TRANSITION BETWEEN MONOSTABILITY AND BISTABILITY OF A GENETIC TOGGLE SWITCH IN ESCHERICHIA COLI

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ABSTRACT. In this paper, we investigate a genetic toggle switch in Escherichia Coli, which models an artificial double-negative feedback loop with two mutually repressors. This model is a planar differential system with three parameters, one of which is an integer power \( n \geq 1 \), in the case that repressors 1 and 2 multimerize with \( n \) and 1 subunits respectively and its equilibria are decided by a polynomial of degree \( n + 1 \). Since one hardly solves such a polynomial equation, a known result on bistability was given by omitting some small terms under the assumption that the promoters are strong and the expression ratio between the ON state and the OFF state is large. In this paper, determining distribution of zeros qualitatively for the polynomial of high degree, we analytically discuss on the system without the assumption and completely give qualitative properties for all equilibria, which corrects the known result of bistability. Furthermore, we prove that there may occur in the system a codimension 2 bifurcation, called cusp bifurcation, which is a collision of two saddle-node bifurcations and manifests the transition between bistability and monostability. We exhibit the global dynamics of repressors in various cases by analyzing equilibria at infinity and proving nonexistence of closed orbits.

1. Introduction. Biological cells are extremely sophisticated systems which can execute a lot of complex behaviors, for example, response with an appropriate change dynamically as monitoring their environment. This attracts great attention to investigate those complex behaviors, one of which is genetic circuit. Explanation to its components of genetic circuit with DNA and RNA can be found from [6, 10, 14, 19, 21, 26]. Along with the advance of genomics and genetic engineering, a subject known as synthetic biology ([16, 30]) is developed to construct synthetic gene circuits which were not found in nature. One of synthetic gene circuits is toggle switch, constructed in Escherichia coli by Gardner, Cantor and Collins ([10]) in 2000. Toggle switch is composed of two repressors and two constitutive promoters, where each promoter is inhibited by the repressor transcribed by the opposing promoter, as shown in Figure 1. In this switch, it is expected to flip between two stable states (high state and low state ([10, 22])), which refers to as a double-negative feedback loop ([7, 8, 22]). It forms a synthetic and addressable cellular unit...
for storing “memory” and involves many fields such as biotechnology, biocomputing and gene therapy. In [10] the change of two repressors with respect to time in toggle switch was modeled by the system of two differential equations

\[
\begin{align*}
\frac{du}{dt} &= \frac{a}{1+u^\beta} - u, \\
\frac{dv}{dt} &= \frac{b}{1+v^\gamma} - v,
\end{align*}
\]

where \(u\) and \(v\) present the concentrations of repressor 1 and repressor 2 respectively, \(a\) and \(b\) are the effective rates of synthesis of repressor 1 and repressor 2 respectively, and \(\beta\) and \(\gamma\) are the cooperativities of repression of promoter 2 and promoter 1 respectively. In the biological sense, \(u, v, a, b, \beta\) and \(\gamma\) are all positive.

The main attention of [10] was paid to bistability ([1, 7, 12, 20, 23]) of system (1), a state having two stable equilibria, which can store memory as shown in [18, 27, 32]. Although it is difficult to solve zeros from the right hand sides of system (1), the authors of [10] plotted numerically the horizontal isocline \(H: v = b/(1+u^\gamma)\) and the vertical isocline \(V: u = a/(1+v^\beta)\) as in Figures 3 and 4 for \(\beta > 1\) and \(\gamma > 1\), showing that system (1) has either exactly one equilibrium or three equilibria. As surveyed in [31], the authors of [10] assumed to work on strong promoters (i.e., parameters \(a\) and \(b\) are both large) with large expression ratio between the ON state and the OFF state. In such a case, the coordinates of equilibrium \(A_2: (u_2, v_2)\) satisfy that \(u_2 \gg v_2\) and therefore were approximated as \(u_2 \approx a\) and \(v_2 \approx b/a^\gamma\).
and the coordinates of $A_0 : (u_0, v_0)$ were similarly approximated as $u_0 \approx a/b^\beta$ and $v_0 \approx b$, which enables them to obtain the condition 

$$a^{\beta\gamma} = \beta \gamma b^\beta \quad (\text{or } b^{\beta \gamma} = \beta \gamma a^\beta)$$

to ensure a vanished determinant $D$ of the Jacobian matrix of system (1) at $A_2$ (or $A_0$). Further, they omitted the relatively small term $\log b/\log (\beta \gamma)$ from the equality $\log a = \log b/\log (\beta \gamma)$, i.e., $\log b = \log a/\log (\beta \gamma)$, an equivalent form of the above condition, and reduced the condition approximately to the following

$$\log a = \frac{\log b}{\gamma} \quad (\text{or } \log b = \frac{\log a}{\beta})$$

Thus, (2) determines those lines in the $(\log b, \log a)$-coordinate as shown in Figure 2, which partition the first quadrant into regions for $D > 0$ or $D < 0$ and therefore give parameter conditions for bistability and monostability. In 2007, Xiu ([33]) investigated the system

$$\begin{align*}
\frac{du}{dt} &= \frac{a}{1+u^\gamma} - u,
\frac{dv}{dt} &= \frac{b}{1+u^\gamma/(1+\frac{1+\gamma}{\beta})^\gamma} - v,
\end{align*}$$

a modification of (1) mentioned in $[15, 25]$, with a tuple $p := (a, b, \beta, \gamma, \eta, K)$ of six parameters and an input $[IPTG]$. Considering $p$ to be a definite choice with a small random change, i.e., $p = (p)/(I+\delta Y)$, where $\langle p \rangle := (156.25, 15.6, 2.5, 1, 20.015, 2.9618 \times 10^{-5})$, $\delta = 0.1$, $I$ is the unit matrix and $Y$ is a $6 \times 6$ matrix composed by 6 random row vectors which distributed in the six-dimensional cube $(-1, 1)^6$ uniformly, they numerically computed for the solution curve of the normalized $v$, which is shown in error bars with respect to varying $[IPTG]$-input, and exhibited a good agreement between numerical error bars and experimental error bars.

As observed above, one hardly simulate the existence of exact two equilibria numerically, the transitional case between one equilibrium and three ones, although the continuity of the vector field makes sure of the existence of two equilibria. Actually, the transitional case as well as the corresponding values of parameters is important to the change of stability and geometric phase structures, which leads to an investigation to bifurcations of equilibria, showing how equilibria arise and how the stability of equilibria changes. Such an investigation needs a more complete discussion to parameters $a, b, \beta$ and $\gamma$ than the approximative analysis with coordinates $u_0, v_0, u_2$ and $v_2$ and condition (2). As shown above, equilibria of system (1) are determined by the equation of fractional power

$$(u - a)(u^\gamma + 1)^\beta + b^\beta u = 0.$$ 

One hardly obtains a coordinate for any one of those equilibria even if $\beta$ and $\gamma$ are restricted to be integers $m \geq 1$ and $n \geq 1$ respectively, not mentioning the computation of eigenvalues at those equilibria.

In this paper, for convenience in computation, we study equation (1) with integers $\beta = 1$ and $\gamma = n$, i.e., the system

$$\begin{align*}
\frac{du}{dt} &= \frac{a}{1+u^n} - u := P(u, v), \\
\frac{dv}{dt} &= \frac{b}{1+u^n} - v := Q(u, v),
\end{align*}$$

where $a > 0$ and $b > 0$. As shown in the beginning of next section, finding equilibria is reduced to finding real zeros of a polynomial of degree $n + 1$ with symbolic coefficients, but one hardly solve such a polynomial. Our strategy is to abandon the routine of qualitative analysis with exact coordinates and eigenvalues but use inequalities to determine signs of some quantities. In section 2, making monotonic
2. Distribution of equilibria. As a routine, equilibria of system (3) are determined by the right-hand sides of (3) being equal to zero, i.e., the system

\[ P(u, v) := \frac{a}{1+u} - u = 0, \quad Q(u, v) := \frac{b}{1+u} - v = 0. \quad (4) \]

However, it is difficult to find real roots of the equation of degree \( n + 1 \)

\[ \Phi(u) := u^{n+1} - au^n + (b+1)u - a = 0, \quad (5) \]

which is deduced by eliminating \( v \) in (4). Actually, we need to find zeros of \( \Phi \) on the interval \((0, a)\) because in the first quadrant the first equation of (4) implies

\[ 0 < u < \frac{a}{1+v} < a. \quad (6) \]

The simplest one is that \( n = 1 \), where the polynomial \( \Phi \) is quadratic, i.e., \( \Phi(u) = u^2 - (a-b-1)u - a = 0 \), and has two different real zeros \( u_{\pm} = \{a-b-1 \pm \sqrt{(a-b-1)^2 + 4a}\}/2 \). Clearly, only \( u_+ \) lies on the interval \((0, a)\). In this case system (3) has exactly one equilibrium \( A : (u_0, v_0) \) in the first quadrant, where \( u_0 = u_+ \) and \( v_0 = a/u_+ - 1 \). We claim that \( A \) is a stable node. In fact, computing the Jacobian matrix of system (3) at \( A \), we get the trace and the determinant

\[ T := \text{trace} \left( \frac{\partial (P, Q)}{\partial (u, v)} \right) \bigg|_A = -2 < 0 \]

\[ D := \det \left( \frac{\partial (P, Q)}{\partial (u, v)} \right) \bigg|_A = \frac{\Omega}{4a^2b^2} \left( (a-b-1)^2 + 4a + (a+b+1) \sqrt{(a-b-1)^2 + 4a} \right) > 0, \]

where \( \Omega = 4a^2b^2/(\{a^2 + b^2 + 2a + 2b + 1\} + (a + b + 1) \sqrt{(a-b-1)^2 + 4a}) > 0 \) for \( a > 0 \) and \( b > 0 \). Moreover,

\[ \Delta := T^2 - 4D = \frac{2}{ab} \left( (a^2 + b^2 + 2a + 2b + 1) - (a + b + 1) \sqrt{(a-b-1)^2 + 4a} \right) > 0. \]

Difficulties mainly come from the case that \( n \geq 2 \), where we hardly solve zeros from equation (5) of degree \( n + 1 \). Those difficulties make the usual routine of equilibrium analysis unavailable. We abandon pursuing the determination of signs for the determinant, trace and discriminant at accurate coordinates of equilibria,
but estimate those quantities near equilibria. For convenience, we need the following
notations:
\[
\begin{align*}
&b_0 := \frac{2}{n-1}, \quad b_* := \frac{4n}{(n-1)^2}, \quad \tilde{u}_2 := \frac{n(n-1)}{n+1}, \\
&a_0(b) := \frac{n+1}{n-1} \left( \frac{(n-1)b-2}{2} \right)^{1/n}, \quad a_\pm(b) := \frac{(n-1)b+2n\pm n}{2n} \left( \frac{(n-1)b-2\pm 2}{2} \right)^{1/n}, \\
&\zeta_\pm(a, b) := \frac{a \left( (n-1)b+2n \pm n \right)}{2n(n+1)}, \quad \mathbb{R} := \left( (n-1)^2b^2 - 4nb^2 \right)^{1/2}.
\end{align*}
\]

**Theorem 2.1.** For \( n \geq 2 \), the following assertions hold in the first quadrant:

(i) In case \( 0 < b \leq b_0 \), system (3) has a unique equilibrium \( A_* : (u_*, b/(1+u_*)^n) \),
where \( u_* \in (\tilde{u}_2, a) \).

