

## AN AGE-PHYSIOLOGY DEPENDENT POPULATION DYNAMICS MODEL WITH POLYGAMY

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**Abstract.** This paper considers a new model of a genetically transmitted disease, namely, Sickle-Cell Anaemia in the form of a first order partial differential equation which uses the *time*, *age* and *physiology* variables. The model developed focusses on the interaction functions  $F_{ij}$  which show the pattern of inheritance of hemoglobin **S** (Hb**S**) gene. Polygamy is captured in this study and could be partially responsible for the widespread of this defect in some regions.

### 1. INTRODUCTION

As was pointed out in the introduction of [9], in the regulation of population growth, age, physiological factors, density dependence, gestation period and the mating pattern are some of the key factors that one would want to include in a realistic mathematical model of the dynamics of a 2-sex population. However, the mathematical convenience imposes constraints on the number of factors that a single model can accommodate. Since the physiological factor appear to have been among the least favoured, this motivates our introduction of such factor into the model. A brief comment on some related works provides the context of this paper.

C. Castillo-Chavez [1] proposed a 1-sex model in which an abstract physiological factor is allowed for, whilst age is discretized. A. T. Dash and R. Cressman [2] developed a 2-sex discrete time model in which polygamy is taken into consideration, and a specific function was chosen to represent the polygamous mating pattern. C. O. A. Sowunmi [9] in contrast to other authors considered polygamy in a way that does not require the specification of a particular mating function. One expects mating patterns to be driven by saturable interactions [6] between males and females, therefore, a critical condition which characterizes saturable processes is known as the *Generalized Law of the Minimum* [6, 9].

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Polygamy is but one out of a myriad of processes – biological, chemical to name but a few, which come under the umbrella name: species interactions and according to Rosen (as reported in [7]), polygamous mating systems can be found in a vast array of animal species including most mammals and many birds. Indeed, in at least 70% of all human societies there is some degree of polygamy. But it is ironical that with the exception of papers [5] and [7], the mathematical study of polygamous mating has never been undertaken [5], though few authors in the recent past as mention above make reference to it. The mathematical difficulties involved in the analysis of such models and the complex nature of the equations involved (though not a sufficient reason to shelve this vital research area) may seem to be some of the basic reasons why most authors ignore polygamy in their models. In fact, polygamy is a non-negligible index that cannot be by-pass in genetic disease transmission. It is in order to understand better the effect of polygamy on the transmission dynamics of genetic diseases that this study is carry out. This paper is therefore a theoretical approach of a model of population dynamics in which SCA, a factor in the health of the individuals provides a basis for elaboration. The structure of the model is based on and earlier successful dynamic model of a genetically transmitted disease [11, 13]. We therefore combine it with theoretical observations to provide a comprehensive model of the effect of polygamy on disease dynamics.

## 2. THE BASIC MODEL

Sickle-Cell Anaemia is the most common inherited genetic defect. The **S** gene which is responsible of this anomaly naturally subdivides the population into three genotypic groups namely: Normal **AA**, Carriers **AS**, and Sickle-Cell patient **SS** (alongside with age cohorts). Moreover, we assume that the population is in a stationary demographic state and the vital dynamics are age-structured [4]. The following assumptions are necessary for the understanding of the rest of this paper.

## 3. NOTATIONS AND ASSUMPTIONS

Since any genetic defect subdivides the population under consideration basically into three phenotypic classes, namely: normal, carriers and affected individuals, the assumptions below form our basis for elucidation. Let  $t, a \in R^+$ ,  $g_i \in \Omega \subset R^+$ ,  $i, j = 1, 2, 3$  and  $1 := AA$ ,  $2 := AS$ ,  $3 := SS$ , also, let  $u_i(t, a, g_i)$  represents the population density of male individuals at time  $t$ , aged  $a$ , with physiological variable  $g_i$ , which may represent mass, length, size or any other attribute that influences the dynamics of

individuals;  $(v_i(t, a', g_i))$  is similarly defined for females). The prime is used to distinguish between the ages of males and females.

Let  $u(t, a) = \int_0^\infty u(t, a, g)dg$  be the total male population at time  $t$ , aged  $a$ , then for  $u(t, a) \geq 0$ ; define the norm in  $L^1(R^+ : R^+)$  as:

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

$$\begin{aligned} \|u(t, \cdot)\|_L^1 &= \|(m_1(t, \cdot), m_2(t, \cdot), m_3(t, \cdot))\|_{L^1} = \\ &= \|m_1(t, \cdot)\|_{L^1} + \|m_2(t, \cdot)\|_{L^1} + \|m_3(t, \cdot)\|_{L^1}, \end{aligned}$$

where we write  $L^1$  for short. All integrals are taken in the sense of Lebesgue.

