbf{A}$. Thus for a solution to exist we have the following.

**Q3**

$$\begin{aligned}
& det(\mathbf{A} - \mathbb{1}\sigma) = 0 \\
\Leftrightarrow \quad & det\left(\begin{pmatrix} A_{11} & A_{12} \\ A_{21} & A_{22}\end{pmatrix} - \begin{pmatrix} 1 & 0 \\ 0 & 1\end{pmatrix}\sigma\right) = 0 \\
\Leftrightarrow \quad & det\left(\begin{pmatrix} A_{11} & A_{12} \\ A_{21} & A_{22}\end{pmatrix} - \begin{pmatrix} \sigma & 0 \\ 0 & \sigma\end{pmatrix}\right) = 0 \\
\Leftrightarrow \quad & det\begin{pmatrix} A_{11}-\sigma & A_{12} \\ A_{21} & A_{22}-\sigma\end{pmatrix} = 0 \\
\Leftrightarrow \quad & (A_{11}-\sigma)(A_{22}-\sigma) - A_{21}A_{12} = 0 \\
\Leftrightarrow \quad & \sigma^2 - (A_{11}+A_{22})\sigma + A_{11}A_{22} - A_{21}A_{12} = 0 \\
\Leftrightarrow \quad & \sigma^2 - tr\mathbf{A}\sigma + det\mathbf{A} = 0 \\
\Leftrightarrow \sigma^{\pm} = & \frac{1}{2}\left(tr\mathbf{A} \pm \sqrt{(tr\mathbf{A})^2 - 4det\mathbf{A}}\right)
\end{aligned} \tag{13}$$

We can then show the general linear solutions of (10) are then given by

$$\delta\mathbf{u} = C^+\mathbf{w}^+exp(\sigma^+ t) + C^-\mathbf{w}^-exp(\sigma^- t)$$

where $C^+$ and $C^-$ are complex coefficients which must be chosen so that $\delta\mathbf{u}$ is real and $\mathbf{w}^+$, $\mathbf{w}^-$ are the solutions (12) corresponding to $\sigma^+$ and $\sigma^-$. Clearly now we have an exponential equation for $\delta\mathbf{u}$ nd we can analyse case by case how the values of $\sigma^+$ and $\sigma^-$ affect the stability of $\delta\mathbf{u}$.

- If $\sigma^+$ and $\sigma^-$ are both real and negative, then clearly $\delta\mathbf{u}$ decreases exponentially with $t$ to 0 and the static solution $u_0$, $v_0$ is then obviously stable as the perturbed solution converges towards it.
- If either $\sigma^+$ or $\sigma^-$ are positve, then clearly at least one component of $\delta\mathbf{u}$ blows up thus $\delta\mathbf{u}$ blows up as a whole h $t$ to 0 and the static solution is unstable as any small perturbation leads to a solution that moves away from it exponentially (at least in the linear limit we have taken).
- If $\sigma^+$ and $\sigma^-$ are complex then in order for $\delta\mathbf{u}$ to be realy they must be complex conguates of each other. The imaginary part will introduce trigonometric functions which correspond to rotations in the $u - v$ plane. The stability is again determined by the real parts of $\sigma^+$ and $\sigma^-$ - we can simply use the above 2 points on the real parts of $\sigma^+$ and $\sigma^-$.
- If the real parts of $\sigma^+$ and $\sigma^-$ are equal to 0 then we will be unable to determine the stability from the above criteria, thus in that case we will analyse the data graphically in an attempt to formulate an opinion on its stability.

Are there other conditions that we can use in order to find the stability of the homogeneous static solutions? If so, how can we formulate these conditions?

**Q4**

Let us interpret the condition for stability, thus far we have considered two cases in which the homogeneous static solutions are stable - the first of which, if $\sigma^+$ and $\sigma^-$ are both real and negative then the solution is stable. We can roughly translate this to the following, let us consider the case $\sigma^+$ and $\sigma^-$ are complex (if one of them is complex then both of them will be as they will both have $(tr\mathbf{A})^2 - 4det\mathbf{A} < 0$. In this case the real part of $\sigma^+$ and $\sigma^-$ is equal to $tr\mathbf{A}$, and for stability we have that the real part must be negative thus we have arrived at the condition $tr\mathbf{A} < 0$.
We will now attempt to use this knowlege to formulate a condition for $det\mathbf{A}$. We will begin by translating the condition $\sigma^+ < 0$ and $\sigma^- < 0$, note that in this case we need only consider the circumstance when $\sigma^+$ and $\sigma^-$ are real as in the case they are complex their stability is dependent entirely on their real part $tr\mathbf{A}$ and independent of $det\mathbf{A}$.

$$
\begin{aligned}
& \tfrac{1}{2}\left(tr\mathbf{A} + \sqrt{(tr\mathbf{A})^2 - 4det\mathbf{A}}\right) < 0 \\
\Leftrightarrow \quad & \left(tr\mathbf{A} + \sqrt{(tr\mathbf{A})^2 - 4det\mathbf{A}}\right) < 0 \\
\Leftrightarrow \quad & \left(\sqrt{(tr\mathbf{A})^2 - 4det\mathbf{A}}\right) < -tr\mathbf{A} \\
\Rightarrow \quad & (tr\mathbf{A})^2 - 4det\mathbf{A} < (tr\mathbf{A})^2 \\
\Rightarrow \quad & -4det\mathbf{A} < 0 \\
\Leftrightarrow \quad & det\mathbf{A} > 0
\end{aligned}
\qquad
\begin{aligned}
& \tfrac{1}{2}\left(tr\mathbf{A} - \sqrt{(tr\mathbf{A})^2 - 4det\mathbf{A}}\right) < 0 \\
\Leftrightarrow \quad & \left(tr\mathbf{A} - \sqrt{(tr\mathbf{A})^2 - 4det\mathbf{A}}\right) < 0 \\
\Leftrightarrow \quad & tr\mathbf{A} < \left(\sqrt{(tr\mathbf{A})^2 - 4det\mathbf{A}}\right) \\
\Rightarrow \quad & (tr\mathbf{A})^2 > \left((tr\mathbf{A})^2 - 4det\mathbf{A}\right) \\
\Rightarrow \quad & -4det\mathbf{A} < 0 \\
\Leftrightarrow \quad & det\mathbf{A} > 0
\end{aligned}
$$

Clearly we see that in either case we have $det\mathbf{A} > 0$, note that at points where we multiply through by $tr\mathbf{A}$ we 'reverse' the inequality as we are aware that $tr\mathbf{A} < 0$.
Thus by considering the stability conditions in all cases for $\sigma^+$ and $\sigma^-$ we are able to formulate the following conditions for stability:

$$
\begin{aligned}
tr\mathbf{A} &< 0 \\
det\mathbf{A} &> 0.
\end{aligned}
$$

These conditions are certainly useful for the matrix equation we have formulated and they offer us a clear method to analyse the stability of the Brusselator when given in the form 9, however in this scenario (only 2 chemical concentrations) both $tr\mathbf{A}$ and $det\mathbf{A}$ are very simple to work out for the 2 x 2 matrix - and this may offer another method of analysing the stability when given similar information (without working with the matrix directly).