(ii) In case \( b_0 < b \leq b_* \), system (3) has a unique equilibrium \( A_* : (u_*, b/(1+u_*)^n) \),
where either (ii-1) \( u_* \in (0, \tilde{u}_2) \) (or \( (\tilde{u}_2, a) \)), if \( 0 < a < a_0(b) \) (or \( a > a_0(b) \)),

or (ii-2) \( u_* = \tilde{u}_2 \), if \( a = a_0(b) \).

(iii) In case \( b > b_* \), system (3) has

(iii-1) a unique equilibrium \( A_* : (u_*, b/(1+u_*)^n) \), where \( u_* \in (0, \zeta_-) \) (or \( (\zeta_+), a) \), if \( 0 < a < a_- (b) \) (or \( a > a_+ (b) \));

(iii-2) exactly two equilibria \( A_1 : (u_1, b/(1+u_1^n)) \) and \( A_2 : (u_0, b/(1+u_0^n)) \),
where \( u_1 \in (\zeta_+, a) \) (or \( 0, \zeta_- \)) and \( u_0 = \zeta_- \) (or \( \zeta_+ \)), if \( a = a_+ (b) \) (or \( a_- (b) \));

(iii-3) exactly three equilibria \( A_1 : (u_1, b/(1+u_1^n)) \), \( A_2 : (u_2, b/(1+u_2^n)) \) and \( A_3 : (u_3, b/(1+u_3^n)) \),
where \( u_1 \in (0, \zeta_-), u_2 \in (\zeta_-, \zeta_+) \) and \( u_3 \in (\zeta_+, a) \),

if \( a_- (b) < a < a_+ (b) \).

**Proof.** As known at the beginning of this section, the equilibria of system (3) are
determined by positive zeros of \( \Phi \). Obviously, \( \Phi \) has at least one zero in the interval
\((0, a)\) because of the continuity of \( \Phi \) and the inequalities
\[
\Phi(0) = -a < 0, \quad \Phi(a) = ab > 0,
\]
but it is hard to find all zeros for an irreducible polynomial of degree \( n+1 \) in general.

Our strategy is to consider the first and second order derivatives
\[
\Phi(u) = (n+1)u^n - anu^{n-1} + b + 1, \quad \Phi''(u) = n(nu^{n-1} - (n+1)u + a(n-1)),
\]
both of which can hardly be factorized well further. Although \( \Phi''(u) \) remains of
higher degree, the factorization in (10) shows that \( \Phi''(u) \) has two different zeros
\( \tilde{u}_1 = 0 \) and \( \tilde{u}_2 = a(n-1)/(n+1) \) as noted in (7). Clearly, only \( \tilde{u}_2 \) lies in the
interval \((0, a)\) as required by (6). Further, we check
\[
\Phi''(\tilde{u}_2) = an^{-2} \left\{ (n+1)u - a(n-1) \right\} > 0,
\]
which implies that function \( \Phi' \) reaches a minimal value at \( u = \tilde{u}_2 \). Substituting
\( u = \tilde{u}_2 \) in (9), we obtain the minimal value
\[
\Phi''(\tilde{u}_2) = (n+1)\tilde{u}_2^n - an\tilde{u}_2^{n-1} + b + 1 = -a^n \left( \frac{n-1}{n+1} \right)^{n-1} + b + 1,
\]
which is actually the minimum of \( \Phi' \) on the interval \((0, a)\). The sign of \( \Phi''(\tilde{u}_2) \) decides the
monotonicity of \( \Phi \) on \((0, a)\). Solving \( \Phi''(\tilde{u}_2) = 0 \), we get
\[
a := a_*(b) = \frac{n+1}{n-1} \left( (n-1)(b+1)^{1/n} \right)\left( \frac{n-1}{n+1} \right)^{n-1} + b + 1.
\]
Thus, from (11) we see that $\Phi'(\tilde{u}_2) > 0$ (or $\Phi'(\tilde{u}_2) < 0$) if $0 < a < a_*(b)$ (or $a > a_*(b)$). In what follows we discuss in the two cases: the case that either $0 < a < a_*(b)$ or $a = a_*(b)$, and the case that $a > a_*(b)$.

In the case that either $0 < a < a_*(b)$ or $a = a_*(b)$, we have $\Phi'(u) \geq 0$ for all $u \in (0, a)$ and $\Phi'$ has at most one zero, as shown in Figures 5 and 6. It follows that $\Phi$ increases strictly on $(0, a)$, implying the uniqueness of zero of $\Phi$ in $(0, a)$ if it exists. Additionally, the zero of $\Phi$ exists because of (8). Let $\tilde{u}_*$ denote the zero, which determines a unique equilibrium of system (3). Although the degree $n + 1$ of the polynomial $\Phi$ prevents from solving the value of $\tilde{u}_*$, it is still possible to determine which of sub-intervals $(0, \tilde{u}_2)$ and $[\tilde{u}_2, a)$ the zero $\tilde{u}_*$ locates in. This can be done by checking the sign of $\Phi(\tilde{u}_2)$ because of (8). Note that $\Phi(\tilde{u}_2) = a \mathcal{F}(a, b)$, where

$$\mathcal{F}(a, b) := -\frac{2(n-1)^n}{(n+1)^{n+1}} a^n + \frac{(n-1)b-2}{n+1}.$$  

Clearly, $\mathcal{F}(a, b)$ either is definitely negative if $b \leq b_0 := 2/(n-1)$, a number defined in (7), or has a unique positive zero

$$a = a_0(b) := \frac{n+1}{n-1} \left(\frac{(n-1)b-2}{2}\right)^{1/n}$$

as denoted in (7) if $b > b_0$. Moreover, $\Phi(\tilde{u}_2) > 0$ (or $< 0$) if $a < a_0(b)$ (or $a > a_0(b)$). Furthermore, one can prove that $a_*(b) = a_0(b)$ (or $<, >$ or $\leq, \geq$) if and only if $b = b_*$ (or $>$, or $<$), where $b_*$ is given in (7). It implies the critical case that

$$\Phi(\tilde{u}_2) = \Phi'(\tilde{u}_2) = 0$$

if and only if $a = a_*(b)$ and $b = b_*$. For convenience, use the notation

$$a_* := a_0(b_*) = a_*(b_*)$$

Thus, we discuss in three cases: (i) $b \leq b_0$, (ii) $b_0 < b \leq b_*$, and (iii) $b > b_*$. 

In case (i), from (12) we see that $\Phi(\tilde{u}_2) < 0$. It implies that $\tilde{u}_*$ lies in the interval $(\tilde{u}_2, a)$, giving the results of the theorem in case (i) except $a > a_*(b)$.

In case (ii), we have $a_0(b) \leq a_*(b)$. The above discussion shows that either $\Phi(\tilde{u}_2) > 0$ if $a \in (0, a_0(b))$, or $\Phi(\tilde{u}_2) = 0$ if $a = a_0(b)$, or $\Phi(\tilde{u}_2) < 0$ if $a \in (a_0(b), a_*(b)]$, implying that $\tilde{u}_*$ locates in $(0, \tilde{u}_2)$, at $\tilde{u}_2$, and in $(\tilde{u}_2, a)$ if $a \in (0, a_0(b))$, $a = a_0(b)$, and $a \in (a_0(b), a_*(b)]$, respectively. In particular, when $a = a_*$ and $b = b_*$ we can obtain the value $\tilde{u}_* = \tilde{u}_2 = a_*(n-1)/(n+1) = ((n+1)/(n-1))^{1/n}$, denoted by $u_*$, and therefore give the coordinate $(u_*, v_*)$ to the corresponding equilibrium $A_*$, where $v_* := b/(u^* n + 1) = 2/(n-1)$ by the second equation of (3). Thus, the results of the theorem in case (ii) are obtained except $a > a_*(b)$. 

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Figure 5. $\Phi'(u_2) > 0$  
Figure 6. $\Phi'(u_2) = 0$  
Figure 7. $\Phi'(u_2) < 0$
In case (iii), we have \( a_0(b) > a_*(b) \). Then \( \Phi(\tilde{u}_2) > 0 \) if \( a \in (0, a_*(b)] \), implying that \( \tilde{u}_* \) lies in the sub-interval \( (0, \tilde{u}_2) \). Further, we claim that \( \tilde{u}_* \) lies in the sub-interval \( (0, \zeta_-(a, b)) \subset (0, \tilde{u}_2) \), where \( \zeta_-(a, b) \) was defined in (7). In fact, from \( \Phi(\tilde{u}_*) = 0 \), i.e., \( \tilde{u}_* + 1 - a \tilde{u}_* + (b + 1)\tilde{u}_* - a = 0 \), we get
\[
\tilde{u}_* = \frac{(b + 1)\tilde{u}_* - a}{a - \tilde{u}_*}. \tag{15}
\]
Substituting (15) in (9), we have
\[
\Phi'(\tilde{u}_*) = \frac{\Xi(\tilde{u}_*)}{(a - \tilde{u}_*)\tilde{u}_*}, \tag{16}
\]
where \( \Xi(u) := n(b + 1)u^2 + a(b - bn - 2n)u + a^2n \). Since \( b > b_* \), one can check that the discriminant \( \Delta \) of \( \Xi \) satisfies
\[
\Delta := a^2b\{(n - 1)^2b - 4n\} > 0, \tag{17}
\]
which implies that \( \Xi \) has two different real zeros
\[
\zeta_{\pm}(a, b) := \frac{a((n - 1)b + 2n \pm \Re)}{2n(b + 1)}, \tag{18}
\]
where \( \Re \) defined in (7) depends on \((b, n)\), as denoted in (7). The convexity of the quadratic function \( \Xi \) implies that \( \Xi(u) < 0 \) if and only if \( u \in (\zeta_-(a, b), \zeta_+(a, b)) \). Thus,
\[
0 < \zeta_-(a, b) < \tilde{u}_2 < \zeta_+(a, b) < a \tag{19}
\]
because \( \Xi(0) = a^2n > 0 \), \( \Xi(a) = a^2b > 0 \) and for \( b > b_* \) we have
\[
\Xi(\tilde{u}_2) = -\frac{a^2((n - 1)^2b - 4n)}{(n + 1)^2} < 0.
\]
On the other hand, from (11) we see that either \( \Phi'(u) > 0 \) on \((0, a)\) if \( a \in (0, a_*(b)) \) or \( \Phi'(u) > 0 \) on \((0, \tilde{u}_2) \cup (\tilde{u}_2, a) \) if \( a = a_*(b) \), which implies that \( \Phi'(\tilde{u}_*) > 0 \) since \( 0 < \tilde{u}_* < \tilde{u}_2 \) at the beginning of the paragraph. It follows from (16) that \( \Xi(\tilde{u}_*) > 0 \). By (19) and the signs of \( \Xi \) on those sub-intervals, we see that \( 0 < \tilde{u}_* < \zeta_-(a, b) \). Thus, the claim that \( \tilde{u}_* \in (0, \zeta_-(a, b)) \) is proved. This completes the proof for results in (iii) of the theorem except \( a > a_*(b) \).