- (i)  $u_0 \in L^1(R^+; R^+); u_0 \in R^{2+}$ .
- (ii)  $R(\cdot, \cdot) \in C(R^+ \times \Omega; R^+)$  is uniformly Lipschitz continuous with respect to its variables and bounded below by a strictly positive constant  $l$ , say.
- (iii)  $F_{ij} : R^{5+} \rightarrow R^+$  is monotone increasing and globally Lipschitz in its first two variables (the Lipschitz continuity being uniform with respect to the last three variables). Also,  $F_{ij}((u_i(t, a); v_j(t, a'), \cdot, \cdot, t) : R^{2+} \rightarrow R^+$  has compact support,  $\text{supp}F_{ij} \subseteq [w_{mr}, w_{ms}] \times [w_{fr}, w_{fs}]$ .
- (iv)  $u(t, \cdot) \in C[R_+, L^1(R^+, R^+)]$  continuously,  $t \in R^+$ .
- (v)  $u$  has directional derivatives along the curves  $t - a = \text{constant}$ , at every point of  $R^{2+}$  and satisfies the system of equations in 1 below.
- (vi)  $\exists \kappa_i, \tau_j > 0$ , continuous over  $R^{2+}$ , and having the same support as  $F_{ij}((u_i(t, a); v_j(t, a'), \cdot, \cdot, t)$ , such that:

$$F_{ij}((u; v), a, a', t) \leq \min[\kappa_i(a, a')u, \tau_j(a, a')v],$$

satisfying the equalities [7]

$$\int k_i(a, a')u_i(t, a)da' = (w_{fr} - w_{fs})k_i(a)u_i(t, a),$$

and

$$\int \tau_j(a, a')v_j(t, a')da = (w_{mr} - w_{ms})\tau_j(a')v_j(t, a'),$$

where  $[w_{fr}, w_{fs}]$  represents the reproductive age interval for females, this means pregnancy cannot occur earlier than age  $w_{fr} > 0$ . For males, the reproductive period spans the age  $w_{mr}$  to  $w_{ms}$ , while  $k_i(a, a')$  is the polygamy factor,  $\tau_i$  is a measure of the maximum relative reproductive load on females aged  $a'$ , induced by males aged  $a$  [7].

The model equations for the male population are given by the following system of first order quasi-linear partial differential equations with appropriate initial conditions.

$$\frac{\partial u_i}{\partial t} + \frac{\partial u_i}{\partial a} + G_i(a) \frac{\partial u_i}{\partial g_i} = -R_i(a, g_i)u_i,$$

and

$$(1) \quad \begin{aligned} u_i(0, a, g_i) &= u_{i0}(a, g_i), \\ u_i(t, 0, g_i) &= B_i(t, g_i), \end{aligned}$$

where  $G_i > 0$  is the velocity of  $g_i$ ,  $R_i > 0$  is the daily death removal rate, while  $B_i(\cdot, \cdot)$  represents the birth or renewal functions, given by (3) below.

For the sake of brevity, we will drop the suffix  $i$  and shall refer to it as appropriate. The general interaction function is given by

$$F((u(t, a, g); v(t, a', g)), a, a', t),$$

and since the dynamics of individuals varies with sex, for the purpose of this study, we modify the above mixing function as follows: If  $m_i(t, a, g)$  represents the density of males of class  $i$ , while  $f_j(t, a', g)$  is that of females, then, we have as interaction function

$$(2) \quad F_{ij}((m_i(t, a, g); f_j(t, a', g)), a, a', t).$$

The function in (2) above representing the general interaction between males of class 'i' and females of class 'j', is well-defined and satisfies the General Law of the Minimum [8] adapted to this particular model. It is to be noted that  $m_i$  and  $f_j$  satisfy the same properties as  $u$  above.

Hence the birth equations are given by:

$$\begin{aligned} B_1(t, g) &= \int_0^\infty \int_0^\infty (\delta_{11}^{(1)} F_{11} + \delta_{12}^{(1)} F_{12} + \delta_{22}^{(1)} F_{22}) da da', \\ B_2(t, g) &= \int_0^\infty \int_0^\infty (\delta_{12}^{(2)} F_{12} + \delta_{12}^{(2)} F_{12} + \delta_{22}^{(2)} F_{22} + \delta_{23}^{(2)} F_{22}) da da', \\ B_3(t, g) &= \int_0^\infty \int_0^\infty (\delta_{22}^{(3)} F_{22} + \delta_{23}^{(3)} F_{23} + \delta_{33}^{(3)} F_{33}) da da', \end{aligned}$$

where  $\delta_{ij}^{(k)}$  denotes the probability of having a child of class 'k' from mating between class  $i$ -males and  $j$ -females and vice-versa,  $i, j, k = 1, 2, 3$ . Since gene transmission is sex-independent, we assume that  $\delta_{ij}^{(\cdot)} = \delta_{ji}^{(\cdot)}$ , that is, the genotypes are indistinguishable, a property known as the principle of the equality of sexes in inheritance [12, 13].  $0 \leq \delta_{ij}^{(\cdot)} \leq 1$ , and  $(\delta_{ii}^{(i)} = 1)$ .

