CUBO *A Mathematical Journal*
Vol. 8, N° 2, (53 - 61). August 2006.

A Uniqueness Theorem In An Age-Physiology Dependent Population Dynamics

Jean. M. Tchuenche [1]
Department of Mathematical Sciences, University of Agriculture
PMB 2240, Abeokuta, Nigeria.
jmtchuenche@yahoo.com

ABSTRACT

A mathematical model describing the evolution of a population dynamics problem in which, a genetically transmitted disease, Sickle-Cell Anaemia, is prevalent is considered. The genotype or physiological structure of individuals divides such a population naturally into three genotypic groups, namely; normal (AA), carriers (AS) and sickle-cell suffers (SS). An *a priori* estimate of the solution is obtained as well as conditions under which such a solution is unique.

RESUMEN

Se considera un modelo matemático que describe la evolución de un problema de dinámica de poblaciones, en el cual una enfermedad transmitida genéticamente, Sickle-Cell Anemia, es prevalente. El genotipo, o estructura fisiológica de los individuos, divide naturalmente tal población en tres grupos genotípicos, a saber: normal (AA), portadores (AS) y pacientes (SS). Se obtiene una estimación *a priori* de la solución y las condiciones bajo las cuales ella es única.

[1] I am forever thankful to my dear parents, Sébastien (late) and Régine Téguia who worked tirelessly, so I could get a good education. They taught me by teaching and examples, what the most important things in life really are. Thanks are also due to my sister Yvonne Moualeu who made it possible to attend university.

Key words and phrases: *age, genotype, population dynamics, interaction function, estimates, renewal equation.*
Math. Subj. Class.: *34C11, 34C60, 35B40, 35B45, 92D40.*

1 Introduction

As early as 1953, Slobodkin demonstrated that neither age nor size of a Daphnia, taken separately, was sufficient information to predict its physiological reactions. Therefore, apart from age a, a second independent variable, g, say, referred to as the physiological factor will also be a basis for classification of individuals within a population. There are many factors one would like to include in a realistic mathematical model, but mathematical convenience imposes constraints on the number of parameters a model can accommodate (Sowunmi, 2004). Since the physiological factor appears to have been among the least favoured key factors to be included in a model, this motivates us to include such a parameter in our study, though, Gurney and Nisbet (1998) posited that continuous time models of populations composed of individuals distinguishable by both age and size are a traditional source of mathematical headaches. The main difficulty in this paper is the estimation of the renewal equation for each genotypic class. Physiologically structured populations have been extensively studied in the literature (see Sinko and Streifer, 1967; Bell and Anderson, 1967, Metz and Diekmann, 1986; Kooi and Kelpin 2003, to name a few).
Motivated by the outcome from the mating system with genotype structure, and the derivation of the renewal equations (Tchuenche, 2005), we decided to carry out the study of the uniqueness of solutions to the model equation given in (2.1) below. The method of solution is via the one-sided Laplace transform (see Tchuenche, 2002). We have extensively considered the *a priori* estimates in Tchuenche$_b$ (2005). But, it is important to point out that the approach here is simpler, since the parameters considered are few. For instance, the effect of polygamy is left out. The system of equations in (2.1), together with the renewal equations in (2.2) look analytically intractable. It is in order to show that the model is well-posed that we decided to go a step further to prove the uniqueness of its solution.

2 The Model Equations

If the physiological factor represents for instance the foetal Haemoglobin **F** level, then, the genotype in the case of genetically transmitted diseases such as Sickle-Cell Anaemia (SCA), subdivides the population into three phenotypic groups, namely: normal (AA), carriers (AS) and sickle-cell patients (SS). We make reference to SCA because it is the most common inherited defect, which is found in tropical regions, where malaria is endemic. Below are the list of some notations and symbols used in

the sequel.

2.1 Notations

$t, a \in \mathbb{R}_+, g \in \Omega \in \mathbb{R}_+$ are the independent variables time, age and physiological variable respectively.