The other case, i.e., \( a > a_*(b) \), is complicated, where \( \Phi' \) has exactly two different real zeros, denoted by \( u_{01} \) and \( u_{02} \) separately as shown in Figure 7, such that
\[
0 < u_{01} < \tilde{u}_2 < u_{02} < a \tag{20}
\]
because \( \Phi'(0) = b + 1 > 0 \) and \( \Phi'(a) = a^n + b + 1 > 0 \). This implies that \( \Phi \) reaches the maximal value at \( u_{01} \) and the minimal value at \( u_{02} \) on \((0, a)\) and \( \Phi \) is strictly increasing on \((0, u_{01}) \) and \((u_{02}, a)\) but decreasing on \((u_{01}, u_{02})\), as shown in Figures 8-12. It follows that
\[
\Phi(u_{01}) > \Phi(u_{02}). \tag{21}
\]
Thus, there are following five situations:

(S1) \( \Phi(u_{01}) < 0 \) and \( \Phi(u_{02}) < 0 \), as shown in Figure 8.
(S2) \( \Phi(u_{01}) = 0 \) and \( \Phi(u_{02}) < 0 \), as shown in Figure 9.
(S3) \( \Phi(u_{01}) > 0 \) and \( \Phi(u_{02}) < 0 \), as shown in Figure 10.
(S4) \( \Phi(u_{01}) > 0 \) and \( \Phi(u_{02}) = 0 \), as shown in Figure 11.
(S5) \( \Phi(u_{01}) > 0 \) and \( \Phi(u_{02}) > 0 \), as shown in Figure 12.
By the continuity of $\Phi$ and the monotonicity of $\Phi$ on intervals $(0,u_{01}), (u_{01}, a)$ and $(u_{02}, a)$, the signs the maximum $\Phi(u_{01})$ and the minimum $\Phi(u_{02})$ show that $\Phi$ has exactly one zero in $(S1)$ and $(S5)$, two zeros in $(S2)$ and $(S4)$, and three zeros in $(S3)$.

We only need to return those situations $(S1)-(S5)$ on signs of $\Phi(u_{0i}) \ (i = 1, 2)$ to relations of parameters $a, b$ and $n$, which gives conditions for different numbers of equilibria. For this purpose, we compute those values of $a, b$ and $n$ in the critical cases $(S2)$ and $(S4)$, i.e.,

$$\Phi(u_{0i}) = \Phi'(u_{0i}) = 0, \quad i = 1 \text{ and } 2,$$

respectively. These are the same requirement as in (13). We hardly do the same routine as in [9, 13, 28], solving $u_{0i}$ as a function of $a, b$ and $n$ from one equation of (22), because the two equations are of degrees $n + 1$ and $n$ separately. Thus we cannot substitute $u_{0i}$ as a function of $a, b$ and $n$ in the other equation to give conditions of $a, b$ and $n$ under which the system has exactly one, two or three equilibria. However, the above discussion of case (iii) suggests an effective elimination, i.e., using $u_{0i}^{-1} = (b+1)/(an-(n+1)u_{0i}) \ (obtained \ from \ the \ second \ equation \ of \ (22))$, to replace the terms of $u_{0i}^{-1}$ in the first equation of (22), which gives

$$\Phi(u_{0i}) = \frac{-\Xi(u_{0i})}{an-(n+1)u_{0i}} = 0, \quad i = 1 \text{ and } 2,$$

where $\Xi$ is the quadratic function defined just below (16).

Knowing the discriminant $\Delta$ of $\Xi$ in (17), we discuss in the three cases: $(C1)$ $\Delta < 0$, i.e., $0 < b < b_*$, $(C2)$ $\Delta = 0$, i.e., $b = b_*$, and $(C3)$ $\Delta > 0$, i.e., $b > b_*$. In case $(C1)$, $\Xi$ has no real zeros, implying that $\Xi(u) > 0$ for all $u \in (0, a)$. It follows from (23) that $\Phi(u_{0i}) < 0$ for $i = 1$ and $2$, which is exactly the situation $(S1)$. This shows that if $0 < b < b_*$ and $a > a_*(b)$ then $\Phi$ has a unique simple zero $u_*$, which satisfies by the continuity of $\Phi$ that $\tilde{u}_2 < u_* < a$, the same results as given in (i) and (ii) of the theorem. Since the case that $b \leq b_*$ and $0 < a \leq a_*(b)$ is completely discussed in the paragraphs of cases (i) and (ii) below (13), we conclude
that results (i) and (ii) of the theorem are proved except that \( b = b_* \) and \( a > a_*(b) \), which however is covered in the following case (C2).

In case (C2), \( \Xi \) has exactly one double zero \( u_0 = a(n-1)/(n+1) \) and \( \Xi(u) > 0 \) on \( (0,a) \) except \( u_0 \). It implies that \( \Xi(u_0) > 0 \), \( i = 1,2 \), since \( u_0 \) exactly coincides with \( \tilde{u}_2 \), the zero of \( \Phi' \) in the interval \( (0,a) \), and \( u_0 < \tilde{u}_2 < u_{02} \) as shown in (20). By (23) we get \( \Phi(u_0) < 0 \) for \( i = 1 \) and 2, which returns to situation (S1) again. Noting that \( a_*(b_*) = a_* \), the number defined in (14), and that \( \Phi(\tilde{u}_2) < 0 \) if \( a > a_* \) as indicated in the paragraph of (12), we conclude that if \( b = b_* \) and \( a > a_* \), then \( \Phi \) has a unique simple zero \( u_* \), which satisfies \( \tilde{u}_2 < u_* < a \). Thus, the exceptional case mentioned above for case (C1) is also proved.

Case (C3), i.e., \( b > b_* \), corresponds to result (iii) of the theorem. In this case, \( \Xi \) has two different real zeros

\[
\zeta_{\pm}(a,b) = \frac{a(b(n-1) + 2n \pm \Re)}{2n(b+1)},
\]

as given in (18). By the order shown in (19), the interval \( (0,a) \) is partitioned as

\[
(0, a) = \left(0, \zeta_-\right) \cup \{\zeta_+\} \cup \left(\tilde{u}_2, \zeta_-\right) \cup \{\tilde{u}_2\} \cup \left(\zeta_+, \zeta_+\right) \cup \{\zeta_+\} \cup (\zeta_+, a),
\]

where \( \zeta_\pm \) denote \( \zeta_{\pm}(a,b) \) respectively. By order (20), \( u_{01} \) and \( u_{02} \) lie in \( (0, \tilde{u}_2) \) and \( (\tilde{u}_2, a) \) respectively and therefore we have the following possible distributions:

| Case          | Condition                                      |
|---------------|------------------------------------------------|
| (C3-1-1)      | \( 0 < u_{01} < \zeta_- < \tilde{u}_2 < \zeta_+ < u_{02} < a \), |
| (C3-1-2)      | \( 0 < u_{01} < \zeta_- < \tilde{u}_2 < u_{02} = \zeta_+ < a \), |
| (C3-1-3)      | \( 0 < u_{01} < \zeta_- < \tilde{u}_2 < u_{02} < \zeta_+ < a \), |
| (C3-2-1)      | \( 0 < u_{01} = \zeta_- < \tilde{u}_2 < u_{02} < \zeta_+ < a \), |
| (C3-2-2)      | \( 0 < u_{01} = \zeta_- < \tilde{u}_2 < u_{02} = \zeta_+ < a \), |
| (C3-2-3)      | \( 0 < u_{01} = \zeta_- < \tilde{u}_2 < \zeta_+ < u_{02} < a \), |
| (C3-3-1)      | \( 0 < \zeta_- < u_{01} < \tilde{u}_2 < \zeta_+ < u_{02} < a \), |
| (C3-3-2)      | \( 0 < \zeta_- < u_{01} < \tilde{u}_2 < u_{02} = \zeta_+ < a \), |
| (C3-3-3)      | \( 0 < \zeta_- < u_{01} < \tilde{u}_2 < u_{02} < \zeta_+ < a \). |

| Table 1. Distribution of zeros \( u_{01} \) and \( u_{02} \) of \( \Phi' \) |

One can check that the cases (C3-1-2), (C3-1-3), (C3-2-1) and (C3-2-2) are invalid. In fact, as indicated just before (19), we see that

\[
\Xi(u) < 0 \quad \forall u \in (\zeta_-, \zeta_+), \quad 
\Xi(u) > 0 \quad \forall u \in (0, \zeta_-) \cup (\zeta_+, a), \quad 
\Xi(u) = 0 \quad \text{for} \quad u = \zeta_\pm.
\]

In case (C3-1-2), \( u_{01} \in (0, \zeta_-) \) and \( u_{02} = \zeta_+ \). It follows that \( \Xi(u_{01}) > 0 \) and \( \Xi(u_{02}) = 0 \), implying that \( \Phi(u_{01}) < 0 \) and \( \Phi(u_{02}) = 0 \), a contradiction to (21). We similarly prove the invalidity for other cases.

To the opposite, we display conditions in terms of parameters \( a, b \) and \( n \) for those valid cases (C3-1-1), (C3-2-3), (C3-3-1), (C3-3-2) and (C3-3-3).

**Lemma 2.2.** Suppose that \( b > b_* \) and \( a > a_*(b) \). Then in Table 1 the case (C3-1-1) (or (C3-3-3)) is true if and only if \( a > a_+(b) \) (or \( a_-(b) < a < a_+(b) \)), the case (C3-2-3) (or (C3-3-2)) is true if and only if \( a = a_+(b) \) (or \( a = a_-(b) \)), and the case (C3-3-1) is true if and only if \( a_-(b) < a < a_+(b) \). Here \( a_\pm(b) \) are defined in (7).
We leave the proof of the lemma to the end of this section. Since the assumption $a > a_*(b)$ was required in the “other case” of case (iii), as shown at the beginning of the paragraph of (20), and the assumption $b > b_*$ was required in (C3) of the “other case”, applying Lemma 2.2, we obtain the following conclusions:

If $a > a_+(b)$, the zeros $u_{01}$ and $u_{02}$ of $\Phi'$ distribute as in case (C3-1-1). By (24), we have $\Xi(u_{0i}) > 0, \ i = 1, 2$, implying from (23) that $\Phi(u_{0i}) < 0, \ i = 1, 2$, i.e., the situation (S1) listed below (21). It implies by the statement just below the list of (S1)-(S5) that $\Phi$ has exactly one zero, denoted by $u_*$, which lies in $(\zeta_+, a)$ by the continuity of $\Phi$. Therefore, in this case system (1) has a unique equilibrium, as stated in (iii-1) of the theorem.

If $a = a_+(b)$, the zeros $u_{01}$ and $u_{02}$ of $\Phi'$ distribute as in case (C3-2-3). By (24) we have $\Xi(u_{01}) = 0$ and $\Xi(u_{02}) > 0$, implying from (23) that $\Phi(u_{01}) = 0$ and $\Phi(u_{02}) < 0$, the situation (S2), in which $\Phi$ has exactly two zeros, denoted by $u_0$ and $u_*$, where $u_0$ locates at $\zeta_-$ and $u_*$ lies in $(\zeta_+, a)$. Therefore, in this case system (1) has exactly two equilibria, as stated in (iii-2) of the theorem.

If $a_-(b) < a < a_+(b)$, the zeros $u_{01}$ and $u_{02}$ of $\Phi'$ distribute as in case (C3-3-1). By (24) we have $\Xi(u_{01}) < 0$ and $\Xi(u_{02}) > 0$, implying that $\Phi(u_{01}) > 0$ and $\Phi(u_{02}) < 0$, the situation (S3), in which $\Phi$ has exactly three zeros, denoted by $u_1, u_2$ and $u_3$, which lie in $(0, \zeta_-), (\zeta_-, \zeta_+)$ and $(\zeta_+, a)$ respectively. Therefore, in this case system (1) has exactly three equilibria, as stated in (iii-3) of the theorem.

If $a = a_-(b)$, the zeros $u_{01}, u_{02}$ distribute as in case (C3-2-2). Similarly to case (C3-2-3), we prove that system (1) has exactly two equilibria, as stated in (iii-2) of the theorem.

If $a_*(b) < a < a_-(b)$, the zeros $u_{01}, u_{02}$ distribute as in case (C3-3-3). Similarly to case (C3-1-1), we prove that system (1) has a unique equilibrium, as stated in (iii-1) of the theorem.