For more details on the above derivation and the properties of  $F_{ij}$  and  $B_i(t, g)$  see [12] and [13].

**Theorem 1.** *System 1 has an integral representation of the form*

$$(3) \quad \begin{cases} u(t, a, g) = H(t - a)\pi(a)B(t - a, g) + H(a - t)u_0(a - t, g)\frac{\pi(a)}{\pi(a-t)}, \\ g(a) = g(0) + \int_0^a G(\alpha)d\alpha. \end{cases}$$

*Remark:* (3) is obtained by applying the Laplace transform (L.T.), with respect to time, and solving the ODE via the method of characteristics. The L.T. method applies easily, if the coefficient of the unknown function and its derivatives are independent of time  $t$ . Unless otherwise stated, we assume throughout that every function  $u(t)$  say, which has a well-defined Laplace transform over some region of the complex plane is a function of exponential order as  $t \rightarrow \infty$ . The transform operation is performed with respect to time  $t$ , with  $p \in C$  as the transform variable. For many applications, it is enough to regard  $p$  as a real, but in general, it should be taken as complex [3]. No approximation is made when the L.T. method is employed, therefore we loose nothing in the equation parameters, and the difficulty usually encounters is to obtain the inverse transform.

*Proof.* The transform of (1) with  $\mathbb{L}$  representing the Laplace transform operator and ' $\hat{u}$ ' the transform of  $u \in L^1$  (which is sufficiently well-behaved) is given by

$$\begin{aligned} & \mathbb{L}[u_t + u_a + G(a)u_g + R(a, g)u] = \\ & = \int_0^\infty e^{-pt} \frac{\partial}{\partial t} u dt + \frac{\partial}{\partial a} \int_0^\infty e^{-pt} u dt + G(a, g) \int_0^\infty e^{-pt} \frac{\partial u}{\partial g} dt + \\ & + R(a, g) \int_0^\infty e^{-pt} u dt = 0, \end{aligned}$$

i.e.

$$(4) \quad \frac{\partial \hat{u}}{\partial a} + G(a) \frac{\partial(\hat{u})}{\partial g} + (p + R)\hat{u} = u_0(a, g).$$

Solving (4) by the method of characteristics yields:

$$(5) \quad g(a) = g(0) + \int_0^a G(\alpha)d\alpha,$$

and

$$\frac{d\hat{u}}{da} + (p + R)\hat{u} = u_0.$$

Therefore,

$$\begin{aligned} \hat{u}(p, a, g) & = e^{-pa} e^{-\int_0^a R(\alpha, g)d\alpha} \int_0^a \{u_0(\xi, g)\} e^{\int_0^\xi (p+R(a, g))da} d\xi + \\ & + K(p) e^{-\int_0^a (p+R)d\alpha}, \end{aligned}$$

where  $K(p)$  is the constant of integration, given by the condition

$$K(p) := \hat{u}(p, 0, g) = \hat{B}(p, g).$$

Define

$$(6) \quad \pi(a) := \exp \left\{ - \int_0^a R(\alpha, g) d\alpha \right\}.$$

Then, (6) now reads:

$$(7) \quad \hat{u}(p, a, g) = \int_0^a e^{-p(a-\xi)} \pi(a) \{u_0(\xi, g)\} e^{\int_0^\xi R(a, g) da} d\xi +$$

$$(8) \quad + \hat{B}(p, g) e^{-pa} \pi(a).$$

The last term on the right hand side of (8) is the transform of

$$(9) \quad B(t-a, g) e^{-\int_0^a R(\alpha, g) d\alpha} H(t-a) = B(t-a, g) \pi(a) H(t-a).$$

Secondly, using the transformation  $\xi = a - s$ ,  $d\xi = -ds$  in the term containing  $u_0$ , we obtain by inspection.

$$(10) \quad u_0(a-t, g) H(a-t) \frac{\pi(a)}{\pi(a-t)} = u_0(a-t, g) \frac{\pi(a)}{\pi(a-t)} H(a-t),$$

$$(11) \quad g(a) = g(0) + \int_0^a G(\alpha) d\alpha.$$

From (9) and (11), the result follows.  $\square$

#### 4. A PRIORI ESTIMATES

Populations can also be regulated by keeping them at equilibrium [8] values and in order to control the rapid growth, bounds must be imposed on them. It is in line with the control measure that we need to establish estimates in order to investigate the behavior in parameter values of the model.