Suffixes $i, j, k = 1, 2, 3$ correspond to 1:=**AA**, 2:=**AS**, 3:=**SS**, respectively.

$f_i(t, a, g), m_i(t, a, g) \geq 0$, represent the population densities of females and males, respectively in group i, at age a with physiological factor g.

$R_i(a, g) = \mu_i(a, g) + \lambda_i(a, g), \quad i = 1, 2, 3$: force of mortality where the μ_i's are the per capita death rates within a cohort due to anaemia and, since there are quite often additional risks of mortality attending some membership of a population, we then suppose that death from other causes occur at a per capita rate $\lambda_i(a, g)$.
$\mu_1(a, g) = 0$, $\mu_2(a, g) \geq 0$, because during certain strenuous activities, when partial pressure of oxygen is low such as high altitudes (Kecton,1972), carriers develop full-blown anaemia (Tribe *et al.*,1978). The age-physiology dependent vital rates $R_i(a, g)$ are assumed to be sex independent.

l is the common lower bound of the R_i's, while l_i is the lower bound of R_i.

$F_{ij}((m_i(t, a, g_i); f_j(t, a', g_j')), a, a', t)$: function governing the interaction between males and females.

δ_{ij}^k: is the probability of having a neonate of class 'k' from mating between class i-males and j-females.

f_i^j: number of females of class 'i' interacting with class j-males, (Hoppensteadt and Peskin (1975), Milner and Babbiolo (1992) refer to this term as the number of couples) .

$A_{ij}^{(k)}$: average number of children of class 'k' arising from interaction between class i-males and j-females.

Using an evolution equation approach, the dynamical behaviour of individuals can best be described by the set of first order quasi-linear partial differential equation below (for a complete derivation see Tchuenche, 2001), where $u_i(:= m_i + f_i) \in C(\mathbb{R}_+^2 \times \Omega : \mathbb{R}_+)$

$$\begin{aligned} &\frac{\partial u_i(t, a, g_i)}{\partial t} + \frac{\partial u_i(t, a, g_i)}{\partial a} + G_i(a)\frac{\partial u_i(t, a, g_i)}{\partial g_i} = R_i(a, g_i)u_i \\ &u_i(0, a, g_i) = u_{i0}(a, g_i) \\ &u_i(t, 0, g_i) = B_i(t, g_i) \end{aligned} \tag{2.1}$$

i is as defined above, while $G_i(a)$ is the rate of increase or decrease of the physiological variable g_i, which could be taken to represents the levels of haemoglobin F. System (2.1) describes the evolution of a population with an additional structure which could be mass, size or any other attribute that influences the dynamical behaviour of individuals. By modifying the exact form of Sowunmi's (1993) interaction function to suit our own purpose, the renewal equation are given by (also see Tchuenche, 2001, 2005),

$$\begin{aligned}
B_1(t,g_1) &= \int_0^\infty\int_0^\infty\int_0^\infty\int_0^\infty \left[\delta_{11}^{(1)}F_{11}+\delta_{12}^{(1)}F_{12}+\delta_{22}^{(1)}F_{22}\right] d\alpha d\alpha' dg_1 dg_1' \\
B_2(t,g_2) &= \int_0^\infty\int_0^\infty\int_0^\infty\int_0^\infty \left(\delta_{12}^{(2)}F_{12}+\delta_{13}^{(2)}F_{13}+\delta_{22}^{(2)}F_{22}+\delta_{23}^{(2)}F_{23}\right) d\alpha d\alpha' dg dg' \\
B_3(t,g_3) &= \int_0^\infty\int_0^\infty\int_0^\infty\int_0^\infty \left(\delta_{22}^{(3)}F_{22}+\delta_{23}^{(3)}F_{23}+\delta_{33}^{(3)}F_{33}\right) d\alpha d\alpha' dg dg' \qquad (2.2)
\end{aligned}$$

where $\delta_{ij}^{(k)}$ is the probability of having a child of class k from mating between a class i-male and j-female or vice-versa (the S gene transmission is sex independent, thus $F_{ij}=F_{ji}$) and,

$$F_{ij} := F_{ij}((m_i(t,\alpha,g_i);f_j(t,\alpha',g_j')),\alpha,\alpha',g_i,g_i',t). \qquad (2.3)$$

represent the interaction functions between males aged α and females aged α' at time t.