As a consequence, we have completed our discussion in the ‘other’ case, i.e., $a > a_*(b)$, as mentioned in the paragraph of (20), and completed the proof of the theorem.

We end this section with the proof of Lemma 2.2.

**Proof of Lemma 2.2.** Since $b > b_*$, we first claim that

$$a_*(b) < a_-(b) < a_+(b),$$

where $a_\pm(b)$ are defined in (7). In fact, as known in (18), $\zeta_\pm(a, b)$ are the two real zeros of the quadratic function $\Xi$. By (16) and (23), we get

$$a \mathcal{H}_\pm(a, b) = \Phi(\zeta_\pm(a, b)) = 0 \quad \forall a > a_*(b), \ b > b_*,$$

where

$$\mathcal{H}_\pm(a, b) := \frac{(n+1)b+N}{2nb+2n} \left( \frac{[n-1]b+2n\pm\sqrt{n^2-b^2}}{2nb+2n} \right)^n a^n + \frac{[n-1]b+\sqrt{n^2-b^2}}{2nb+2n}.$$

One can check that $a = a_\pm(b)$ solve the equation $\mathcal{H}_\pm(a, b) = 0$, i.e.,

$$\mathcal{H}_\pm(a_\pm(b), b) = 0 \quad \forall b > b_*.$$  \hspace{1cm} (27)

On the other hand, as indicated at the beginning of case (iii) in the proof of Theorem 2.1, if $b > b_*$ and $a = a_*(b)$ then the zero $\tilde{u}_*$ of $\Phi$ lies in the interval $(0, \zeta_-)$, implying that $\Phi(\zeta_-) > 0$ and $\Phi(\zeta_+) > 0$ because $\Phi$ increases strictly on $(0, a)$ as mentioned before (12). It follows that

$$\mathcal{H}_\pm(a_*(b), b) = \frac{\Phi(\zeta_+(a_*(b), b))}{a_*(b)} > 0 \quad \forall b > b_*.$$  \hspace{1cm} (28)
Note that
\[ \frac{\partial}{\partial a} \mathcal{H}_\pm(a, b) = \pm \frac{\partial}{\partial a} \left( \frac{(n-1)b + 2n \pm R}{2(n-1)b + 2n + 2n + R} \right)^n a^{n-1} < 0, \]
namely, \( \mathcal{H}_\pm \) is decreasing in \( a \), because
\[ (n + 1)b - R = \frac{8n^2}{(n+1)b+R} > 0 \quad \text{and} \quad (n - 1)b + 2n - R = \frac{4n^2(b+1)}{(n-1)b+2n+R} > 0. \]
It follows from (27) and (28) that \( a_\pm(b) > a_\pm(b) \). In order to prove \( a_\pm(b) > a_\pm(b) \)
for all \( b > b_* \), we note the five situations \((S1)-(S5)\) in the case that \( a > a_\pm(b) \),
stated below (21). For \( a = a_\pm(b) \) (or \( a_\pm(b) \)), the corresponding situation is \((S2)\)
or \((S4)\) by (27), i.e.,
\[ \Phi(u_{01}) = \Phi(\zeta_-(a, b)) = 0 \quad \text{and} \quad \Phi(u_{02}) < 0 \]
(or \( \Phi(u_{01}) > 0 \) and \( \Phi(u_{02}) = \Phi(\zeta_+(a, b)) = 0 \)).
It follows from (20) that \( \Phi(\tilde{u}_2) < 0 \) (or \( > 0 \)) because \( \Phi \) decreases strictly on \((u_{01}, u_{02})\)
as mentioned just before (21). By the equality \( aF(a, b) = \Phi(\tilde{u}_2) \) given just above (12), we get
\[ a_\pm(b)F(a_\pm(b), b) < 0 \quad \text{or} \quad a_\pm(b)F(a_\pm(b), b) > 0 \quad \forall b > b_* \quad (29) \]
On the other hand, as stated before (13), we have that \( \Phi(\tilde{u}_2) > 0 \) (or \( < 0 \)) if and
only if \( a < a_0(b) \) (or \( a_0(b) \)) for all \( b > b_* \). It implies that \( aF(a, b) > 0 \) (or
\( < 0 \)) if and only if \( a < a_0(b) \) (or \( a_0(b) \)) for all \( b > b_* \). It follows from (29) that
\( a_\pm(b) < a_0(b) < a_\pm(b) \) for all \( b > b_* \). Thus, the claim is proved.

Meanwhile, by (26) and (27), we see that
\[ \Phi(\zeta_-) = 0 \quad \text{if and only if} \quad a = a_\pm(b), \quad \Phi(\zeta_+) = 0 \quad \text{if and only if} \quad a = a_\pm(b). \quad (30) \]
Moreover, one can check that
\[ \Phi(\zeta_-) < 0 \quad \text{if and only if} \quad a > a_\pm(b); \quad \Phi(\zeta_+) < 0 \quad \text{if and only if} \quad a > a_\pm(b); \]
\[ \Phi(\zeta_-) > 0 \quad \text{if and only if} \quad a < a_\pm(b); \quad \Phi(\zeta_+) > 0 \quad \text{if and only if} \quad a < a_\pm(b). \quad (31) \]
Thus, (30) and (31) enable us to convert the conditions that \( a > a_\pm(b), a = a_\pm(b), a = a_\pm(b) > a = a_\pm(b) \) and \( a > a_\pm(b) \), which correspond
to cases \((C3-1-1), (C3-2-3), (C3-3-1), (C3-3-2) \) and \((C3-3-3) \) respectively, to various signs of \( \Phi(\zeta_-) \) and \( \Phi(\zeta_+) \), namely, \( \Phi(\zeta_-) < 0, \Phi(\zeta_-) = 0, \Phi(\zeta_-) > 0 \) and \( \Phi(\zeta_+) < 0, \Phi(\zeta_+) = 0, \Phi(\zeta_+) > 0 \) respectively.

**Assertion 1:** Case \((C3-1-1)\) is true if and only if \( a > a_\pm(b) \).

In fact, in case \((C3-1-1)\), we see that \( 0 < u_{01} < \zeta_- \) and \( \zeta_+ < u_{02} < a \). From (24) we have \( \Xi(u_{01}) > 0 \), implying by (23) that \( \Phi(u_{01}) < 0 \). Since \( \Phi \) is strictly decreasing
on \((u_{01}, u_{02})\) as mentioned just before (21), we get that \( \Phi(\zeta_-) < 0 \) and \( \Phi(\zeta_+) < 0 \),
namely, \( a > a_\pm(b) \) and \( a > a_\pm(b) \). It follows from (25) that \( a > a_\pm(b) \), which proves
the necessity. Conversely, assuming that \( a > a_\pm(b) \), by (31) we have \( \Phi(\zeta_-) < 0 \).
In order to prove that \( \Phi(u_{01}) < 0 \), we indirectly assume that \( \Phi(u_{01}) \geq 0 \). In
the case that \( \Phi(u_{01}) = 0 \), we have \( \Phi(u_{02}) < 0 \) by (21). Thus it lies in the situation
\((S2)\) stated below (21) and therefore (23) holds for \( i = 1 \). Since \( 0 < u_{01} < \tilde{u}_2 \) by (20)
and \( \zeta_- \) is the unique zero of \( \Xi \) on the interval \( (0, \tilde{u}_2) \), we see \( u_{01} = \zeta_- \),
implying that \( \Phi(\zeta_-) = 0 \), a contradiction. The complicated case is the other one,
i.e., \( \Phi(u_{01}) > 0 \). Since \( \Phi(\zeta_-) < 0 \), by the continuity, \( \Phi \) has at least one zero between
\( u_{01} \) and \( \zeta_- \). Note that \( \Phi \) is strictly increasing on \((0, u_{01})\) and strictly decreasing on
\((u_{01}, u_{02})\) as mentioned just before (21) but \( 0 < \zeta_- < u_{02} \) by (19) and (20). The
monotonicity implies that the zero of \( \Phi \) between \( u_{01} \) and \( \zeta_- \) is unique, denoted by
\( \hat{u}_1 \). If \( \zeta_- < \hat{u}_1 < u_{01} \), then \( \Xi(\hat{u}_1) < 0 \) by (24) and therefore \( \Phi(\hat{u}_1) < 0 \) by (16).
This contradicts to the fact $\Phi(\hat{u}_1) > 0$, which is implied by the monotonicity of $\Phi$ given below (20). If $u_{01} < \hat{u}_1 < \zeta_-$, we can obtain a contradiction similarly. Since we have proved that $\Phi(u_{01}) < 0$, we can see that $\Phi(u_{02}) < 0$ because $\Phi$ is strictly decreasing on $(u_{01}, u_{02})$. It follows from (23) that $\Xi(u_{01}) > 0$ and $\Xi(u_{02}) > 0$, which implies by (24) that $0 < \hat{u}_1 < \zeta_-$ and $\zeta_+ < u_{02} < a$ since $0 < \zeta_- < \hat{u}_2 < \zeta_+ < a$ by (19) and $0 < u_{01} < \hat{u}_2 < u_{02} < a$ by (20). This completes the proof of the sufficiency and Assertion 1.

**Assertion 2:** Case (C3-2-3) is true if and only if $a = a_+(b)$.

In fact, in case (C3-2-3), we see $u_{01} = \zeta_-$ and $\zeta_+ < u_{02} < a$. Since $\Xi(\zeta_-) = 0$ by (24), we see from (23) that $\Phi(\zeta_-) = \Phi(u_{01}) = 0$, implying by (30) that $a = a_+(b)$. On the other hand, $\zeta_+ \in (u_{01}, u_{02})$ and $\Phi$ is strictly decreasing on $(u_{01}, u_{02})$ as indicated below (20). It follows that $\Phi(\zeta_+) < 0$, implying from (31) that $a > a_+(b)$. Hence, in this case we have $a = a_+(b)$ and $a > a_+(b)$, which is equivalent to $a = a_+(b)$ by (25) and therefore proves the necessity. Conversely, assuming $a = a_+(b)$, by (30) we have $\Phi(\zeta_-) = 0$. It follows from (16) that $\Phi(\zeta_-) = 0$ since we know $\Xi(\zeta_-) = 0$ by (24). Noting that $\Phi$ has a unique zero $u_{01}$ on the interval $(0, \hat{u}_2)$ and $0 < \zeta_- < \hat{u}_2$ by (19), we see that $u_{01} = \zeta_-$ and therefore $\Phi(u_{01}) = 0$. Furthermore, $\Phi$ is strictly decreasing on $(u_{01}, u_{02})$, implying that $\Phi(u_{02}) < 0$. Then, $\Xi(u_{02}) > 0$ by (23). It proves by (24) that $\zeta_+ < u_{02} < a$ because $\hat{u}_2 < u_{02} < a$ by (20) and $\hat{u}_2 < \zeta_+$ by (19). This completes the proof of the sufficiency and Assertion 2.