For the Brusselator model we had the matrix $\mathbf{A} = \begin{pmatrix} b-1 & a^2 \\ -b & -a^2 \end{pmatrix}$.
Clearly,

$$\begin{aligned} det\mathbf{A} &= (b-1)(-a^2) - a^2(-b) = -a^2b + a^2 + a^2b = a^2 \\ tr\mathbf{A} &= b - 1 + a^2 \end{aligned}$$

using these expressions for $det\mathbf{A}$ and $tr\mathbf{A}$ we can translate the above conditions/constraints (inequalities) for $det\mathbf{A}$ and $tr\mathbf{A}$ to conditions for $a$ and $b$, giving us the following conditions:

$$det\mathbf{A} > 0 \Longrightarrow a^2 > 0$$

$$\begin{aligned} tr\mathbf{A} < 0 &\Rightarrow b - 1 + a^2 < 0 \\ &\Longrightarrow b < 1 + a^2 \end{aligned}$$

**Q5**

I now feel that we have covered the stability conditions sufficiently in theory, let us now consider some practical examples where they are applied, in the following we will first let $a = 2$, then we shall consider a multitude of cases where $\sigma^+$ and $\sigma^-$ take different values and later we consider the stability of the solution in each case.

1. Taking $a = 2$, we have the following

$$\begin{aligned} tr\mathbf{A} = &\quad b - 1 - a^2 = b - 1 - 4 = b - 5 \\ det\mathbf{A} = &\quad a^2 = 4 \\ \sigma^{\pm} = &\frac{1}{2}\left(b - 5 \pm \sqrt{(b-5)^2 - 16}\right) \end{aligned} \tag{14}$$

   (a) The smallest value of $b$ for which $\sigma^+ = \sigma^- < 0$.
   We translate the above to the following:
   $\frac{1}{2}\left(b - 5 + \sqrt{(b-5)^2 - 16}\right) = \frac{1}{2}\left(b - 5 - \sqrt{(b-5)^2 - 16}\right) < 0.$
   From the fact $\frac{1}{2}\left(b - 5 + \sqrt{(b-5)^2 - 16}\right) = \frac{1}{2}\left(b - 5 - \sqrt{(b-5)^2 - 16}\right)$ we know the following:

$$\begin{aligned} &\sqrt{(b-5)^2 - 16} = -\sqrt{(b-5)^2 - 16} = 0 \\ \Leftrightarrow &\sqrt{(b-1)(b-9)} = -\sqrt{(b-1)(b-9)} = 0 \end{aligned}$$

   Thus we have either $b = 9$ or $b = 1$, however it is also a condition that $\sigma^{\pm} < 0$ thus $b = 1$ is the only value for which the conditions are satisfied, as $b - 5 = 4 > 0$ for

$b = 9$.
In order to be certain this is the case we calculate the values of $\sigma^{\pm}$ for $b = 1$:

$$\sigma^{+} = b - 5 + \sqrt{(b-5)^2 - 16} = 1 - 5 + \sqrt{(1-5)^2 - 16} = -4 + \sqrt{0} = -4$$
$$\sigma^{-} = b - 5 - \sqrt{(b-5)^2 - 16} = 1 - 5 - \sqrt{(1-5)^2 - 16} = -4 - \sqrt{0} = -4$$

We can clearly see $\sigma^{+} = \sigma^{-} < 0$.

(b) Let us find a value of $b$ for which $\sigma^{+} \neq \sigma^{-}$ are both real and negative.
For $\sigma^{+} \neq \sigma^{-}$ real we must have that:

$$\begin{aligned} & (b-5)^2 - 16 > 0 \\ \Leftrightarrow \quad & b^2 - 10b + 9 > 0 \\ \Leftrightarrow \quad & (b-9)(b-1) > 0 \end{aligned}$$

Clearly therefore for $\sigma^{\pm} = Re(\sigma^{\pm})$ we must have $b > 9$ or $b < 1$ - see the graph (Figure 2) presented below if necessary.

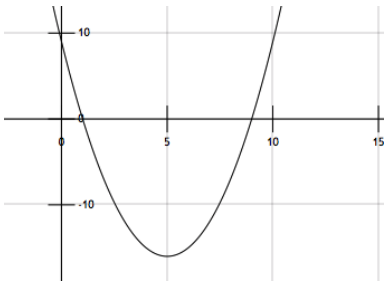


Figure 2: The behaviour of $b^2 - 10b + 9$ presented in a graph over a range of values.

We now wish to seek when $\sigma^{\pm} < 0$, from analysing the previous bullet point we can deduce that $\sigma^{\pm} > 0$ for $b > 9$ and $\sigma^{\pm} < 0$ for$b < 1$. As $\sigma^{\pm} = 0$ never holds and it is complex in the range $1 \geq b \leq 9$, if $\sigma^{\pm}$ is positve at $b = 9$ it will continue to be for $b > 9$ as $b - 5$ 'grows' at a faster rate than $\sqrt{(b-1)^2 - 16}$. Similarly, as $b - 5$ also 'falls' at a faster rate than $\sqrt{(b-1)^2 - 16}$ if it is negative at $b = 1$ it will continue to be for $b < 1$. Thus we have $b < 1$ satisfies the criteria for this value of $\sigma^{\pm}$ and we can deduce the following:
Thus let us consider the first valid integer $b = 0$.
$\sigma^{\pm} = \frac{1}{2}\left(0 - 5 \pm \sqrt{(0-5)^2 - 16}\right) = \frac{1}{2}\left(-5 \pm \sqrt{(9)}\right)$
$\Rightarrow \sigma^{+} = \frac{1}{2}\left(-5 + \sqrt{(9)}\right) = -2$ and $\sigma^{+} = \frac{1}{2}\left(-5 - \sqrt{(9)}\right) = -8$
Clearly we have in both cases that $\sigma^{+} \neq \sigma^{-}$, $Re(\sigma\pm) = \sigma\pm$ (i.e. they are both real) and $\sigma\pm < 0$ (i.e. they are both negative).

(c) A value of $b$ for which $\sigma^{+} \neq \sigma^{-}$ are complex and with a negative real value.
We have in this case that $(b-1)(b-9) < 0$ which is satisfied by $1 < b < 9$ - throughout this range it is ensured that $\sigma^{\pm}$ are complex that is that $Im(\sigma^{\pm}) \neq 0$. It must also be the case that the real part of $\sigma^{\pm}$ is negative, $Re(\sigma^{\pm}) < 0$.
Which translates to $b - 5 < 0 \Longrightarrow b < 5$, so we can now condense our range of values to $1 < b < 5$.