Without any ambiguity, let

$$m_i(t, a) = \int_{\Omega} m_i(t, a, g) dt.$$

The appropriate renewal equation will be denoted by  $B_i(t)$ . The interaction function  $F_i((m_i(t, a); f_i(t, a')), a, a', t)$  satisfies assumption (vi):

$$\int_0^\infty k_i(a, a') m_i(t, a) da' = (w_{fr} - w_{fs}) k_i(a) m_i(t, a).$$

Without loss of reality, let  $k_i(a, a') = k_i(\geq 1)$ ,  $\tau_j(a, a') = \tau_j(\geq 1)$ , be two positive constants, and  $a_{ij}$  represents the proportions of individuals of class 'i' who are married to those of the j-class (the  $a'_{ij}$ s are often referred to as acceptance probabilities [11], [12] and [13], or preference functions [8]; these functions may depend on age, time, sex, etc.).

If  $i$  is fixed, then,  $\sum_{j=1}^3 a_{ij} \leq 1$ .  $a_{ij} (\geq 0) \in R^+$  is a bio-social parameter which may vary greatly, if genetic screening is carried out before any legal union. The table below shows all the possible combination of  $a_{ij}$ .

	$f_1$	$f_2$	$f_3$
$m_1$	$a_{11}$	$a_{12}$	$a_{13}$
$m_2$	$a_{21}$	$a_{22}$	$a_{23}$
$m_3$	$a_{31}$	$a_{32}$	$a_{33}$

**Theorem 2.** Let  $u > 0$ , if  $l (> 0)$  is the common lower bound of  $l_1, l_2$  and  $l_3$ , then

$$\|u(t, \cdot)\| \leq U_0 e^{(b_1 + b_2 + b_3 - l)t},$$

where

$$U_0 = U_{01} + U_{02} + U_{03}.$$

*Proof.* Since  $u(t, a) = m_1(t, a) + m_2(t, a) + m_3(t, a)$ ; the following obvious inequality is true and will prove useful in the sequel

$$m_1(t, a) + m_2(t, a) \leq u(t, a).$$

Now we have the following:

If  $\min(k_i \times m_i, \tau_j \times f_j) = k_i m_i(t, a)$ , then

$$\begin{aligned} B_1(t) &= \int_0^\infty \int_0^\infty (F_{11} + \delta_{12}^{(1)} F_{12} + \delta_{22}^{(1)} F_{22}) da da' \leq \\ &\leq \int_0^\infty \int_0^\infty (k_1 a_{11} m_1 + \delta_{12}^{(1)} k_1 a_{12} m_1 + \delta_{12}^{(1)} k_1 a_{21} m_2 + k_1 a_{22} \delta_{22}^{(1)} m_2) da da' \leq \\ (12) &\leq k_1 (w_{fr} - w_{fs}) \int_0^\infty \left\{ (a_{11} + a_{12} \delta_{12}^{(1)}) m_1 + m_2 (a_{21} \delta_{12}^{(1)} + a_{22} \delta_{22}^{(1)}) \right\} da \leq \\ &\leq k_1 \bar{a}_1 (w_{fr} - w_{fs}) \int_0^\infty \{m_1(t, a) + m_2(t, a)\} da, \end{aligned}$$

where

$$\bar{a}_1 = \max \left( a_{11} + a_{12} \delta_{12}^{(1)}, a_{21} \delta_{12}^{(1)} + a_{22} \delta_{22}^{(1)} \right).$$

Similarly,

$$B_2(t) \leq k_2 \bar{a}_2 (w_{fr} - w_{fs}) \int_0^\infty (m_1(t, a) + m_2(t, a) + m_3(t, a)) da,$$

where

$$\bar{a}_2 = \max \left( a_{12} \delta_{12}^{(2)}, a_{21} \delta_{12}^{(2)} + a_{22} \delta_{22}^{(2)} + a_{23} \delta_{23}^{(2)}, a_{32} \delta_{32}^{(2)} \right).$$

$$B_3(t) \leq k_3 \bar{a}_3 (w_{fr} - w_{fs}) \int_0^\infty (m_2(t, a) + m_3(t, a)) da,$$

where

$$\bar{a}_3 = \max \left( a_{22}\delta_{22}^{(3)} + a_{23}\delta_{23}^{(3)}, a_{32}\delta_{32}^{(3)} \right) + a_{33}$$