**Assertion 3:** Case (C3-3-1) is true if and only if $a = a_+(b)$.

In fact, in case (C3-3-1), $\zeta_- < u_{01} < \hat{u}_2$ and $\hat{u}_2 < u_{02} < \zeta_+$. From the first inequality we claim that $\Phi(\zeta_-) > 0$. In fact, $\Xi(u_{01}) < 0$ by (24), implying from (23) that $\Phi(u_{01}) > 0$. Since $\Phi(0) = -a < 0$ by (8) and $\Phi$ is strictly increasing on $(0, u_{01})$ as indicated just before (21), we see that $\Phi$ has a unique zero, denoted by $\hat{u}_2$, in $(0, u_{01})$. Clearly, $\Phi(\hat{u}_2) > 0$. It follows from (16) that $\Xi(\hat{u}_2) > 0$. Thus, $0 < \hat{u}_2 < \zeta_-$ by (24), implying the claimed result by the monotonicity of $\Phi$. On the other hand, from the second inequality, i.e., $\hat{u}_2 < u_{02} < \zeta_+$, we get $\Xi(u_{02}) < 0$ by (24), implying from (23) that $\Phi(u_{02}) > 0$. It implies $\Phi(\zeta_+) > 0$ because $\Phi$ is also strictly increasing on $(u_{02}, a)$ as mentioned just before (21). Having known $\Phi(\zeta_-) > 0$ and $\Phi(\zeta_+) > 0$ above, we see from (31) that $a < a_+(b)$ and $a > a_-(b)$. It follows from (25) that $a_+(b) < a < a_-(b)$ since $a > a_+(b)$ as required at the beginning of paragraph of (20), which proves the necessity. Conversely, assume that $a_+(b) < a < a_-(b)$. By (31) we have $\Phi(\zeta_+) > 0$. As done for the inequality $\Phi(u_{01}) < 0$ in the above case (C3-1-1), reducing to an absurdity, we similarly prove that $\Phi(u_{02}) > 0$. On the other hand, we easily see that $\Phi(u_{01}) > 0$ because $\Phi$ is strictly decreasing on $(u_{01}, u_{02})$. It follows from (23) that $\Xi(u_{01}) < 0$ and $\Xi(u_{02}) < 0$, implying from (24) that $\zeta_- < u_{01} < \hat{u}_2$ and $\hat{u}_2 < u_{02} < \zeta_+$ since $0 < \zeta_- < \hat{u}_2 < \zeta_+ < a$ and $0 < u_{01} < \hat{u}_2 < u_{02} < a$ by (19) and (20). This proves the sufficiency and Assertion 3.

**Assertion 4:** Case (C3-3-2) is true if and only if $a = a_-(b)$.

In fact, in case (C3-3-2), $\zeta_- < u_{01} < \hat{u}_2$ and $u_{02} = \zeta_+$. By (24) we have $\Xi(u_{01}) < 0$, implying by (23) that $\Phi(u_{01}) > 0$. For the same reason as in case (C3-3-1), $\Phi$ has a unique zero $\hat{u}_2$ in $(0, u_{01})$ and $\Phi'(\hat{u}_2) > 0$, implying that $\Xi(\hat{u}_2) > 0$ and therefore $0 < \hat{u}_2 < \zeta_-$. Since $\Phi$ is strictly increasing on $(0, u_{01})$, we get $\Phi(\zeta_-) > \Phi(\hat{u}_2) = 0$. On the other hand, since $u_{02} = \zeta_+$, we get $\Xi(\zeta_+) = 0$ by (24), which implies from (23) that $\Phi(\zeta_+) = \Phi(u_{02}) = 0$. Having known $\Phi(\zeta_-) > 0$ and $\Phi(\zeta_+) = 0$ above, we see from (31) and (30) that $a < a_+(b)$ and $a = a_-(b)$, implying by (25) that $a = a_-(b)$, which proves the necessity. Conversely, assuming
that $a = a_-(b)$, by (30) we have $\Phi(\zeta_+)=0$. As done in the end of discussion in case (C3-2-3), where we gave results $u_{01} = \zeta_-$ and $\zeta_+ < u_{02} < a$, we can similarly prove that $u_{02} = \zeta_+$ and $0 < u_{01} < \zeta_-$ and therefore proves the sufficiency and Assertion 4.

Assertion 5: Case (C3-3-3) is true if and only if $a_+(b) < a < a_-(b)$.

In fact, in case (C3-3-3), i.e., $\zeta_- < u_{01} < u_2$ and $\zeta_+ < u_{02} < a$, from (24) we have $\Xi(u_{01}) < 0$ and $\Xi(u_{02}) > 0$, implying by (23) that $\Phi(u_{01}) > 0$ and $\Phi(u_{02}) < 0$. Since $\Phi(0) < -a < 0$ and $\Phi(a) = ab > 0$ as given in (8) and $\Phi$ strictly increases on $(0, u_{01}) \cup (u_{02}, a)$ and decreases strictly on $(u_{01}, u_{02})$ as mentioned just before (21), we see that $\Phi$ has exactly three zeros. Let $u_1', u_2'$ and $u_3'$ denote those zeros such that $0 < u_1' < u_{01} < u_2' < u_{02} < u_3' < a$. By the monotonicity of $\Phi$, $\Phi'(u_1') > 0, \Phi'(u_2') < 0$ and $\Phi'(u_3') > 0$ and therefore $\Xi(u_1') > 0, \Xi(u_2') < 0$ and $\Xi(u_3') > 0$ by (16). It follows from (24) that $0 < u_1' < \zeta_- < u_2' < \zeta_+ < u_3' < a$.

Note that $\Phi(\zeta_-) = 0$ for all $u \in (u_1', u_2')$ and $\Phi(u) < 0$ for all $u \in (u_2', u_3')$ since $\Phi(u_1') = 0$ for all $j = 1, 2, 3, u_1' < u_{01} < u_2' < u_{02} < u_3'$, and $\Phi$ is strictly increasing on $(0, u_{01}) \cup (u_{02}, a)$ but strictly decreasing on $(u_{01}, u_{02})$. It follows that $\Phi(\zeta_-) > 0$ and $\Phi(\zeta_+) < 0$, implying by (31) that $a_-(b) < a < a_+(b)$, which proves the necessity. Conversely, assuming that $a_-(b) < a < a_+(b)$, by (31) we see that $\Phi(\zeta_-) > 0$ and $\Phi(\zeta_+) < 0$. Noting that $\Phi$ reaches the maximal value at $u_{01}$ and the minimal value at $u_{02}$ on $(0, a)$ as indicated just below (21), we get that $\Phi(u_{01}) > 0$ and $\Phi(u_{02}) < 0$. Then, $\Xi(u_{01}) < 0$ and $\Xi(u_{02}) > 0$ by (23), and therefore $\zeta_- < u_{01} < \hat{u}_2$ and $\zeta_+ < u_{02} < a$ by (24) because of the orders given in (19) and (20), which proves the sufficiency and Assertion 5. This completes the proof of Lemma 2.2. □

3. Properties of equilibria. In section 3 we gave conditions of parameters for exact numbers of equilibria but did not obtain coordinates of those equilibria, which prevents us from determining qualitative properties of those equilibria by computing determinant and trace of the Jacobian matrix at each of them in the usual routine. In what follows, we only use the interval distributions of those equilibria obtained in last section to give their qualitative properties.

Theorem 3.1. For the system (3) with $n \geq 2$, equilibria obtained in Theorem 2.1 have the following properties: In case (i) of Theorem 2.1, i.e., $0 < b \leq b_0$ and $a > 0$, $A_s$ is a stable node. In case (ii-1) of Theorem 2.1, i.e., $b_0 < b < b_s$ and either $0 < a < a_0(b)$ or $a = a_0(b)$, $A_s$ is a stable node. In case (ii-2), i.e., $b_0 < b \leq b_s$ and $a = a_0(b)$, $A_s$ is a stable node if $b_0 < b < b_s$ and $A_s$ is a degenerate stable node if $b = b_s$. In case (iii-1) of Theorem 2.1, i.e., $b > b_s$ and either $0 < a < a_-(b)$ or $b > a_2(b)$, $A_s$ is a stable node. In case (iii-2), i.e., $b > b_s$ and either $a = a_-(b)$ or $a = a_2(b)$, $A_s$ is a stable node and $A_0$ is a saddle-node. In case (iii-3), i.e., $b > b_s$ and $a_-(b) < a < a_+(b)$, $A_1$ and $A_3$ are both stable nodes and $A_2$ is a saddle.

Proof. Let $E: (\bar{v}, \bar{v})$ present a general equilibrium of system (3), where $\bar{v} = b/(\bar{u}^n + 1)$ by (4). Although the coordinate $\bar{u}$ is unknown yet, we can formally compute the Jacobian matrix of system (44) at $E$, i.e.,

$$J|_E := \begin{pmatrix} P_\bar{u}(\bar{u}, \bar{v}) & P_\bar{v}(\bar{u}, \bar{v}) \\ Q_\bar{u}(\bar{u}, \bar{v}) & Q_\bar{v}(\bar{u}, \bar{v}) \end{pmatrix} = \begin{pmatrix} -\frac{ab}{u^2} + \frac{abn}{u^{n+1}} & -\frac{2ab}{u^2} \\ -\frac{abn}{u^{n+1}} & -\frac{2ab}{u^2} \end{pmatrix}. $$

Then one can compute the trace, the determinant and the discriminant

$$T(\bar{u}) := \text{tr}(J|_E) = -\frac{2ab}{u^2}, \quad D(\bar{u}) := \det(J|_E) = \frac{abn(\bar{u})}{u^{n+1}(u-a)}, \quad \Delta(\bar{u}) := T^2(\bar{u}) - 4D(\bar{u}) = \frac{4abn(\bar{u})(\bar{u}+1)(u-a)}{u^{n+1}(u-a)}.$$

(32)
where $\Xi$ is the quadratic function defined just below (16). Clearly,
\[
T(\tilde{u}) < 0 \quad \text{and} \quad \Delta(\tilde{u}) > 0
\]  
(33)
since $0 < \tilde{u} < a$ as required in (6) and $0 < \tilde{u} < a/(b + 1)$ by (15). In order to
determine the sign of $D(\tilde{u})$, we cannot compute its exact value as usual because
we did not obtain precise coordinates of $E$ in section 2. However, the monotonic
interval where $\tilde{u}$ locates gives enough information for the sign of $D(\tilde{u})$.

In case (i) of Theorem 2.1, $0 < b \leq b_0$. As indicated at the beginning of the
second paragraph below (23), we have $\Xi(\tilde{u}) > 0$ for all $u \in (0, a)$, implying by (32)
that $D(\tilde{u}) > 0$ since $\tilde{u} \in (0, a)$. By (33) and [24, pp.21-22] or [34, p.48] we see that
$A_*$ is a stable node.

In case (ii) of Theorem 2.1, $b_0 < b \leq b_*$. From the second and third paragraphs
below (23) similarly, we see that if $b_0 < b < b_*$ then $\Xi(u) > 0$ for all $u \in (0, a)$; if
$b = b_*$, then either $\Xi(u) > 0$ for all $u \in (0, a)$ or $\Xi(u) = 0$ for $u = \tilde{u}_2$. It follows from (32)
that if $b_0 < b < b_*$ then $D(\tilde{u}) > 0$ since $\tilde{u} \in (0, a)$; if $b = b_*$, then
either $D(\tilde{u}) > 0$ when $0 < a < a_0(b)$ since $\tilde{u} \in (0, \tilde{u}_2)$ or $D(\tilde{u}) = 0$ when $a = a_0(b)$
since $\tilde{u} = \tilde{u}_2$ or $D(\tilde{u}) > 0$ when $a > a_0(b)$ since $\tilde{u} \in (\tilde{u}_2, a)$. Hence, in subcase
(ii-1), i.e., $b_0 < b < b_*$ and either $0 < a < a_0(b)$ or $a > a_0(b)$, the above results
on the sign of $D(\tilde{u})$ together with (33) imply by [24, pp.21-22] or [34, p.48] that
$A_*$ is a stable node. In subcase (ii-2), i.e., $b_0 < b \leq b_*$ and $a = a_0(b)$, we still use
the results on the sign of $D(\tilde{u})$ and (33) to see that $A_*$ is either a stable node if
$b_0 < b < b_*$ or degenerate if $b = b_*$. 