The properties of F_{ij} and $B_i(\cdot,\cdot)$ are enumerated in Tchuenche (2005).

The following assumptions will enable us to prove Theorem 1 below.

(i) $u_0(>0)\in L^1(\mathbb{R}_+;\mathbb{R}_+)$

(ii) $R(\cdot,\cdot),\cdot\in C(\mathbb{R}_{2+}\times\Omega;\mathbb{R}_+)$ is uniformly Lipschitz continuous with respect to its variables and bounded below by a strictly positive constant l, say.

(iii) $F_{ij}((m_i(t,a,g_i);f_j(t,a',g_j),\ \cdot\ ,\ \cdot\ ,\ t)\ :\ \mathbb{R}_+^2\to\mathbb{R}_+$ has compact support, is L^1-measurable for each $(m_i(\cdot,\cdot,\cdot)\ ;\ f_j(\cdot,\cdot,\cdot))$ and for any fixed t.

Let C denote the function space $C(\mathbb{R}_+^3;L^1(\mathbb{R}_+,\mathbb{R}_+))$ and C_T^2 denote the product space $C([0,T];L^1(\mathbb{R}_+,\mathbb{R}_+))$ with itself, for any finite time $T>0$. The operator on C into C defined by the RHS of equation (4.3) below is positive. Let H denote this operator. It is important to point out here that our approach is somewhat different form that of Thieme (1990) and Magal (2001). Our results with hold in $L^1(\mathbb{R}_+^2\times\Omega;\mathbb{R}_+)$, with some little modifications, but since we need to apply Gronwall's lemma, the existence of solutions in C_T^2 is more appropriate.

For $u(t,a,g)\geq 0$; define the norm in L^1 as:

$$u(t,g) := \|u(t,\cdot,g)\|_{L^1(\mathbb{R}_+,\mathbb{R}_+)} := \int_0^\infty |u(t,a,g)|da$$

$$\|u(t,\cdot,g)\| = \|(u_1(t,\cdot,g),u_2(t,\cdot,g),u_3(t,\cdot,g))\|_{L^1}$$

$$= \|u_1(t,\cdot,g)\|_{L^1} + \|u_2(t,\cdot,g)\|_{L^1} + \|u_3(t,\cdot,g)\|_{L^1}$$

where we write L^1 for short.

3 Formulation of problem I

Find $u(t,a,g) \in C_T^2$, such that system (2.1) is solved uniquely for all t, $a \geq 0$, $g \in \Omega$.

Theorem 1. Provided

$$\frac{C}{l+\gamma} < 1,$$

there exists a unique solution $u(t,a,g)$ in C_T^2 that solves Problem I above.

$\gamma(>0)$ and C are constants to be determined. Before attempting a demonstration, we first need some estimates.

4 A Priori Estimate of Solutions

In the regulation of population growth, boundedness and stability of equilibria are two concepts to be given prominence (Sowunmi, 1993). In working towards estimation of parameters, certain assumptions must be made.
Let l represents the common lower bound of $R_i(a,g_i)$, define

$$\begin{aligned} \|u(t,\cdot,\cdot)\|_{L^1(\mathbb{R}_+\times\Omega)} &= \|(u_1,u_2,u_3)\| = \|u_1\| + \|u_2\| + \|u_3\| \\ &= \int_0^\infty \int_0^\infty u(t,a,g)dadg \qquad (4.1) \end{aligned}$$

$$P(t) := \|u(t,\cdot,\cdot)\|_{L^1(\mathbb{R}_+\times\Omega)} \qquad (4.2)$$

where

$P(t)$ is the total population

The first integral representation of system (2.1) is given by:

$$\begin{cases} u_i(t,a,g_i) = H(t-a)\pi_i(a)B_i(t-a,g) + H(a-t)u_{i0}(a-t,g)\dfrac{\pi_i(a)}{\pi_i(a-t)} \\ \\ g_i(a) = g_i(0) + \displaystyle\int_0^\infty G_i(\alpha)d\alpha \end{cases} \qquad (4.3)$$