$\bar{a}_1, \bar{a}_2, \bar{a}_3$  are positive constants. Also, from (3) and (12), we have

$$\|u(t, \cdot)\|_{L^1(R^+)} = \int_0^t \sum_{n=1}^3 B_n(t-a)\pi_n(a)da + \int_t^\infty \sum_{n=1}^3 u_{0n}(a-t)\pi_n(t)da,$$

where

$$\pi_n(t) := \frac{\pi_n(a)}{\pi_n(a-t)}.$$

Considering the term involving  $B_1$  first, we have

$$\begin{aligned} & \int_0^t B_1(t-a)\pi_1(a)da \leq \\ & \leq k_1\bar{a}_1(w_{fr} - w_{fs}) \int_0^t \pi_1(a) \int_0^\infty m_1(t-a, \alpha) + m_2(t-a, \alpha) d\alpha da \leq \\ & \leq k_1\bar{a}_1(w_{fr} - w_{fs})e^{-l_1t} \int_0^t e^{l_1a} \|m_1(a, \cdot) + m_2(a, \cdot)\|_{L^1} da \leq \\ & \leq b_1e^{-l_1t} \int_0^t e^{l_1a} \|u(a, \cdot)\|_{L^1} da, \end{aligned}$$

where  $l_1 > 0$ , is the lower bound of the death rate  $R_1$ ,

$b_1 := k_1\bar{a}_1(w_{fr} - w_{fs}) > 0$ .

Also,

$$\int_t^\infty u_0(a-t)\pi_1(t)da \leq U_{01}e^{-l_1t},$$

where

$$U_{01} := \int_0^t u_{01}(a)e^{l_1a} da.$$

We estimate  $B_2$  and  $B_3$  similarly. Thus,

$$\begin{aligned} \|u(t, \cdot)\|_{L^1(R^+)} & \leq U_{01}e^{-l_1t} + b_1e^{-l_1t} \int_0^t e^{l_1a} \|u(a, \cdot)\| da + \\ & \quad + U_{02}e^{-l_2t} + b_2e^{-l_2t} \int_0^t e^{l_2a} \|u(a, \cdot)\| da + \\ & \quad + U_{03}e^{-l_3t} + b_3e^{-l_3t} \int_0^t e^{l_3a} \|u(a, \cdot)\| da. \end{aligned}$$

Hence, if  $l(> 0)$  is the common lower bound of  $l_1, l_2$  and  $l_3$ , on applying the classical Gronwall's Lemma, we obtain

$$\|u(t, \cdot)\| \leq U_0e^{(b_1+b_2+b_3-l)t},$$

where

$$U_0 = U_{01} + U_{02} + U_{03}.$$

□

Establishing a lower bound for this population model is quite difficult, but the biologically relevant lower bound is 0, that is;  $0 < \|u(t, \cdot)\| \leq U_0 e^{(b_1 + b_2 + b_3 - l)t}$ . Negative solutions are biologically irrelevant or meaningless [14]. After obtaining the above result, one therefore asks: How can we minimize the occurrence of genetic defects? To answer this question, we need to apply the result obtained to a specific example. This is the purpose of the next section.

## 5. AN APPLICATION

The above dynamic model can serve as a standard for quantitative analysis of the effect of polygamy on disease dynamics, and as a basis for investigating the behavior in parameter value of the estimates of the population. The question earlier posed is as important as stability, because we use the concept of sensitivity analysis to give answer in the mathematical setting, which is interesting from the biological point of view, and suggestions are made afterwards. So,

*How can we or what are the best ways to reduce the population of carriers?*

This Section is concerned with the best possible ways to reduce the population of carriers (**AS**), provided sickle-cell patients are not allowed to marry at all (a realistic and natural constraint). The theoretical way to prevent most genetic disorders is to control mating with carriers of the defective gene, because in general, they are quite normal in appearance and have virtually no increase in morbidity and mortality above the normal population. A lot of work has been done on the biology of SCA, but none or very little on the dynamics of its population [11].

The birth modulus  $\beta_i > 0$ , is introduced here for the simple reason that family planning affects the number of offsprings and consequently the rate of birth.

Let the population densities of males and females be

$$u(t, a) = m_1(t, a) + m_2(t, a); \quad v(t, a') = f_1(t, a') + f_2(t, a'),$$

respectively,  $m_3(t, a)$  and  $f_3(t, a')$  are neglected here, if we assume that their contribution to population feedback is sufficiently small. The method of estimating the renewal equations is the same as that in (2), the only addition being the birth rate  $\beta_i$ .

Let  $\min(k_i \times m_i, \tau_j \times f_j) = k_i \times m_i(t, a)$ , then

$$\begin{aligned} B_1(t) &= \int_0^\infty \int_0^\infty \beta_1 \left( F_{11} + \delta_{12}^{(1)} F_{12} + \delta_{22}^{(1)} F_{22} \right) da da' \leq \\ &\leq \beta_1 \int_0^\infty \int_0^\infty \left( k_1 a_{11} m_1 + \delta_{12}^{(1)} k_1 a_{12} m_1 + \delta_{12}^{(1)} k_1 a_{21} m_2 + k_1 a_{22} \delta_{22}^{(1)} m_2 \right) da da' \leq \\ &\leq \beta_1 k_1 (w_{fr} - w_{fs}) \int_0^\infty \left\{ \left( a_{11} + \delta_{12}^{(1)} a_{12} \right) m_1 + m_2 \left( a_{21} \delta_{12}^{(1)} + a_{22} \delta_{22}^{(1)} \right) \right\} da. \end{aligned}$$