In case (iii) of Theorem 2.1, $b > b_*$. From (24) and (32) we see that if $\tilde{u} \in
(0, \xi_-) \cup (\xi_+, a)$ then $D(\tilde{u}) > 0$, if $\tilde{u} = \xi_\pm$ then $D(\tilde{u}) = 0$, and if $\tilde{u} \in (\xi_-, \xi_+)$
then $D(\tilde{u}) < 0$. In subcase (iii-1), i.e., $b > b_*$ and either $0 < a < a_-(b)$ or $a > a_+(b)$, by
Theorem 2.1 the system has a unique equilibrium, the abscissa $u_*$ of which lies in
either $(0, \xi_-)$ or $(\xi_+, a)$. The above results on the sign of $D(\tilde{u})$ together with (33)
imply by [24, pp.21-22] or [34, p.48] that $A_*$ is a stable node. In subcase (iii-2), i.e.,
b > b_* and either $a = a_-(b)$ or $a = a_+(b)$, Theorem 2.1 shows that the system
has exactly two equilibria and their abscissas $u_*$ and $u_0$ either lies in $(0, \xi_-)$ and
hits $\xi_+$ respectively or lies in $(\xi_+, a)$ and hits $\xi_-$ respectively. We similarly use the results
on the sign of $D(\tilde{u})$ together with (33) to see that $A_*$ is a stable node and
$A_0$ is degenerate. In subcase (iii-3), i.e., $b > b_*$ and $a_-(b) < a < a_+(b)$, the system
has exactly three equilibria, whose abscissas $u_1, u_2$ and $u_3$ lie in $(0, \xi_-), (\xi_-, \xi_+)$
and $(\xi_+, a)$ respectively. For the same reason, $A_1, A_3$ are both stable nodes and $A_2$ is a saddle.

The above discussion indicates two degenerate situations: (ii-2D) $b = b_*$ and
$a = a_*$, and (iii-2) $b > b_*$ and $a = a_+(b)$, which are included in subcases (ii-2) and
(iii-2) respectively and in which $D(\tilde{u}) = 0$. In both situations exact one eigenvalue
vanishes since $T(\tilde{u}) < 0$ by (32). In what follows, we give qualitative properties for
the two degenerate equilibria.

In situation (ii-2D), by Theorem 2.1 (ii-2), the system has a unique equilibrium
$A_* : (a_*(n-1)/(n+1), 2/(n-1))$, where $a_*$ is defined in (7). The eigenvalues are 0 and
$-4n(n+1)/(n-1)^2$, which is negative. Expanding system (44) at $A_*$, we get
\[
du {\dot{u}} = \frac{2n(n+1)}{a(n-1)^2} u - \frac{2n(n+1)}{a(n-1)^2} v - \frac{n(n+1)^2}{a(n-1)^2} u^2
\]
\[
- \frac{n(n+1)^2}{a(n-1)^2} u^2 v + O((u, v)^4),
\]
\[
dv {\dot{v}} = \frac{2n(n+1)}{a(n-1)^2} u - \frac{2n(n+1)}{a(n-1)^2} v - \frac{n(n+1)^2}{a(n-1)^2} u^2
\]
\[
- \frac{n(n+1)^2}{a(n-1)^2} u^2 v - \frac{n(n+1)^2}{a(n-1)^2} u^2 v + O((u, v)^4).
\]  
(34)
Using the invertible linear transformation

\[ u = \frac{a_+(n-1)^2}{(n+1)^2} \nu + \frac{a_-(n-1)^2}{(n+1)} \omega, \quad v = \nu + \omega, \]

to diagonalize the linear part of system (34), we obtain

\[
\frac{du}{dt} = -\frac{4n-1}{n} \nu \omega - \frac{n(n-5)(n+5)}{12(n+1)} \nu^3 + \frac{n(n-1)(n+9)}{4(n+1)} \nu \omega^2 - \frac{n(n^2+8n-1)}{4(n+1)} \nu \omega^2
\]
\[ + \frac{b(n-1)}{12} \omega^3 + O(|\nu|, \omega) := \Theta(\nu, \omega), \]

\[
\frac{dv}{dt} = -\frac{4n(n+1)}{n} \nu^2 + 2n \nu \omega - \frac{8n^2+2n-1}{n} \omega^2 - \frac{n(n-1)(n+13)}{12(n+1)} \nu \omega^3 \]
\[ + O(|\nu, \omega|)^4 := \Lambda(\nu, \omega). \]

By the Center Manifold Theorem ([4, Theorem 1] and [11, Theorem 3.2.1]), system (35) has a one-dimensional center manifold \( W^c \) near the origin, where \( h_+ \) is \( C^\infty \) such that \( h_+(0) = 0 \) and \( h'_+(0) = 0 \). Thus we can formally consider the second order expansion \( h_+(\nu) = h_{+,2} \nu^2 + O(|\nu|^3) \). By the invariance of the center manifold \( \omega = h_+(\nu) \), we can differentiate its both sides and get \( \frac{dw}{dt} \mid_{W^c} = h'_+(\nu) \frac{dw}{dt} \mid_{W^c} \), i.e., \( \Lambda(\nu, h_+(\nu)) = h'_+(\nu) \Theta(\nu, h_+(\nu)) \). Substituting the second order expansion of \( h \) in the above equation and comparing the coefficient of \( \nu^2 \), we get \( h_{+,2} = (n-1)/(2(n+1)) \). Then we obtain the equation

\[
\frac{dv}{dt} = -\frac{n(n-1)}{12} \nu^3 + O(|\nu|^4), \tag{36}
\]
the restriction of system (35) to \( W^c \). With degree 3 and a negative coefficient in the main term of (36), \( A_+ \) is a stable node. This proves the result of case (ii-2) in Theorem 3.1.

In situation (iii-2), \( b > b_+ \) and \( a = a_+(b) \). Since the discussion for \( a = a_-(b) \) is similar, we concentrate to properties of \( A_0 \) for \( a = a_+(b) \). By Theorem 2.1 (iii-2), the coordinates of \( A_0 \) are given by \( (bn - b - 2n - \Re) a_+(b)/(2n + b + \Re)/(2n) \), where \( \Re \) defined in (7) depends on \( b, n \). The eigenvalues are 0 and \( -bn - b + \Re \), which is negative. Expanding system (44) at \( A_0 \), we get

\[
\frac{du}{dt} = -\frac{bn + b - \Re}{4n} u + a_+(bn + b - 2n - \Re) u - \frac{(bn - b + 2n + \Re)^2 (bn - b - 2 - \Re)}{8n} u^2 \]
\[ - \frac{bn + 2b - \Re}{b} \frac{bu}{u} + O(|u, v|^3), \]

\[
\frac{dv}{dt} = -\frac{(bn - b + 2n + \Re)^2 (bn - b - \Re)}{8n a_+ n^2} u^2 - \frac{bn - b - \Re}{2} \frac{u}{u} - \frac{(bn - b - 2n - \Re)^2 (bn - b + 2n + \Re)}{32 n^2} u^2 \]
\[ + \Re((u, v)^3) \tag{37}
\]
where \( a_+ \) presents \( a_+(b) \) for simplicity. Using an invertible linear transformation

\[ u = \xi z - \xi w, \quad v = z + w, \]
where \( \xi := -a_+(bn - b - 2n - \Re)^2/(4n^2(b + 1)^2) \), we normalize the linear part of (37) and obtain

\[
\frac{dz}{dt} = -\frac{\Re(bn - b - \Re)}{8b} z^2 - \frac{(4b - \Re)(bn - b - \Re)}{4b} zw - \Re(bn - b - \Re) w^2 + O(|(z, w)|^3), \tag{38}
\]

\[
\frac{dw}{dt} = -(bn + b - \Re) w + \frac{(4b - \Re)(bn - b - \Re)}{4b} z^2 + \frac{(2bn - 2b - \Re)(bn - b - \Re)}{4b} zw \]
\[ - \frac{(bn - b - \Re)(4bn + 8b - 3\Re)}{8b} w^2 + O(|(z, w)|^3), \]

By the Center Manifold Theorem ([4, Theorem 1] and [11, Theorem 3.2.1]), system (38) has a one-dimensional center manifold \( W^c_0 := \{(z, w) : w = h_0(z)\} \) near the origin, where \( h_0 \) is \( C^\infty \) such that \( h_0(0) = 0 \) and \( h'_0(0) = 0 \). As done in situation (ii-2D), the restriction of system (38) to \( W^c_0 \) is the equation

\[
\frac{dz}{dt} = -\frac{\Re(bn - b - \Re)}{8b} z^2 + O(|z|^3),
\]

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where we compute
\[-\frac{b(n-1)^2b-4n}{8b} = -\sqrt{b(n-1)^2b-4n} \left\{ (n-1)b - \sqrt{b(n-1)^2b-4n} \right\} < 0\]
because \(b > b_*=4n/(n-1)^2\) as given in (7). It implies that \(A_0\) is a saddle-node. This proves the results of Theorem 3.1 in case (iii-2), and therefore the proof of the theorem is completed.

\[\square\]

4. Bifurcations. In last section a transition is exhibited between a monostable state and a bistable state. In this section we show how those transitions arise. Theorem 3.1 indicates that system (44) has exactly two degenerate situations, i.e., (ii-2D) \(b=b_0\) and \(a=a_+\), and (iii-2) \(b>b_0\) and \(a=a_+(b)\), as given in the paragraph just above (34). The relation between (ii-2D) and (iii-2) can be seen from the limit \(\lim_{b \to b_+} a_+(b) = a_+\), which was shown in the proof of Theorem 2.1.

Near those situations, transition of states may occur and will be displayed by the following discussion of bifurcations.

**Theorem 4.1.** For \(n \geq 2\), a stable node and an unstable saddle arise from a saddle-node bifurcation of system (3) at \(A_0\) as \((a, b)\) varies across the curve \(\Sigma_+ := \{(a, b) \in \mathbb{R}^2 : b > b_0\text{ and } a = a_+(b)\}\) (resp. \(\Sigma_- := \{(a, b) \in \mathbb{R}^2 : b > b_0\text{ and } a = a_-(b)\}\)) to the region \(\{(a, b) \in \mathbb{R}^2 : b > b_0\text{ and } a < a_+(b)\}\) (resp. \(\{(a, b) \in \mathbb{R}^2 : b > b_0\text{ and } a > a_-(b)\}\)), as shown in Figure 14. The curves \(\Sigma_\pm\) meet at point \(C : (a_+, b_0)\) and divide the first quadrant of the \((a, b)\)-plane into the region \(\mathcal{B} := \{(a, b) \in \mathbb{R}^2 : b > b_0\text{ and } a_-(b) < a < a_+(b)\}\), called the bistability region, and the outside one \(\mathcal{M}\), called the monostability region. When \((a, b)\) varies from \((a_+, b_0)\) to \(\Sigma_+ \cup \mathcal{B}\), a codimension 2 bifurcation called the cusp bifurcation happens, producing an unstable saddle-node as \((a, b) \in \Sigma_+ \text{ (or } \Sigma_-)\) and a stable node and an unstable saddle as \((a, b) \in \mathcal{B}\).