Selecting $b = 2$:

$$\begin{aligned}\sigma^{\pm} = \frac{1}{2}\left(b - 5 \pm \sqrt{(b-5)^2 - 16}\right) &= \frac{1}{2}\left(2 - 5 \pm \sqrt{(2-5)^2 - 16}\right) \\ &= \frac{1}{2}\left(-3 \pm \sqrt{(-3)^2 - 16}\right) \\ &= \frac{-3 \pm \sqrt{-7}}{2} \\ &= \frac{-3 \pm i\sqrt{7}}{2},\end{aligned}$$

clearly the above again both satisfy the conditions we sort as we have a negative real part for both as $Re(\sigma^{\pm}) = -\frac{3}{2} < 0$, and they are both complex as $Im(\sigma^{\pm}) = \pm\frac{\sqrt{7}}{2} \neq 0$.

(d) The value of $b$ for which $\sigma^+ = -\sigma^-$ are both complex. Again we will start by translating the above condition:

$$\begin{aligned}& \sigma^+ = -\sigma^- \\ \Leftrightarrow\ & \tfrac{1}{2}\left(b - 5 + \sqrt{(b-5)^2 - 16}\right) = -\left(\tfrac{1}{2}\left(b - 5 - \sqrt{(b-5)^2 - 16}\right)\right) \\ \Rightarrow\ & b - 5 + \sqrt{(b-5)^2 - 16} = 5 - b + \sqrt{(b-5)^2 - 16} \\ \Rightarrow\ & b - 5 = 5 - b \\ \Rightarrow\ & 2b = 10 \\ \Rightarrow\ & b = 5\end{aligned}$$

Thus again it is clear that the above is satisfied for $b = 5$, we can clarify this by substituting $b = 5$ into our expressions for $\sigma^{\pm}$:

$$\begin{aligned}\sigma^+ = \frac{1}{2}\left(b - 5 + \sqrt{(b-5)^2 - 16}\right) &= \frac{1}{2}\left(0 + \sqrt{(0)^2 - 16}\right) \\ &= \frac{1}{2}\left(\sqrt{-16}\right) \\ &= \frac{1}{2}\left(i4\right) \\ &= i2 \\ -\sigma^- = -\frac{1}{2}\left(b - 5 - \sqrt{(b-5)^2 - 16}\right) &= -\frac{1}{2}\left(0 - \sqrt{(0)^2 - 16}\right) \\ &= \frac{1}{2}\left(\sqrt{-16}\right) \\ &= \frac{1}{2}\left(i4\right) \\ &= i2\end{aligned}$$

Clearly $\sigma^+ = i2 = \sigma^- \Longrightarrow \sigma^- = \sigma^+$ , thus we have confirmed that the value of $b$ for which $\sigma^- = \sigma^+$ is satisfied is $b = 5$.

(e) The value of $b$ for which $\sigma^+ \neq \sigma^-$ are both complex with a positive real value. In order for $\sigma^{\pm}$ to be complex we must have that $(b-5)^2 - 16 < 0$ as this is the expression

we take the square root of.

$$\begin{aligned}(b-5)^2-16&<0\\ \Leftrightarrow (b-5)^2&<16\\ \Leftrightarrow -4<b-5&<4\\ \Leftrightarrow 1<b&<9\end{aligned}$$

We also have that the real part of $\sigma^{\pm}$ is positive this is $Re(\sigma^{\pm}) = b-5>0$

$$\begin{aligned}b-5&>0\\ b&>5\end{aligned}$$

We can then condense our first inequality to $5<b<9$. In both cases we will have $\sigma^+ \neq \sigma^-$ are complex with positive real value - we can show this for $b=6$.

$$\begin{aligned}\sigma^+ = \frac{1}{2}\left(b-5+\sqrt{(b-5)^2-16}\right) &= \frac{1}{2}\left(1+\sqrt{(1)^2-16}\right)\\ &= \frac{1}{2}\left(1+\sqrt{-15}\right)\\ &= \frac{1+i\sqrt{15}}{2}\\ \sigma^- = \frac{1}{2}\left(b-5-\sqrt{(b-5)^2-16}\right) &= \frac{1}{2}\left(1-\sqrt{(1)^2-16}\right)\\ &= \frac{1}{2}\left(1-\sqrt{-15}\right)\\ &= \frac{1-i\sqrt{15}}{2}\end{aligned}$$

2. Below we can see the above results tabulated (with respect to their varying parameter values):

| $a$ | $b$ | $u_0$ | $v_0$ | $trA$ | $\sqrt{trA^2-4detA}$ | $\sigma^+$ | $\sigma^-$ |
|---|---|---|---|---|---|---|---|
| 2 | 0 | 2 | 0 | $-5$ | 3 | $-2$ | $-8$ |
| 2 | 1 | 2 | $\frac{1}{2}$ | $-4$ | 0 | $-4$ | $-4$ |
| 2 | 2 | 2 | 1 | $-3$ | $i\sqrt{7}$ | $\frac{-3+i\sqrt{7}}{2}$ | $\frac{-3-i\sqrt{7}}{2}$ |
| 2 | 5 | 2 | $\frac{5}{2}$ | 0 | $i2$ | $i2$ | $-i2$ |
| 2 | 6 | 2 | 3 | 1 | $i\sqrt{15}$ | $\frac{1+i\sqrt{15}}{2}$ | $\frac{1-i\sqrt{15}}{2}$ |

3. The following is all with regards to the above table with reference to the graphs we have produced. We shall consider the stability of each of the solutions $u$ and $v$ in each of the cases that we have formulated.

   In the $1^{st}$ case where we have that $a=2$ and $b=0$, we see that $\sigma^+ = -2$ and $\sigma^- = -8$, we again see the case discussed ealier, where both $\sigma^+$ and $\sigma^-$ are real and negative. In this case we have that $\delta\mathbf{u}$ decreases exponentially to 0 and the static solution $u_0$, $v_0$ is stable - as the perturbed solution converges to it. Thus this is stable. If we refer to (Figure 3)

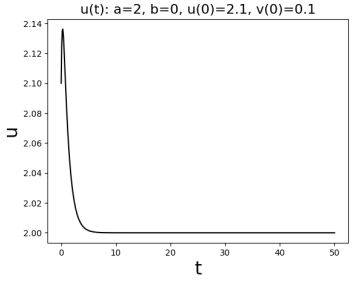


Figure 3: $u(t)$ plotted with initial value $u(0) = 2.1$ and parameter values $a = 2$ and $b = 0$, and $dt = 10^{-4}$.