Let  $\bar{a}_1 := \max \left( a_{11} + \delta_{12}^{(1)} a_{12}, a_{21} \delta_{12}^{(1)} + a_{22} \delta_{22}^{(1)} \right)$ , then

$$B_1(t) \leq \beta_1 k_1 \bar{a}_1 (w_{fr} - w_{fs}) \int_0^\infty \{m_1(t, a) + m_2(t, a)\} da.$$

In the case where carriers are not allowed to interact (i.e., inter-marry),  $a_{22}$  is identically zero and so,  $\bar{a}_1$  can be redefined as

$$a_1 := \max \left( a_{11} + a_{12} \delta_{12}^{(1)}, a_{21} \delta_{12}^{(1)} \right).$$

Hence,

$$B_1(t) \leq \beta_1 k_1 a_1 (w_{fr} - w_{fs}) \int_0^\infty \{m_1(t, a) + m_2(t, a)\} da.$$

Similarly,

$$\begin{aligned} B_2(t) &= \int_0^\infty \int_0^\infty \left( (\delta_{12}^{(2)} F_{12} + \delta_{13}^{(2)}) F_{12} + \delta_{22}^{(2)} F_{22} + \delta_{23}^{(2)} \right) da da' \leq \\ &\leq \beta_2 k_2 (w_{fr} - w_{fs}) \int_0^\infty \left( a_{12} \delta_{12}^{(2)} m_1 + \delta_{12}^{(2)} a_{21} m_2 + \delta_{22}^{(2)} a_{22} m_2 + \right. \\ &\quad \left. + \delta_{23}^{(2)} a_{23} m_2 + \delta_{23}^{(2)} a_{32} m_3 \right) da. \end{aligned}$$

Let

$$\bar{a}_2 := \max \left( a_{12} \delta_{12}^{(2)}, a_{21} \delta_{12}^{(2)} + a_{22} \delta_{22}^{(2)} + a_{23} \delta_{23}^{(2)}, a_{32} \delta_{23}^{(2)} \right),$$

then

$$B_2(t) \leq \beta_2 k_2 \bar{a}_2 (w_{fr} - w_{fs}) \int_0^\infty \{m_1(t, a) + m_2(t, a) + m_3(t, a)\} da.$$

If  $a_{22} = a_{23} = a_{32} \equiv 0$ , then define

$$a_2 := \max \left( \delta_{12}^{(2)} a_{12}, \delta_{12}^{(2)} a_{21} \right),$$

and

$$B_2(t) \leq \beta_2 k_2 a_2 (w_{fr} - w_{fs}) \int_0^\infty \{m_1(t, a) + m_2(t, a)\} da.$$

$$\begin{aligned}
B_3(t) &= \int_0^\infty \int_0^\infty \left( \delta_{22}^{(3)} F_{22} + \delta_{23}^{(3)} F_{23} + F_{33} \right) da da' \leq \\
&\leq \beta_3 k_3 (w_{fr} - w_{fs}) \int_0^\infty \left( \delta_{22}^{(3)} a_{22} m_2 + \delta_{23}^{(3)} a_{23} m_2 + \delta_{23}^{(3)} a_{32} m_3 + a_{33} m_3 \right) da \leq \\
&\leq \beta_3 k_3 \bar{a}_3 (w_{fr} - w_{fs}) \int_0^\infty \{m_2(t, a) + m_3(t, a)\} da,
\end{aligned}$$

where

$$\bar{a}_3 = \max \left( a_{22} \delta_{22}^{(3)} + \delta_{23}^{(3)} a_{23}, a_{32} \delta_{23}^{(3)} + a_{33} \right).$$

If  $a_{22} = a_{23} = a_{32} \equiv 0$ , then

$$B_3(t) = 0.$$

Now the case  $\min(k_i m_i, \tau_j f_j) = \tau_j(a, a') f_j(t, a')$  can be considered, but for the sake of brevity we shall not dwell into the computations here. The only difference is that the expression  $w_{fr} - w_{fs}$  is replaced by  $w_{mr} - w_{ms}$ .