**Proof.** Concerning the saddle-node bifurcation, we only consider the case that \((a, b)\) varies across \(\Sigma_+\) to \((a, b) \in \mathbb{R}^2 : b > b_0\text{ and } a < a_+(b)\). The other case can be discussed similarly. For simplicity we write \(a_+(b)\) as \(a_+\). Let \(\varepsilon := a - a_+\) and consider \(|\varepsilon|\) to be small enough. Expanded at \(A_0 : ((b + b - 2n) a_+/(2n b + 1)), (b(b - b + R))/2n)\), the coordinates of which are given in Theorem 2.1, system (44) is rewritten as the following

\[
\begin{align*}
\frac{du}{dt} &= \frac{3}{2} \varepsilon - \frac{b n + b - R}{2} u - a_+ \frac{\varepsilon (b n - b + 2n - R)}{4(n - 1)b} v + \frac{(b n + b - R)^2}{2b} \varepsilon u \\
&\quad - \frac{\varepsilon (b n - b + 2n - R)^2 (b n + b - R)}{4b} u^2 - \frac{\varepsilon (b n + 3b - R)}{4b} u v + O(\varepsilon, u, v^3), \\
\frac{dv}{dt} &= -\frac{(b n - b + 2n + R)^2 (b n + b - R)}{8a_+^2} u - \frac{b n - b + 2n - R}{2} v - \frac{(b n - b + 2n + R)^2 (b n + b - R)}{32a_+^2} u^2 \\
&\quad - \frac{(b n - b + 2n + R) (b n + 2n + R) (b n - b + 2n - R)}{4a_+^2} u v - \frac{\varepsilon}{2} v^2 + O(\varepsilon, u, v^3),
\end{align*}
\]

where \(\Sigma_- = bn - b - R\). Suspending system (39) with \(\dot{\varepsilon} = 0\), we obtain a 3-dimensional system with eigenvalues 0, 0 and \(-(b n + b - R)\) at the equilibrium \(\hat{O} : (0, 0, 0)\). Use the notation \(\Sigma_+ := bn + b + R\) for simplicity. Applying an invertible linear transformation

\[
\varepsilon = \frac{a_+ \varepsilon (b n - b + 2n - R)}{2n (b + 1)} \varepsilon, \quad u = \frac{a_+ \varepsilon^2 \varepsilon^2}{16n^2(b + 1)^2} (x + y), \quad v = -\frac{\varepsilon}{2n (b + 1)} \varepsilon + x + y,
\]

to normalize the linear part, we change the suspended system into the form
to normalize the suspended system, we obtain

\[ \frac{dx}{dt} = \frac{(bn+b-\Re)(bn+b+2n-\Re)}{8n^2b(\lambda+1)} x \quad \frac{dy}{dt} = \frac{\Re}{8n} y + O(\varepsilon, x, y^3) \]

Thus the restriction equation of system (40) to \( W \)

Using an invertible linear transformation

Thus the restriction equation of system (40) to \( W \)

in which the (generalized) eigenspace of the linearized matrix corresponding to two zero eigenvalues is the \((\varepsilon, x, y)\)-plane. By the Center Manifold Theorem (Theorem 1 of [4] and Theorem 3.2.1 of [11]), system (40) has a 2-dimensional center manifold \( W^c := \{ (\varepsilon, x, y) : y = \hat{h}(\varepsilon, x) \} \) near the origin, where \( h \) is \( C^\infty \) such that \( h(0,0) = 0 \) and \( D\hat{h}(0,0) = 0 \). As done in proof of Theorems 3.1, computing second-order approximation \( \hat{h}_2(\varepsilon, x) := \hat{h}_{20}\varepsilon^2 + \hat{h}_{11}\varepsilon x + \hat{h}_{02}x^2 \) of \( \hat{h} \), we get

\[ \hat{h}_{20} = \frac{3\Re}{32b^6(\lambda+1)^2} \varepsilon^2, \quad \hat{h}_{11} = -\frac{3\Re}{64b^6(\lambda+1)^2} \varepsilon x, \quad \hat{h}_{02} = -\frac{3\Re}{256b^6(\lambda+1)^2} x^2. \]

Thus the restriction equation of system (40) to \( W^c \) is that

\[ \dot{x} = \varepsilon - \frac{3\Re}{8b} x^2 - \frac{3\Re}{4b} \varepsilon x - \frac{3\Re}{8b} \varepsilon y + O(\varepsilon, x, y^3) \]

By Theorem 3.1 of [17] and case (i) of [5, pp.197-200], it implies that system (44) experiences a saddle-node bifurcation at \( A_0 \) at the bifurcation value \( \varepsilon = 0 \). More precisely, exactly two equilibria occur when \( \varepsilon > 0 \), coincide when \( \varepsilon = 0 \), and finally vanish when \( \varepsilon < 0 \). This proves the results of Theorem 4.1 for the saddle-node bifurcation.

Concerning the cusp bifurcation, let \( \nu := a-a_+ \) and \( \rho := b-b_+ \) and consider \( |\rho| \) to be small enough. Expanding system (44) at \( A_* : (a_+(n-1)/(n+1), 2/(n-1)) \), the coordinates of which are given in Theorem 2.1, we get

\[ \frac{d\rho}{dt} = \frac{2n+1}{a_+(n-1)^3} \theta + \frac{2n+1}{a_+(n-1)^3} \nu - \frac{a_+(n-1)^3}{2a_+(n-1)^3} \theta^2 - \frac{2n+1}{a_+(n-1)^3} \theta \nu + O(||(\rho, u, v)||^4), \]

SUSPENDING SYSTEM (41) WITH \( \rho = 0 \) AND \( i = 0 \), WE OBTAIN A 4-DIMENSIONAL SYSTEM WITH EIGENVALUES 0, 0, 0 AND \(-4n(n+1)/(n-1)^2\) AT THE EQUILIBRIUM \( \hat{O} : (0, 0, 0, 0) \).

Using an invertible linear transformation

\[ \rho = \frac{2n+1}{a_+(n-1)^3} \theta + \frac{2n+1}{a_+(n-1)^3} \nu, \quad \nu = \frac{a_+(n-1)^3}{2a_+(n-1)^3} \theta^2 - \frac{2n+1}{a_+(n-1)^3} \theta \nu, \quad v = \tilde{u} + \tilde{v} \]

TO NORMALIZE THE SUSPENDED SYSTEM, WE OBTAIN

\[ \frac{d\theta}{dt} = 0, \quad \frac{d\nu}{dt} = 0, \]

\[ \frac{d\rho}{dt} = \frac{2n+1}{a_+(n-1)^3} \theta^2 + \frac{(n+1)^2}{2a_+(n-1)^3} \nu + \frac{n(n+1)^2}{2a_+(n-1)^3} \theta \nu - \frac{n(n+1)^2}{2a_+(n-1)^3} \theta^2 \]

\[ \frac{d\tilde{u}}{dt} = -\frac{n(n+1)^2}{4(n+1)} \tilde{u} + \frac{(n+1)(n+3)}{4(n+1)} \tilde{v}, \quad \frac{d\tilde{v}}{dt} = -\frac{n(n+1)(n+3)}{6(n+1)^2} \tilde{v} \]
Clearly, from the above equation we have η = \eta^3 of codimension 2, which by the normal form theory (17) has the versal unfolding \eta = \mu_0 + \mu_1 \eta - \eta^3 with unfolding parameters \mu_0 and \mu_1. Its equilibria depending on unfolding parameters form the cusp manifold 

\mathcal{M} = \{(\eta, \mu_0, \mu_1) : \mu_0 + \mu_1 \eta - \eta^3 = 0\}

in \mathbb{R} \times \mathbb{R}^2 and the projection of the manifold on the (\mu_1, \mu_0)-plane consists of two curves \mu_0 = \pm(2\mu_1/3)^{3/2}, which meet tangentially at the origin (0,0).
5. **Global dynamics.** The above given results on qualitative properties and bifurcations, concerning local behaviors near equilibria only, are not enough to show global changes of repressors. The following theorem show dynamical behaviors of the system globally.

**Theorem 5.1.** System (3) has no closed orbits. Moreover, in case $a = a_\pm(b)$ and $b > b_*$, system (3) has an orbit linking equilibria $A_0$ and $A_1$; in case $a_-(b) < a < a_+(b)$ and $b > b_*$, system (3) has an orbit linking $A_1$ and $A_2$ and an orbit linking $A_2$ and $A_3$; in other cases, system (3) is globally asymptotically stable.

In order to prove the theorem, we need to investigate equilibria at infinity and closed orbits. For convenience, we use the time-scaling $t = \tau(v + 1)(u^n + 1)$ to simplify system (3) as

\[
\begin{aligned}
\frac{du}{d\tau} &= a(u^n + 1) - u(v + 1)(u^n + 1), \\
\frac{dv}{d\tau} &= b(v + 1) - v(v + 1)(u^n + 1),
\end{aligned}
\] (44)
a polynomial system orbitally equivalent to system (3).

**Lemma 5.2.** For any positive integer $n$, system (44) has two equilibria $I_u$ and $I_v$ at infinity in the first quadrant, where $I_u$ lies on the $u$-axis and $I_v$ lies on the $v$-axis. $I_u$ is a saddle-node with a one-dimensional unstable manifold tangent to the $u$-axis at infinity. $I_v$ is a saddle-node with a one-dimensional unstable manifold tangent to the $v$-axis at infinity if $n = 1$. For $n \geq 2$, $I_v$ is of fully null degeneracy and there is a unique orbit leaving from $I_v$, which goes in the direction of the positive $v$-axis. No orbits connect to $I_u$ and $I_v$ in other directions.

**Proof.** Applying the Poincaré transformation $u = 1/z$ and $v = x/z$ to project all points at infinity but the two on the $v$-axis to the $x$-axis of the new $(x, z)$-coordinate, we change system (44) into the form

\[
\begin{aligned}
\frac{dx}{dz} &= -axz + bxz^n + bz^{n+1} - axz^{n+1} := X(x, z), \\
\frac{dz}{dz} &= x + z - az^2 + xz^n + z^{n+1} - az^{n+2} := Z_1(x, z),
\end{aligned}
\] (45)
where $d\varrho = d\tau/z^n$, so that we only need to consider equilibria of (45) on the $x$-axis. From the equations $X(x, 0) = 0$ and $Z(x, 0) = 0$, we obtain a unique zero $x = 0$, showing that system (45) has a unique equilibrium on the $x$-axis. This equilibrium, denoted by $O_1$, locates at the origin of $(x, z)$-plane, and therefore corresponds to an equilibrium of system (44) at infinity on the positive $u$-axis, denoted by $I_u$. In order to determine if there is an equilibrium at infinity on the $v$-axis, denoted by $I_v$, we apply another Poincaré transformation $u = y/z$ and $v = 1/z$ to change system (44) into the form

\[
\begin{aligned}
\frac{dy}{dz} &= ay^nz - byz^n + az^{n+1} - byz^{n+1} := Y(y, z), \\
\frac{dz}{dz} &= y^n + z^n + ynz - (b - 1)z^{n+1} - bz^{n+2} := Z_2(y, z),
\end{aligned}
\] (46)
where $d\varrho = d\tau/z^n$, so that we only need to consider if system (46) has an equilibrium at the origin $O_2$ of the $(y, z)$-plane because $O_2$ corresponds to the point at infinity on the positive $v$-axis. One can check that this is true because $Y(0, 0) = Z_2(0, 0) = 0$. 