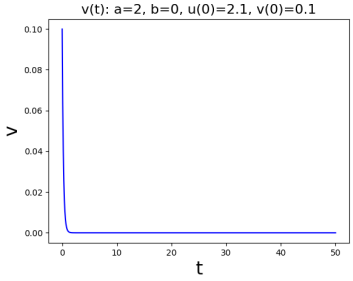


Figure 4: $v(t)$ plotted with initial value $v(0) = 1.1$ and parameter values $a = 2$ and $b = 0$, and $dt = 10^{-4}$.

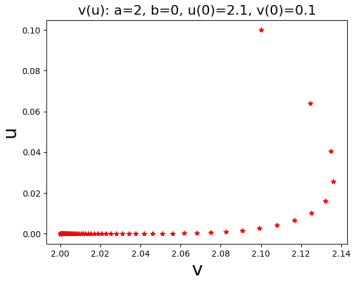


Figure 5: $v(u)$ plotted with initial values $v(0) = 1.1$ and $u(0) = 2.1$, and parameter values $a = 2$ and $b = 0$, and $dt = 10^{-4}$.

and (Figure 6) we can clearly see this behaviour exhibited, the curves in both figures quite obviously converge and this helps to clarify that the nature of the numerical data plotted is indeed stable. We also see that (Figure 5) is different to a lot of the other figures for example (Figure 14) this is again due to the fact that the $u$ and $v$ are both convergent, and this convergence is clear in the plot in (Figure 5). We see that the graph of (Figure 5) converges to a fixed point (around $(v, u) = (2, 0)$) - this is because both $u$ and $v$ converge, this same logic can be applied to the other $v - u$ graphs that converge to a fixed point.

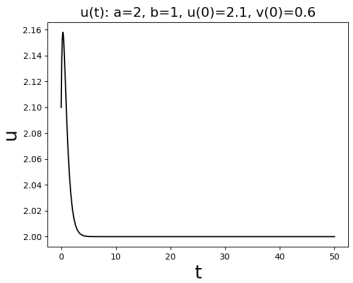


Figure 6: $u(t)$ plotted with initial value $u(0) = 2.1$ and parameter values $a = 2$ and $b = 1$, and $dt = 10^{-4}$.

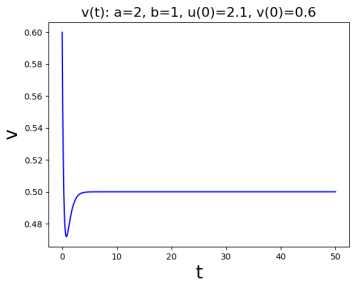


Figure 7: $v(t)$ plotted with initial value $v(0) = 1.1$ and parameter values $a = 2$ and $b = 1$, and $dt = 10^{-4}$.

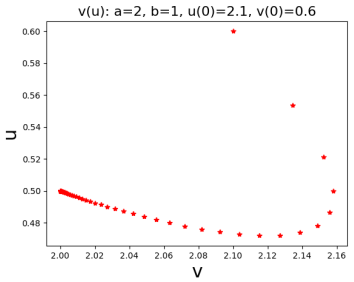


Figure 8: $v(u)$ plotted with initial values $v(0) = 1.1$ and $u(0) = 2.1$, and parameter values $a = 2$ and $b = 1$, and $dt = 10^{-4}$.

In the $2^{nd}$ case where we have that $a = 2$ and $b = 1$, we see that $\sigma^+ = -4$ and $\sigma^- = -4$, and with the exact same reasoning as above we can conclude that this is stable - it can be interpreted in exactly the same way as the figures (Figure 6), (Figure 7) and (Figure 8) were earlier. We an also see that (Figure 6) and (Figure 7) both converge as we expected from our numerical analysis. It is then of no surprise that (Figure 8) converges to a fixed point as both of the graphs it models converge to fixed values. We see that as $v$ becomes smaller $u$ converges to a fixed point at around (around $(v, u) = (2, 0.5)$).

In the $3^{rd}$ case where we have that $a = 2$ and $b = 2$, we see that $\sigma^+ = \frac{-3+i\sqrt{7}}{2}$ and $\sigma^- = \frac{-3-i\sqrt{7}}{2}$. Here the stability of the solution is more difficult to interpret as both solutions are complex. Here as the imaginary values of $\sigma^+$ and $\sigma^-$ are complex conjugate of one another and correspond to rotations in the $u - v$ plane (despite this not being exhibited here). The stability is again determined by the real parts of $\sigma^+$ and $\sigma^-$, in this

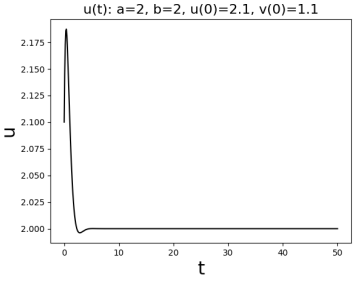


Figure 9: $u(t)$ plotted with initial value $u(0) = 2.1$ and parameter values $a = 2$ and $b = 2$, and $dt = 10^{-4}$.

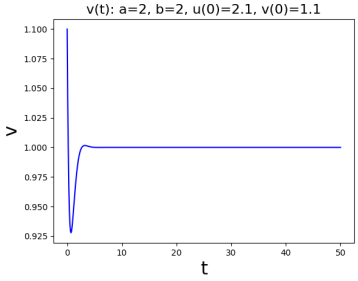


Figure 10: $v(t)$ plotted with initial value $v(0) = 1.1$ and parameter values $a = 2$ and $b = 2$, and $dt = 10^{-4}$.

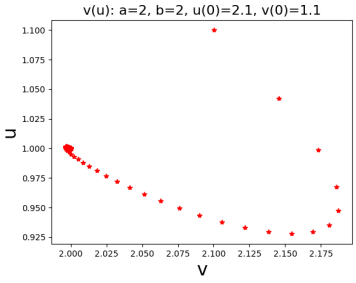


Figure 11: $v(u)$ plotted with initial values $v(0) = 1.1$ and $u(0) = 2.1$, and parameter values $a = 2$ and $b = 2$, and $dt = 10^{-4}$.

case they are both negative $-\frac{3}{2}$ and thus we are assured by the same reasoning as in the first case but with respect to the real part of $\sigma^+$ and $\sigma^-$ rather than $\sigma^{\pm}$ as a whole that the solutions are stable. If we refer to (Figure 9), (Figure 10) and (Figure 11) we can clearly see that the graphical representation supports the numerical analysis as the gaphs (Figure 9) and (Figure 10)converge thus the solutions are stable. We also see that similarly to the first case (Figure 11), regardless of the fact that in the $3^{rd}$ case $\sigma^+$ and $\sigma^-$ are complex, as they are still both stable and both converge to single values. thus the plot present in (Figure 11) converges to a single point $((v, u) = (2, 1))$.