The *a priori* estimates are obtained as follows:

**Lemma 1.** *Let  $l$  be common lower bound of  $l_1$  and  $l_2$ , and  $U_0 = U_{01} + U_{02}$ , then*

$$\|u(t, \cdot)\| \leq U_0 e^{(b_1 + b_2 - l)t}.$$

*Proof.* Since

$$\begin{aligned}
u(t, a) &= \{B_1(t - a)\pi_1(a) + B_2(t - a)\pi_2(a) + B_3(t - a)\pi_3(a)\}H(t - a) + \\
&+ \{u_{01}(a - t)\pi_1(t) + u_{02}(a - t)\pi_2(t) + u_{03}(a - t)\pi_3(t)\}H(a - t),
\end{aligned}$$

then

$$\|u(t, \cdot)\|_{L^1} = \int_0^t \sum_{n=1}^3 B_n(t - a)\pi_n(a) da + \int_t^\infty \sum_{n=1}^3 u_{0n}(a - t)\pi_n(t) da.$$

Now,

$$\begin{aligned}
\int_0^t B_1(t-a)\pi_1(a)da &\leq \\
&\leq \beta_1 k_1 a_1 (w_{fr} - w_{fs}) \int_0^t \pi(a) \int_0^\infty (m_1(t-a, \alpha) + m_2(t-a, \alpha)) d\alpha da \leq \\
&\leq \beta_1 k_1 a_1 (w_{fr} - w_{fs}) \int_0^t \int_0^\infty (m_1(a, \alpha) + m_2(a, \alpha)) \pi(a-t) d\alpha da \leq \\
&\leq \beta_1 k_1 a_1 (w_{fr} - w_{fs}) e^{-l_1 t} \int_0^t e^{l_1 a} \|m_1(a, \cdot) + m_2(a, \cdot)\|_{L^1} da \leq \\
&\leq b_1 e^{-l_1 t} \int_0^t e^{l_1 a} \|m_1(a, \cdot) + m_2(a, \cdot)\|_{L^1} da \leq \\
&\leq b_1 e^{-l_1 t} \int_0^t e^{l_1 a} \|u(a, \cdot)\|_{L^1} da.
\end{aligned}$$

Also,

$$\begin{aligned}
\int_t^\infty u_{01}(a-t)\pi_1(t)da &\leq e^{-l_1 t} \int_0^\infty u_{01}(a) e^{l_1 a} da \leq \\
&\leq U_{01} e^{-l_1 t},
\end{aligned}$$

where  $U_{01} := \int_0^\infty u_{01}(a) e^{l_1 a} da$ ,  $b_1 := \beta_1 k_1 a_1 (w_{fr} - w_{fs})$ , and  $l_i > 0$  is as defined earlier. Similarly,

$$\int_0^t B_2(t-a)\pi_2(a)H(t-a)da \leq b_2 e^{-l_2 t} \int_0^t e^{l_2 a} \|m_1(a, \cdot) + m_2(a, \cdot)\| da.$$

Hence,

$$\begin{aligned}
\|u(t, \cdot)\| &\leq b_1 e^{-l_1 t} \int_0^t e^{l_1 a} \|u(a, \cdot)\| da + U_{01} e^{-l_1 t} + \\
&\quad + b_2 e^{-l_2 t} \int_0^t e^{l_2 a} \|u(a, \cdot)\| da + U_{02} e^{-l_2 t} + \\
&\quad + b_3 e^{-l_3 t} \int_0^t e^{l_3 a} \|u(a, \cdot)\| da + U_{03} e^{-l_3 t}.
\end{aligned}$$

Since we assume no interactions among **AS**, and also that the contribution of **SS** is small, then

$$\begin{aligned}
\|u(t, \cdot)\| &\leq U_{01} e^{-l_1 t} + b_1 e^{-l_1 t} \int_0^t e^{l_1 a} \|u(a, \cdot)\| da + \\
&\quad + U_{02} e^{-l_2 t} + b_2 e^{-l_2 t} \int_0^t e^{l_2 a} \|u(a, \cdot)\| da.
\end{aligned}$$

Let  $l < \min(l_1, l_2)$ , and  $U_0 = U_{01} + U_{02}$ , then

$$\|u(t, \cdot)\| \leq U_0 e^{(b_1 + b_2 - l)t},$$

by Gronwall's Lemma.  $\square$

For the population of males of class **AS** to decrease, the parameters of the equation show, that  $b_2 = \beta_2 k_2 a_2 (w_{fr} - w_{fs})$  should be small, and this can happen, if  $\beta_2$ ,  $k_2$  and  $a_2$  are arbitrarily small.  $w_{fr} - w_{fs}$  is fixed since it is the reproductive interval for females.

$\beta_2$ : birth rate of carriers can be reduced by a proper family planning.

$k_2$ : polygamy should be discouraged among heterozygous, especially, if we impose the general condition

$$\int_0^\infty \max_a k_i(a, a') da \geq 1.$$

$a_2$ : proportion of heterozygous (**AS**) married to homozygous (**AA**) could as well be reduced, if some carriers agree not to marry at all. They may choose celibacy.  $b_2$  can be interpreted as the birth rate of male carriers from reproductive females in the age bracket  $[w_{fr}, w_{fs}]$ .