The complete method of solution can be found in Tchuenche (2002) and Tchuenche$_b$ (2005). If g is taken as the level of haemoglobin **F**, then it becomes an increasing

function of age. We do not wish to belabor the integration with respect to g, because the result is biologically meaningless, and the analysis will appeal to Abelian or Tauberian theorems. We can now estimate u_1 as follows:,

$$\begin{aligned} P_1(t) = \|u_1\| &\leq \int_0^\infty \int_0^\infty e^{-l_1 a} B_1(t-a, g_1) da dg_1 + \\ &+ \int_0^\infty \int_0^\infty e^{-l_1 t} u_{10}(a-t, g_1) da dg_1 \\ &\leq \int_0^t \int_0^\infty e^{-l_1(t-a)} B_1(a, g_1) da dg_1 + \\ &+ \int_0^\infty \int_t^\infty e^{-l_1 t} u_{10}(a-t, g_1) da dg_1 \end{aligned} \tag{4.4}$$

Using the transformation $v = a - t$ in the last expression yields

$$\int_0^\infty \int_0^\infty u_{10}(a, g_1) da dg_1 = U_{10} \tag{4.5}$$

where, after making the aforementioned substitution, and replacing v again by a (since they are dummy variables), with some little algebra, we obtain (4.5). It is a more delicate matter to estimate $B(t, g)$.
Now, we define

$$\int_0^\infty \int_0^\infty F_{ij} d\alpha' dg_1' := A_{ij}^{(k)} f_i^j(t, \cdot, \cdot) \tag{4.6}$$

with the parameters as defined earlier.
Also, let

$$K_{ij}^{(\cdot)} := \delta_{ij}^{(\cdot)} A_{ij}^{(\cdot)} \tag{4.7}$$

Hence, substituting equations (4.5-4.6) in the first expression on the RHS of (4.4) gives

$$\begin{aligned} B_1(a, g_1 &= \int_0^\infty \int_0^\infty \left\{ \delta_{11}^{(1)} A_{11}^{(1)} f_1^1(a, \cdot, \cdot) + \delta_{12}^{(1)} A_{22}^{(1)} f_1^2(a, \cdot, \cdot) + \right. \\ &\left. + \delta_{22}^{(1)} A_{22}^{(1)} f_2^2(a, \cdot, \cdot) \right\} da dg_1 \\ &\leq K_{11}^{(1)} \|f_1^1(a, \cdot, \cdot)\| + K_{12}^{(1)} \|f_1^2(a, \cdot, \cdot)\| + K_{22}^{(1)} \|f_2^2(a, \cdot, \cdot)\| \\ &\leq K_1 \left(\|f_1^1(a, \cdot, \cdot)\| + \|f_1^2(a, \cdot, \cdot)\| + \|f_2^2(a, \cdot, \cdot)\| \right) \\ &\leq K_1 P_1^*(a) \leq K_1 P_1(a) \end{aligned} \tag{4.8}$$

where $K_1 := \max\left(K_{11}^{(1)}, K_{12}^{(1)}, K_{22}^{(1)}\right)$ and $P_1^*(\cdot)$ is the population of interacting females having normal neonates.
Therefore,

$$P(t) \leq \rho K e^{-lt} \left[\int_0^t \int_0^\infty e^{la} (P_1(a) + P_2(a) + P_3(a)) da + U_{10} + U_{20} + U_{30} \right]$$

$U_0 = U_{10} + U_{20} + U_{30}$ and $K = \max(K_1, K_2, K_3)$
$\rho = \max(\rho_1, \rho_2, \rho_3)$; $\rho_i = |g_i(a) - g_i(0)\|$

$$P(t) \leq \rho K e^{-lt}\left[\int_0^t \int_0^\infty e^{la} P(a)dadg + U_0\right]$$

$$P(t) \leq U_0 e^{(\rho K - l)t} \tag{4.9}$$

by the classical Gronwall's lemma [1].