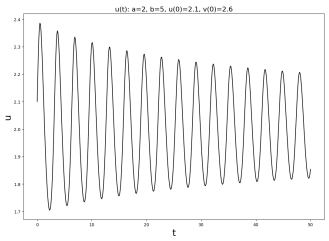


Figure 12: $u(t)$ plotted with initial value $u(0) = 2.1$ and parameter values $a = 2$ and $b = 5$, and $dt = 10^{-4}$.

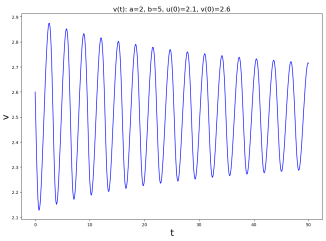


Figure 13: $v(t)$ plotted with initial value $v(0) = 1.1$ and parameter values $a = 2$ and $b = 5$, and $dt = 10^{-4}$.

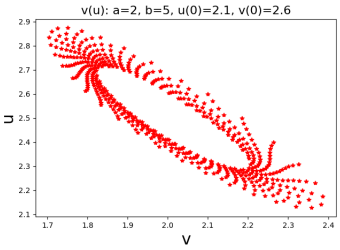


Figure 14: $v(u)$ plotted with initial values $v(0) = 1.1$ and $u(0) = 2.1$, and parameter values $a = 2$ and $b = 5$, and $dt = 10^{-4}$.

In the $4^{th}$ case where we have that $a = 2$ and $b = 5$, we see that $\sigma^+ = i2$ and $\sigma^- = i2$. Here the stability of the solution is more difficult to interpret as both solutions are complex, we also don't have a real part of the solution to refer to and we thus we cannot draw any conclusion on the stability of the two eigenvalues using numerical data alone. In this case we refer to (Figure 12), (Figure 13) and (Figure 14), here we see that the graph diverges and is clearly unstable and displays bizarre oscillatory behaviour for (Figure 12) and (Figure 13). I say this as I have reference to the numerical eigenvalues, and I can make an educated judgement that (Figure 12) and (Figure 13) are unstable. However, it does appear tat the peaks of the graphs in both (Figure 12) and (Figure 13) suggesting their may be some convergence, one method of confirming it does not converger would be to plot graphs over a huge range of $t$. However, this is somewhat inefficient instead we refer to (Figure 14) and see that this graph convergese to a patterm, and not a singular point - this is because both (Figure 12) and (Figure 13) are undulatory - and are characterised

by wave-like patterns.

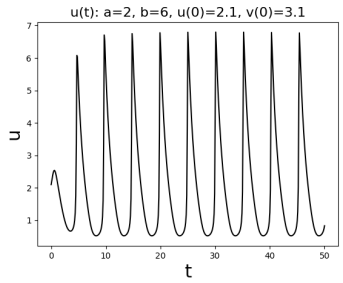


Figure 15: $u(t)$ plotted with initial value $u(0) = 2.1$ and parameter values $a = 2$ and $b = 6$, and $dt = 10^{-4}$.

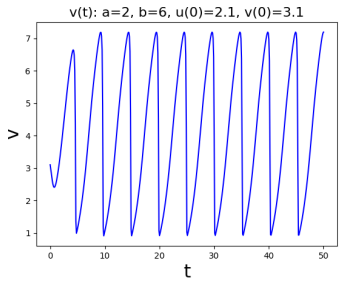


Figure 16: $v(t)$ plotted with initial value $v(0) = 1.1$ and parameter values $a = 2$ and $b = 6$, and $dt = 10^{-4}$.

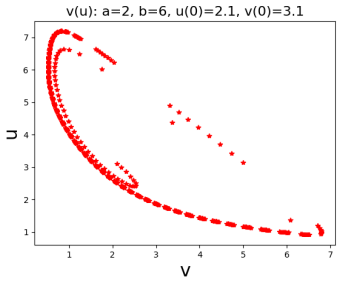


Figure 17: $v(u)$ plotted with initial values $v(0) = 1.1$ and $u(0) = 2.1$, and parameter values $a = 2$ and $b = 6$, and $dt = 10^{-4}$.

In the $5^{th}$ case where we have that $a = 2$ and $b = 6$, we see that $\sigma^+ = \frac{1+i\sqrt{15}}{2}$ and $\sigma^- = \frac{1-i\sqrt{15}}{2}$. This case is somewhat similar to that in case 3, however here we have the real part of the eigenvalues to refer to in order to draw our conclusions on the stability of $u$ and $v$. In both cases the real part of the eigenvalue is $\frac{1}{2}$ - clearly a positive value. We can therefore conclude numerically that $\delta\mathbf{u}$ blows up and the static solution is unstable as any small perturbation leads to a solution that moves away from it exponentially (at least in the linear limit we have taken). Again we see oscillary behaviour in (Figure 15) and (Figure 16) and the fuinction diverges supporting our numerical analysis. However, in (Figure 17) we clearly see the figure displays some of the roational characteristics we have come to expect when $u$ and $v$ are not convergent. The graph (Figure 17) converges to a fixed pattern again this is due to the fact (Figure 15) and (Figure 16) are both undulatory. The figure displays the nature of a funciton that is clearly unstable however it differs a great deal to that of (Figure 14) - this is due to the fact that instability of (Figure 15) and (Figure 16) is more clear and the distance between peaks in the graphs does not get smaller as it did in. (Figure 12) and (Figure 13).

In general our numerical analysis seems to have been somewhat confirmed by the analysis of the figures we have produced. However, we must consider that we stated that our predicted behaviours are only valid for small $\partial\mathbf{u}$ and $\partial\mathbf{v}$ this could maybe explain why we get strange oscillatory behaviour in the figures when we expect a more clear divergence. Also I believe that we could look into the case when $Re(\sigma^{\pm}) = 0$ a great deal more as the behaviour of the graphs we produced in this case were by no means transparent. In general if we analyse the information above we see that the prediction of the stability analysis is generally confirmed by the numerical solution. I also altered the value of $\epsilon$ vastly throughout the production of these graphs and whilst the information presented was sometimes displaying clearer changes it did not affect the stability on the graph, there were no apparent changes in the graphs. The lack of clartiy at points may again be due to the fact that our analysis is only value for small $\partial\mathbf{u}$ and $\partial\mathbf{v}$ and thus the graph may exhibit some characteristics that are difficult to interpret at least from the numerical data we have available.

Alternatively, we could choose to analyse the numerical data differently through our general stability analysis (i.e. $tr\mathbf{A} < 0$ and $det\mathbf{A} > \mathbf{0}$ implies stability rather than analysing the eigenvalues $\sigma^{\pm}$) however, as we have already gained information on how the values of $\sigma^+$ and $\sigma^-$

relate to stability it is not necessary.

In the above we computed a number of eigenvalues with varying criteria for each of the values, we went on to analyse the stability of each of the solutions corresponding to these values using numerical analysis (i.e. by analysing the sign of the eigenvalues) and we confirmed this information using graphs produced for our basic model. This was rather tedious and time-consuming in order to analyse the information appropriately, thus both for more realism and efficiency in analysis it is time we progressed to a more developed model.