In the case of females, we use similar parameters distinguishable from the ones above.

$$\begin{aligned} \tilde{B}_1(t) &\leq \tilde{\beta}_1 \tau_1 \tilde{a}_1 (w_{mr} - w_{ms}) e^{-\tilde{l}_1 t} \int_0^t e^{\tilde{l}_1 a} \|f_1(a, \cdot) + f_2(a, \cdot)\| da \leq \\ &\leq \tilde{b}_1 e^{\tilde{l}_1 t} \int_0^t e^{\tilde{l}_1 a} \|v(a, \cdot)\|_{L^1} da. \end{aligned}$$

Hence,

$$\begin{aligned} \|v(t, \cdot)\|_{L^1} &\leq \tilde{b}_1 e^{\tilde{l}_1 t} \int_0^t e^{\tilde{l}_1 a} \|v(a, \cdot)\| da + v_{01} e^{-\tilde{l}_1 t} + \\ &+ \tilde{b}_2 e^{\tilde{l}_2 t} \int_0^t e^{\tilde{l}_2 a} \|v(a, \cdot)\| da + v_{02} e^{-\tilde{l}_2 t} + \\ &+ \tilde{b}_3 e^{\tilde{l}_3 t} \int_0^t e^{\tilde{l}_3 a} \|v(a, \cdot)\| da + v_{03} e^{-\tilde{l}_3 t}. \end{aligned}$$

If  $a_{22} = a_{23} = a_{33} \equiv 0$ , then

$$\|v(t, \cdot)\| \leq V_0 e^{(\tilde{b}_1 + \tilde{b}_2 - \tilde{l})t},$$

where  $V_0 = V_{01} + V_{02}$ ,  $\tilde{l}$  is the common lower bound for  $\tilde{l}_1$  and  $\tilde{l}_2$ . The estimate of the total population  $P(t)$  is given by

$$\begin{aligned} P(t) &= \int_0^\infty (u(t, a) + v(t, a)) da \leq \|u(t, \cdot)\| + \|v(t, \cdot)\| \leq \\ &\leq U_0 e^{(b_1 + b_2 - l)t} + V_0 e^{(\tilde{b}_1 + \tilde{b}_2 - \tilde{l})t}. \end{aligned}$$

If  $b_1 + b_2 - l = \tilde{b}_1 + \tilde{b}_2 - \tilde{l}$  and  $U_0 + V_0 = P_0$ , then

$$P(t) \leq P_0 e^{(b_1 + b_2 - l)t}.$$

If  $U_0 = V_0$ , then since  $|e^x + e^z| \geq |x + y| \quad \forall x, y \in R^+$ , we have

$$\begin{aligned} P(t) &\geq U_0(b_1 + b_2 + \tilde{b}_1 + \tilde{b}_2 - l_1 - \tilde{l}_1 - l_2 - \tilde{l}_2) = \\ &= U_0(\bar{b}_1 + \bar{b}_2 - \bar{l}_1 - \bar{l}_2) = \\ &= U_0(\bar{b} - \bar{l}), \end{aligned}$$

where  $\bar{b}_1 = b_1 + \tilde{b}_1$ ;  $\bar{b} = \bar{b}_1 + \bar{b}_2$ , and  $\bar{l}_1 = l_1 + \tilde{l}_1 + l_2 + \tilde{l}_2$ .

From (5), the population of female carriers may decrease, if  $\tilde{b}_2$  is small, i.e.,  $\tilde{\beta}_2$  could be made arbitrarily small, if  $\tau_2$  has a strict maximum value which is very small. (5) and (13) give the upper and lower bounds of the population. If the contribution of individuals of class '3' is non negligible, together with the fact that  $m_3(t, a) < m_1(t, a)$ , we obtain our previous result given by (4). If there is no mating between individuals of class '3' and none between those of class '2', then there would be no birth of sickle-cell sufferers and in the long run the initial population of sickle-cell patients will die out (a difficult achievable state indeed!).

## 6. CONCLUSION

This model is an attempt to analyze mathematically an age-structured population dynamic model with an additional structure, in which polygamy is a substantial index. For mathematical convenience, density dependence and gestation period are ignored, but the mating patterns are accounted through the introduction of the interaction function.

(4) tells us that the population of carriers (AS) and sickle-cell sufferers (SS) will increase, if  $b_2, b_3 \gg 1$ , the main contributing parameters being  $k_2$  and  $k_3$ , the polygamy factors. Couples with a parent having a defective gene should minimize the number of their offsprings by an appropriate family planning and genetic counselling. Such individuals should avoid polygamy. From the aforementioned, it is obvious therefore that, polygamy factor is an index to be given prominence in the study of 2-sex population models and

polygamous mating deserves due consideration in genetic disease transmission.

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