Since $\Psi(\nu,\omega)$ on the $(\nu,\omega)$-plane, we rewrite (45) as

\[
\begin{align*}
\frac{d\nu}{d\rho} &= -av^2 - av\omega + b\nu(\nu + \omega)^n - b(\nu + \omega)^{n+1} - a\nu(\nu + \omega)^{n+1} \\
&=: \Phi(\nu,\omega), \\
\frac{d\omega}{d\rho} &= \omega - av\omega - a\omega^2 - (b + 1)\nu(\nu + \omega)^n + (b + 1)(\nu + \omega)^{n+1} \\
&+ a\nu(\nu + \omega)^{n+1} - a(\nu + \omega)^{n+2} := \Psi(\nu,\omega).
\end{align*}
\]

Since $\Psi(\nu,\omega)$ has a common factor $\omega$, we easily see that $\omega = 0$ is a center manifold. Restricted to this center manifold, system (47) is reduced to the equation $\frac{d\nu}{d\rho} = \frac{d\omega}{d\rho}$, showing that $O_1^*$ is a saddle-node with a saddle sector on the side of the positive $\nu$-axis. Further, we claim that the branch of the unstable manifold on the side of the positive $\omega$, denoted by $W^u_+$, lies in the second quadrant of $(\nu,\omega)$-plane, as shown in Figure 13(a). In fact, we know that $W^u_+$ is tangent to the $\omega$-axis at $O_1^*$ and, on the other hand, $\frac{d\nu}{d\rho} = \frac{d\omega}{d\rho} = \Phi(0,\omega) = -b\omega^{n+1} < 0$ on the positive $\omega$-axis, implying that the positive half $\omega$-axis lies in the saddle sector. This proves the claim. Correspondingly, by the linear transformation as mentioned just before (47), on the $(x,z)$-plane system (45) has a center manifold $z = -x$ and an unstable manifold tangent to the $z$-axis at $O_1$. By the claim, the branch of the unstable manifold which corresponds to $W^u_+$ lies in the first quadrant of $(x,z)$-plane (see Figure 13(b)). It follows that system (45) has at most one orbit near $O_1$ in the first quadrant. Actually, system (45) has exactly one orbit near $O_1$ in the first quadrant, which leaves from $O_1$, because $dx/d\rho = b\omega^{n+1} > 0$ by (45), restricted to the positive half $z$-axis. This gives the results of Lemma 5.2 on $I_u$.

Concerning $I_v$, we discuss equilibrium $O_2$ of system (46) in the two cases: $n = 1$ and $n \geq 2$. The case $n = 1$ is simple, where system (46) has eigenvalues 0 and 1 and can be simplified by the linear transformation $y = -\nu_1, z = \nu_1 + \omega_1$ as

\[
\begin{align*}
\frac{d\nu_1}{d\tau} &= -(a + b)\nu_1\omega_1 - a\omega_1^2 - b\nu_1^3 - 2b\nu_1^2\omega_1 - b\nu_1\omega_1^2 := \Phi_1(\nu_1,\omega_1), \\
\frac{d\omega_1}{d\tau} &= \omega_1 + (a - b + 1)\nu_1\omega_1 + (a - b + 1)\omega_1^2 - b\nu_1^2\omega_1 - 2b\nu_1\omega_1^2 - b\omega_1^3 := \Psi_1(\nu_1,\omega_1).
\end{align*}
\]

Similarly to $I_u$, we can reduce the system to the center manifold $\omega_1 = 0$ and see that the origin $O_2$ is a saddle-node, which gives the result of Lemma 5.2 on $I_v$ for $n = 1$.

For $n \geq 2$, $O_2$ is of fully null degeneracy, i.e., the Jacobian at $O_2$ is a zero matrix. Using the Briot-Bouquet transformation $(y,z) \to (y,\eta_1)$, where $y = y$ and $z = \eta_1y$,
to desingularize $O_2$, we change system (46) into the form
\[
\begin{align*}
\frac{dy}{dt} &= (a - b)y^2\eta_1 + ay^2\eta_1^{n+1} - by^2\eta_1^{n+1}, \\
\frac{d\eta_1}{dt} &= 1 + y\eta_1 - (a - b)y\eta_1^2 + \eta_1^n - (b - 1)y\eta_1^{n+1} - ay\eta_1^{n+2}.
\end{align*}
\] (48)

The common factor $y$ in the first equation of (48) shows that the $\eta_1$-axis is an orbit. Hence, by the uniqueness, no orbits intersect the $\eta_1$-axis. This shows by the geometric sense of the Briot-Bouquet transformation that in the first quadrant of the $(y, z)$-plane system (48) has no orbits connecting to $O_2$ in a direction other than the positive $z$-axis. In order to determine if there is an orbit connecting to $O_2$ in the direction of the positive $z$-axis, we use another Briot-Bouquet transformation $(z, y) \rightarrow (z, \eta_2)$, where $z = z$ and $y = \eta_2z$, which rewrites system (46) as
\[
\begin{align*}
\frac{dz}{dt} &= z - (b - 1)z^2 - bz^3 + z\eta_2^n + z^2\eta_2^n, \\
\frac{d\eta_2}{dt} &= az - \eta_2 + (b - 1)z\eta_2 + (a - b)z\eta_2^n - \eta_2^{n+1} - z\eta_2^{n+1}.
\end{align*}
\] (49)

One can check that the origin $O_2^*$ of the $(z, \eta_2)$-plane is a saddle of system (49) with eigenvalues $1$ and $-1$. Note that $d\eta_2/dt = az > 0$ if we restrict (49) to the positive $z$-axis. This shows that a branch of the unstable manifold of the saddle lies in the first quadrant of the $(z, \eta_2)$-plane and therefore, by the geometric sense of the Briot-Bouquet transformation, in the first quadrant of the $(y, z)$-plane system (46) has exactly one orbit near $O_2$, which leaves from $O_2$ in the direction of the $z$-axis. This implies the results on $I_v$ for $n \geq 2$. Hence, the proof of Lemma 5.2 is competed. \hfill \blacksquare

Now, we are ready to prove the main theorem of this section.

**Proof of Theorem 5.1.** The first result of no closed orbits comes from the Bendixson Criterion ([3] or [24, p.264]) by computing
\[\text{div}(P(\hat{u}(t), \hat{v}(t)), Q(\hat{u}(t), \hat{v}(t))) = (P_u(u(t), v(t)) + Q_v(u(t), v(t)))|_{(\hat{u}(t), \hat{v}(t))} = -2 \neq 0.\]

In case $a = a_+(b)$ and $b > b_*$, the system has exactly two equilibria $A_0$ and $A_+$ by Theorem 2.1. Moreover, $A_+$ is a stable node and $A_0$ is a saddle-node by Theorem 3.1. Since $Q(u, 0) = b/(u^2 + 1) > 0$ on the positive $u$-axis and $P(0, v) = a/(v + 1)$ on the positive $v$-axis by (4), all orbits initiating either the $u$-axis or the $v$-axis enter the first quadrant. Additionally, we see from (45), the system reduced by the Poincaré transformation in the proof of Lemma 5.2, that $Z_1(x, 0) = x > 0$ on the positive half $x$-axis, which implies by Lemma 5.2 that all orbits in the first quadrant are eventually bounded. Thus, the branch of a center manifold at $A_0$ which lies in the saddle sector links with $A_+$.

In case $a_- < a < a_+(b)$ and $b > b_*$, by Theorems 2.1 and 3.1 the system has exactly three equilibria $A_1$, $A_2$ and $A_3$, the middle one $A_2$ of which is a saddle and the other two $A_1$ and $A_3$ are both stable nodes. It follows that the two branches of the unstable manifold at $A_2$ link with $A_1$ and $A_3$ separately for the same reason as in the last paragraph.

In remaining cases, system (3) has exactly one equilibrium $A_+$, which is a stable node, showing that system (3) is globally asymptotically stable. Thus, the proof of Theorem 5.1 is completed. \hfill \blacksquare

Summarizing Theorems 2.1-5.1 and some assertions given in their proofs, we see that system (3) has exactly one equilibrium as $(a, b)$ lies in $\mathcal{M} \cup C$, exactly two equilibria as $(a, b)$ lies on $\mathcal{T}_Z$, exactly three equilibria as $(a, b)$ lies in $B$, as shown in Figure 14.
6. **Conclusions.** Clearly, saddle-node bifurcation occurs on the curves $\Upsilon_+$ and $\Upsilon_-$ and cusp bifurcation occurs at the point $C$ in Figure 14. These bifurcations show that the genetic toggle switch changes from monostability to bistability as $(a, b)$ enters $\mathcal{B}$ (the angular sector between $\Upsilon_+$ and $\Upsilon_-$) from $\mathcal{M}$ (outside $\mathcal{B}$).

For an intuitive observation, we plot the broader curves $\Upsilon_{\pm}$ for $n = 5$ in Figure 15. They actually correspond in the $(\log a, \log b)$-coordinate to the lines $\log a = \beta \log b$ and $\log a = \log b / \gamma$ respectively, which were given in [10] as shown in Figure 2 and can be plotted precisely in the case $n = 5$ as the finer curves $\tilde{\Upsilon}_{\pm}$: $a = b$ and $\tilde{\Upsilon}_- : a = b^{1/5}$ in Figure 15. As indicated in [10] and our Introduction, the curve $\tilde{\Upsilon}_+$ (resp. $\tilde{\Upsilon}_-$) being the critical conditions of transition between monostability and bistability were obtained approximatively in the special case that the degenerate equilibrium $E : (u, v)$ lies closely near the $v$-axis, i.e., $u \ll v$ (resp. the $u$-axis, i.e., $v \ll u$) under the assumption that both $a$ and $b$ are large. In our paper we obtain the curves $\Upsilon_{\pm}$ accurately without their assumption and prove that they are both saddle-node bifurcation curves. Therefore, our results correct the boundary $\tilde{\Upsilon}$ of bistable region. Choosing $(b, a) = (3, 2.8)$, which lies between $\tilde{\Upsilon}_+$ and $\Upsilon_+$, and $(b, a) = (3, 1.8)$, which lies between $\tilde{\Upsilon}_-$ and $\Upsilon_-$, we make numerical simulations with the software PPLANE, showing that the system is monostable rather than bistable in Figures 16 and 17. This demonstrates that the region between $\Upsilon_+$ and $\Upsilon_-$ in Figure 15 is true but was not found in [10].

In comparison with the work [2] by the iGEM Duke Team in 2013, which plots intersection between the horizontal isocline and the vertical isocline numerically to shows that system (1) has exactly three equilibria for the choice $(a, b, \beta, \gamma) = (4, 4, 3, 3)$ and a unique equilibrium for the choice $(a, b, \beta, \gamma) = (3, 3, 1, 2)$, our results do not specify any choice but generally give conditions for exact number of equilibria analytically.

The genetic toggle switch is a synthetically constructed circuit in *Escherichia coli* to control gene expression. Although some dynamical properties such as multistability and oscillations have been found in the natural genetic circuit, researchers want to build genetic circuits artificially for desired properties. One of desired properties in a gene-regulatory network is the switching behavior between two equilibria. Our paper presents global dynamics of system (3) and gives a condition for bistability. In the bistable state (seen in Figure 15), the stable manifold of the saddle $A_2$ divides the first quadrant into two basins of attraction. On the other hand, the unstable
manifold of the saddle $A_2$, being heteroclinic connections with $A_1$ and $A_3$, makes a separatrix of the two basins so that the upper (lower) half-basin above (below) the separatrix preserves evolution inside the half-basin. The two basins make a mechanism for such a switching and the bifurcation values given in our Theorem 4.1 provide accurate parameter choices which lead to bistability and regulate the capacity to achieve switching behavior.

In this paper we only consider system $S(1, n)$ for convenient computation. Because of the symmetry of (1), one can discuss system $S(m, 1)$ similarly. Our discussion on system (3) exhibits a routine for the general system $S(m, n)$ or system (1) but the computation will be more complicated.

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