## 5 General Stability Analysis

A lot of the information discussed in this section is covered in more detail in the appendix of the assignment sheet, and should you require full explanations for some relationships stated then I reccommend you refer to it.
The model we currently use provides useful information, but it is limited to the static homogeneous case and whilst this gives us an idea of initial stability or stability at a point its validity is limited and its applications in a real-life scenario such as tumor growth are unlikely to be massively helpful. In order to provide a more general stability analysis of the system formed by (1) and (2) we must now consider perturbations $\delta u(x,t)$ and $\delta v(x,t)$ which now depend both on $t$ and $x$ (are non homogeneous). These take into account both the time $t$ and spatial $x$ parameters and provide a more realistic analysis that is likely to depict more accurately the behaviour of the chemicals over time. In vector form the perturbations are both time and space dependent, and are of the form

$$\delta \mathbf{u} = \mathbf{w}_q exp(\sigma_q t) exp(iqx),$$

where $\sigma_q$ and $q$ are constants which must be determined and $\mathbf{w}_q$ a constant vector as (9) is linear. Thus our previous condition (12) is replaced by

$$(\mathbf{A} - \mathbf{D}q^2)\mathbf{w}_q = \sigma_q \mathbf{w}_q \tag{15}$$

which leads to the following:

$$\begin{aligned} & det(\mathbf{A} - \mathbf{D}q^2 - \mathbb{1}\sigma_q) = 0 \\ \Leftrightarrow \quad & det\left(\begin{pmatrix} A_{11} & A_{12} \\ A_{21} & A_{22} \end{pmatrix} - \begin{pmatrix} D_u & 0 \\ 0 & D_v \end{pmatrix} q^2 - \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \sigma_q \right) = 0 \\ \Leftrightarrow \quad & det\left(\begin{pmatrix} A_{11} - D_u q^2 & A_{12} \\ A_{21} & A_{22} - D_v q^2 \end{pmatrix} - \begin{pmatrix} \sigma_q & 0 \\ 0 & \sigma_q \end{pmatrix}\right) = 0 \end{aligned}$$

If we denote $\mathbf{B} = \begin{pmatrix} A_{11} - D_u q^2 & A_{12} \\ A_{21} & A_{22} - D_v q^2 \end{pmatrix}$ then similarly to the derivation we used for (13) we arrive at:

$$\sigma_q^{\pm} = \frac{1}{2}\left(tr\mathbf{B} \pm \sqrt{(tr\mathbf{B})^2 - 4det\mathbf{B}}\right) \tag{16}$$

if more detail is required then please refer to the appendix of the assignment document, although this is intuitive from the first derivation. If we utilise the stability conditions $tr\mathbf{A} < \mathbf{0}$ and $det\mathbf{B} > \mathbf{0}$ with respect instead to our new more general matrix $\mathbf{B}$ then our conditions for

stability now become

$$tr\mathbf{B} = A_{11} + A_{22} - (D_u + D_v)q^2 < 0$$
$$det\mathbf{B} = (A_{11} - D_u q^2)(A_{22} - D_v q^2) - A_{12}A_{21} > 0$$

.

As we are aware $D_u, D_v$ and $q^2$ are all positive the condition $tr\mathbf{B} < \mathbf{0}$ translates to $A_{11}+A_{22} < 0$, however the question we know ask ourselves is for what parameter values do $det\mathbf{B} > 0$ hold, and do the conditions for stability still have any validity?
We can begin to approach this by noticing the expression for $det\mathbf{B}$ is a parabola in $q$, if we differentiate this expression we arrive at the following equation:

$$\frac{ddet\mathbf{B}}{dq^2} = 2D_u D_v q^2 - (D_u A_{22} + D_v A_{11}).$$

We can find the minimum point of the parabola by setting this equation to 0 at some $q$-value, call this $q_m$ such that $2D_u D_v q_m^2 - (D_u A_{22} + D_v A_{11}) = 0$ and thus this minimum point occurs at $q_m^2 = \frac{D_u A_{22} + D_v A_{11}}{2D_u D_v}$. Thus we can now consider when the determinant of the minimum point is less than 0 to simplify the problem for ourselves.
An expression for $det(\mathbf{B}(q_m))$ is:

$$det(\mathbf{B}(q_m)) = -\frac{1}{4D_u D_v}(D_u A_{22} + D_v A_{11})^2 + A_{11}A_{22} - A_{12}A_{21}.$$

Then the condition $det(\mathbf{B}(q_m)) < 0$ implies

$$D_u A_{22} + D_v A_{11} > 2\sqrt{D_u D_v (A_{11}A_{22} - A_{12}A_{21})}.$$

This provides us with a clear method of finding when the solution are and aren't stable.

### 5.1 Providing a Computational Model

In order to better understand the properties of the Brusselator, and better understand our new model we can provide a computer program which helps to detail its behaviour. In order to do this we must transform equation (1) into a discreted system of equations. Using the fact that for any function $u(x)$,

$$\frac{d^2u}{dx^2} \approx \frac{u(x + \Delta x) + u(x - \Delta x) - 2u(x)}{\Delta x^2}$$

we may then represent the equation set (1) by

$$\frac{du_i}{dt} = D_u \frac{u_{i+1} + u_{i-1} - 2u_i}{\Delta x^2} + f_1(u_i, v_i)$$
$$\frac{dv_i}{dt} = D_v \frac{v_{i+1} + v_{i-1} - 2v_i}{\Delta x^2} + f_2(u_i, v_i).$$

In order to integrate this we will make use of the $4^{th}$ order Runge-Kutta method to perform the time integration. The boundary conditions that we use are that $\frac{\partial u}{\partial x}$ and $\frac{\partial v}{\partial x}$ vanish on the edges of the domain.
There are many different concepts of stability, for instance:

- A chemical concentration may be considered stable if its among-environment variance is small, this is something we have discussed throughout this essay.
- A chemical contentration is considered to be stable if its response to environments is paraallel to the average responses of all chemicals within the model (this may be applied more aptly to larger more involved models).

These are just two of many ways people often consider chemical stability. I shall focus on the first bullet point, 'a chemical concentration may be considered stable if its among-environment variance is small' essentially stating that over time the concentration of the chemical does not change very much. Whilst this was considered somewhat in our initial model in order to provide a more realistic model (and not just gain some useful theoretical analysis) we must extend this model to take into account both spatial and time variables.