Proof of Theorem 1.
Let C_T^2 denote the product space

$$C([0,T]; L^1(\mathbb{R}_+ \times \Omega, \mathbb{R}_+))$$

with itself, where $L^1(\cdot)$ has been given the L^1-norm. On C_T^2, we use the upper bound norm

$$\|\cdot\|_{C_T^2} = \sup_{0\leq t\leq T} e^{-\gamma t}\|\cdot\|(t)$$

for $\gamma \geq 0$ and arbitrary. This is known as the Bielecki's norm (Light, 1990).
Let $u_1, u_2 \in C([0,T]; L^1(\mathbb{R}_+ \times \Omega))$ be two weak solutions of system (2.1), where suffixes 1 and 2 denote the solutions and not the population cohort (AA, AS, SS),
Let $Q = \{(u_1, u_2) \in C_T^2\}$ be closed and convex, then, let the right hand side of (4.3) represents an operator $H : Q \to Q$ such that for arbitrary $u_1, u_2 \in Q$,

$$\begin{aligned}
\|u_1 - u_2\| &= \|H(u_1)(t) - H(u_2)(t)\| = \|H(u_1) - H(u_2)\|(t) \\
&= \int_0^\infty \int_0^\infty \{u_1(t,a,g) - u_2(t,a,g)\}dadg \\
&\leq e^{-lt}\int_0^\infty \int_0^t e^{la}\{B_1(a,g) - B_2(a,g)\}dadg \\
&\leq \rho K\sigma e^{-lt}\int_0^t e^{la}\|u_1 - u_2\|(\alpha)d\alpha \\
&\leq Ce^{-lt}\int_0^t e^{l\alpha}\|u_1 - u_2\|(\alpha)d\alpha,
\end{aligned} \tag{4.10}$$

where $C = \rho K\sigma$, and $\int_0^\infty B(a,g)dg = \sigma B(a) \leq u$.
Since $\|\cdot\|_{C_T^2} = \sup e^{-\gamma l}\|\cdot\|(t)$, $\gamma(>0)$ is arbitrary, then

$$\begin{aligned}
\|H(u_1) - H(u_2)\| &\leq C\int_0^t e^{-l(l-a)}\|u_1 - u_2\|e^{\gamma a}da \\
&\leq C\|u_1 - u_2\|e^{-lt}\int_0^t e^{(l+\gamma)a}da \\
&\leq \frac{C}{l+\gamma}\|u_1 - u_2\|e^{\gamma t} \\
\Rightarrow \|H(u_1) - H(u_2)\|_{C_T^2} &\leq \frac{C}{l+\gamma}\|u_1 - u_2\|_{C_T^2}.
\end{aligned} \tag{4.11}$$

Hence, H is a contraction if and only if $\frac{C}{l+\gamma} < 1$. For γ large enough, the result follows. ∎

Conclusion: The uniqueness Theorem 1, shows that the operator H has a unique fixed point in C_T^2. Thus, system (2.1) is well-posed, its solution exists and is unique. This means there is a unique function in C_T^2 which solves system (2.1). The proof is without any appeal to a general theory which depends on a deep argument, hoping to avoid going through complicated arguments in the particular case to which our theorem is applied, for the sake of simplicity and mathematical convenience.
The renewal function $B_i(t, g_i)$ captures the pattern of inheritance of the haemoglobin **S** gene (Tchuenche, 2005), without any reference to the selective advantage of haemoglobin **S** over haemoglobin **A** in the transmission dynamics of the gene.

Received: March 2005. Revised: April 2005.

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