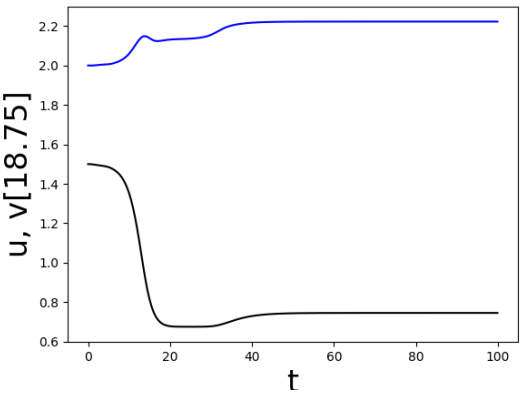


Figure 18: Concentrations $u$ and $v$ plotted over time.

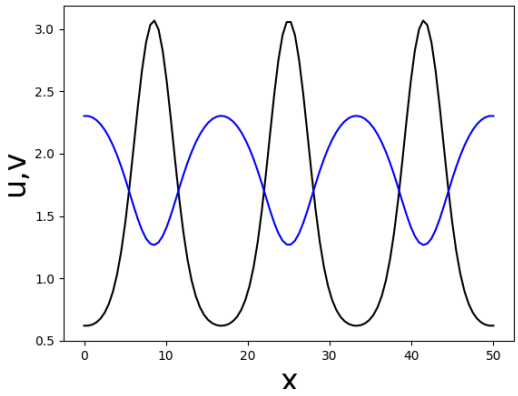


Figure 19: Concentrations $u$ and $v$ plotted against spatial parameter $x$.

Here in (Figure 18) we see a clear contrast in the nature of the graph here to that of the earlier graphs, as the presence of diffusion essentially incorporates 'random' behaviour to the chemical molecules that is present in real life, this provides a more realistic representation of the variance of the $u$ and $v$, and the affect diffusion has on their behaviour. This figure presents a stable solution however it displays some variation for a longer period earlier in the graph than that of the graphs from the earlier model when diffusion wasn't present. While (Figure 19) clearly presents oscillations of $u(x)$ and $v(x)$ results from an unstable solution, this seemingly uniform behaviour when implemented into the larger model allows for a better representation of the non-uniform formations we see present in organisms such as patterns or cell formations (including tumors). We will provide a more structured comparison for the two models.

In the images above (Figure 20) and (Figure 21), for various parameter values (stated in Q6

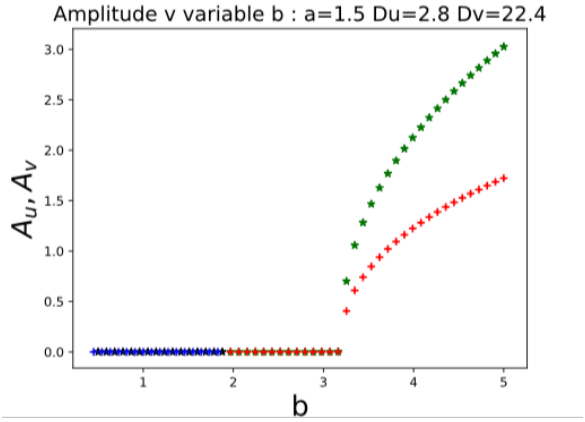


Figure 20: Amplitudes of $u$ and $v$ for the parameters stated in the title.

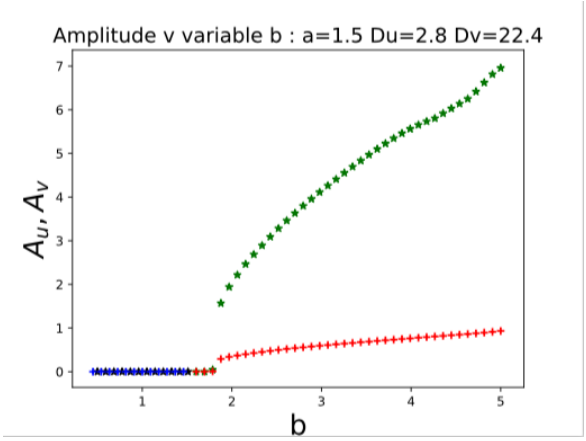


Figure 21: Amplitudes of $u$ and $v$ for the parameters stated in the title.

the title) many solutions are plotted for various 50 different values of $b$, the stability of the

solution is then presented quite clearly by colours, black and blue indicate stable, green and red indicate instable. We know that a constant solution should always be stable, thus if $A_u = 0$ and $A_v = 0$ this indicates the solution is stable, where as instable solutions are always such that $A_u \neq 0$ and $A_v \neq 0$ thus we can clearly see that the theoretical prediction is a good one, as in each case that the amplitude is non-zero we have the marker for that point in the graph is green or red indicating instability. However, the prediction is not perfect, as in some cases we see $A_u = A_v = 0$ seemingly however the markers are coloured green or red respectively, suggesting that they do not satisfy the criteria for stability. Thus whilst every case that the solution is instable, the criteria is not satisfied and it is presented correctly as instable, we also have some cases where the marker suggests instability however the the amplitude is 0. Thus the prediction is very good for identifying instable points as it identified all of them, but it is misleading as it also identified some stable points. We should note that as $D_u$ increased there were more stable markers that did not satisfy the stability criteria.

It is important to understand the contrast between the two models provided. The initial homogeneous model that depended on a single variable $t$ representing time, we explored plots of this model of the concentrations of $u$ and $v$, and gained some clear information on how stability/instability effects the nature of these chemicals when time is the only factor. We often observered quick convergences of $u$ and $v$ when plotting stable solutions, and oscillatory behaviour when they were instable, however the behaviour seemed uniform and consistent regardless. Whilst this information was useful for gaining an understanding it lacked depth, and the 'overly consistent' behaviours dispayed in the $u/v$-time graphs was not representative of behaviours of chemicals in vivo environments. A huge factor in this was clearly the lack of spatial parameters in the model, this lack of a spatial parameter meant that diffusion could not be incorporated effectively, thus diffusion was not present in the model. This clearly had a huge effect on the results as without diffusion or any element of randomness the reaactions between activators and inhibitors in the system would be exactly the same throughout the time the model was run for. This has has a huge contrast to reality, whilst hard to model within the body there are numerous factors which can effect the reaction between molecules, and diffusion is merely one of these. Whilst similar reactions take place in both models, the reactions within the model that includes the spatial parameter (and thus diffusion) incorporates a variation in these reactions which is more similar to that of an organism and certainly that of cells near tumor tissue. As the tumor tissue requires energy it secretes chemical signals more frequently and they will diffuse in order to source a blood vessel for energy. If this model was based on the growth of tumor tissue then the tissue would never develop its structure and grow, nor would it diffuse around the incurring metastasis - in this case all of the cancers modelled would be easily containable and not provide a realistic representation of some of the key difficulties in treating cancer. In an effort to improve the model, and acquire more realistic results diffusion was incorporated into the model, this was through the method of perturbing the static solutions, the spread of chemicals across the system was now no longer uniform in unstable cases, and this provided us with a better idea of how $u$ and $v$ are effected in such conditions. Its clear that incorporating diffusion provided an element of non-uniformity and this simulated 'non-uniformity' provides a more realistic representation of cell behaviour in organisms than the entirely uniform behaviour of the earlier model. This clear difference between the models highlights the affect of diffusion in cells, and by viewing the graphical images providing by both models it identifies the huge effect altering biological processes has. Through analysing (Figure 19) we are able to see a variety of information modelled, the most prominent of which being the magnitude of peaks and troughs in the figure, as well as the frequency of oscillations in the figure. However, you may be asking yourself how does the profile of each of these curves relate to morphogenesis, more specifically how do the characteristics of the graph relate to morphogenesis. The peaks of the curves $u(x)$ and $v(x)$ correspond to the peak chemical concentration and the troughs correspond to the lowest concentration of chemicals in the systems, and this can be applied to

reaction diffusion in order to predict the rate at which reaction-diffusion is occuring at these $x$ values. Thus, we can understand how varying or maintaining $x$ will effect reaction diffusion, this corresponds to effecting morphogenesis. This includes biological process such as the formation of structures within organisms like the formation of cancerous tissues, or in zebras this may affect the presence of a pigment in its hair cells, and thus effect how the pattern appears to other organisms. You may ask yourself, why we have only taken an interest in the graph (19) where the graph is clearly unstable throughout. This simply put is because we are interested in the effects the changing chemical concentrations have in terms of morphogenesis as a constant chemical concentration is unlikely to occur in morphogenesis, as this would mean a constant activator and inhibitor, and just from basic knowledge of patterns/structures we are aware that they are unlikely to be formed under constant conditions as if there is no strange it can only really be considered a basic structure at most. For example if we apply this to Zebra, then we see that there are periods when the activator is high for the sake of it clarity, we may call $u$ the activator, when $u$ is high this may cause the black pigment to be more prominent in hair cells, though as $u$ falls and the inhibitor $v$ rises this will diminish the presence of the black pigment and cause the hair cells to be white. The repeated oscillations of this effectively form a pattern of black and white stripes. Similarly we could consider this to be a pattern within genes in a red blood cell that is incorrectly formed and effectively mutated, this is likely to make them cancerous. However, in a stable solution we have that the concentrations are constant and no pattern is formed.

# 6 Conclusions

## 6.1 Observations and Potential

I believe that both the initial system (lacking diffusion) and more general system had some benefit, and the two together were a useful tool to exhibit the effect that the presence of diffusion has on concentrations of chemicals and thus the effect it has on morphogenesis. I also believe that this provides an us with an avenue to research further into engineer methods in which we can alter reaction diffusion rates effectively, and thus stimulate morphogenesis in a beneficial manner. For example, we saw in (Figure 18) that as the inhibitor rose, the stimulator fell and this will directly effect how morphogenesis occurs and the patterns it formulates, on a more intricate manner if we could manage this diffusion we could help to utilise morphogenesis to mould many important natural structure (e.g. organs).

It is clear that reaction diffusion has a huge impact on the concentrations of chemical, and that when we implemented this into our model it provided us with a significantly different characteristics in our graphs to that of the graphs when diffusion was not present. Even in stable solutions when diffusion was not present there was some initial variation before the graphs quickly converged (this comment is respect to our u-t and v-t graphs such as Figures (3) and (4)). In comparison to our graphs in the model which incorporated diffusion there were significant differences in the early stages prior to convergence, for example in (Figure 18) we see that the graph varies for a significantly longer period of time before it converges, this makes sense when considering that diffusion will affect the time it takes for $\delta\mathbf{u}$ to converge to 0. This suggests that if were able to alter the diffusion rate of chemicals within an organism this may reduce the time it takes for the formation of the stable pattern to occur. In the case that the pattern being formed was a cell to replace a damaged cell this could greatly reduce the time that it took the organism to recover.

We also saw in the model incorporating diffusion that at higher diffusion rates specifically for higher values of $D_v$, we had a much greater amplitude of $v$. This suggest the greater the diffusion rate the greater level of instability see (Figures 20 and 21) for reference. Similarly, in the same two figures we also saw that as we increased $b$ essentially increasing the values of the static solution, this also resulted in a greater amplitude of $v$ as well as a greater amplitude of $u$.

## 6.2 Improvements

I think from the observations we made it was clear that the simplified model provided a really good basis for the model developed later, it also displayed the general behaviours of the concentrations in a variety of situations as it facilitated change under numerous parameters. Unfortunately, the model still lacked many of the beahviours I would expect from a model based around real-life, and I believe whilst its a useful learning tool and a definite aid in developing a more advanced mode (as it gives helpful guidance for equations in the model), it still has limited use when analysing morphogenesis in real life.
The latter model was a significant improvement from this through the introduction of a spatial parameter and thus the introduction of the biological process reaction diffusion, the development of more realism in the results was noticable and I feel that should I pursue another model with more resources and time, I would aim to try and introduce more biological processes. I even feel that comprising a singular model that takes into account the more aspects of morphogenesis that would offer realism (for instance intracellular processes, cellular character, intercellular interraction and tissue level characteristics).
I feel that the identification of pattern formation in both models provided real food for thought, and I would be interested to investigate further how we are able to mould this pattern formation in order to put morphogenesis to good use.
I also believe that the fact that there is no way of introducign new reactants, and the fact that the Brusselator does not depend on the number of reactants is a rather large assumption to be making when modelling a biological process with the aims of understanding morphogenesis. This is because the vast majority of biological processes are dependent on reactants, and if there is no way to introduce new reactants or for that matter, utilise/remove products then the model is very simple and has comparatively limited use to what it would have. In order to address this I would specialise the model significantly, if I were to apply this to the body I would aim to iteratively introduce new blood cells and formulate products (tissues) in order to effectively 'use up' the products. However, I do see that this is more simply said than done and that the model I have utilised is produced simply in order to identify some complex trends in a simple manner without having to produce a model that is too vast.

## 6.3 Applying morphogenesis to the motive for the essay (cancer research)

Throughout my investigation and research I have gained a vast amount of knowledge on the effect of chemicals on morphogenesis, and more simply put the effect of chemicals on the formations of patterns. One formation of a pattern that we are all familiar with is the development and growth of cancerous tissues (tumors) from mutated cells. This development is hugely reliant on the dispersal of chemical signals such as those that we have discussed. We have clearly seen that the concentrations of chemicals is massively reliant on numerous factors, some of the key ones we have taken into account are stability of the concentrations and diffusion rates. We utilise chemicals in so much of cancer research already (such as in chemotherapy and medical imaging), however I believe that from developing a more complex model there is much more we could learn about the formation of tumors with respect to the chemicals involved and morphogenesis. Potentially, with much further research we could inhibit the activity of the chemicals produced by cancerous tumors and depending on the stage at which this occured it could massively affect the extent to which metastasis occured and the tumor growed.

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