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# Non linear dynamic equation for deoxyhemoglobins aggregation: A phenomenological approach

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***Abstract***

***In a previous work Dejardin and Olatunji* [1], *a mathematical model is derived for the kinetics of the Deoxyhemoglobin S (deoxy-HbS). The analytical function A(t) obtained for the time evolution of the absorbance measured in turbidity, satisfactorily fits the experimental data of Poyart et al* [2]. *In the present paper, starting with the function A(t), we used a phenomenological approach to derive a nonlinear dynamic equation for the aggregation of deoxy-HbS. Every parameter of the governing equation can be assigned a clear physical meaning. Moreover, drawing on the work of Quemada* [3], *we introduced in the parameters base a scalar structural parameter $\lambda(t, x)$ which depends on the time t and on a set of controlling factors denoted x Furthermore, the set of controlling factor x can be limited to, say, the volume fraction $\phi$, a constant shear rate $\dot{\gamma}$, the deoxy-HbS concentration c, the temperature T, and other factors which influence the aggregation dynamics. In this paper, we developed the solution of the governing equation under steady conditions and applied the results to some rheological properties of deoxy-HbS gel.***

***Keywords:*** Deoxyhemoglobin S aggregation, Nonlinear dynamic equation, Steady properties of HbS gel.

## 1.0 Introduction

**S**ickle cell hemoglobin (HbS) is a genetic variant of the human normal hemoglobin (HbA) in which the vanyl residue at the β-position replaces the normally occurring glutamyl residue. In the deoxygenated state, and under certain experimental conditions, HbS molecules can polymerize in solution as well as inside the red blood cell. The deformation of erythrocytes is caused by the formation of liquid crystalline tactoid of deoxy-HbS in the cell. The formation of liquid deoxy-HbS crystalline factoid constitutes the main pathogenic process in sickle cell anaemia patients.

Thanks to the extensive research, there is a rich amount of information on the molecular and cellular properties of deoxy-HbS as well as on its polymerization as studied by Poyart et al [2]. To test our theoretical model, we use the numerical values of absorbance measured in turbidity experiments [2]. As some experimental factors, we indicate that after rapid variation of the temperature from 0 to 30˚C, the turbidity of the deoxy-HbS solution is measured at 700 nm, i.e. at a wavelength of spectrum in the zone of small absorbance for oxy-HbA and deoxy-HbA. Moreover, the absorbance maximum shift is highly sensitive to deoxy-HbS concentration, temperature, and ionic strength of the buffer.

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In the present theoretical model, we assumed that the polymerization of deoxy-HbS is closely relatedto the time-dependent variation of the absorbance measured in turbidity. This hypothesis is consistent with spectrophotometric experiments [2] which clearly indicate that in the same conditions, the solution of deoxy-HbA does not present any molar absorbance modification.

Therefore, the equation governing the molecular dynamics of sickle cell hemoglobin polymerization can be readily derived without considering explicitly, the details of the double nucleation mechanism, as described by (Hofrichter et al [4].

More precisely, this double nucleation molecular mechanism postulates that there are two pathways for the polymer formation: polymerization initiation by homogenous nucleation in the solution phase, followed by heterogeneous nucleation on the surface of polymers formed via homogeneous process.

Moreover, it is worth noting that this nucleation mechanism of deoxy-HbS polymerization, leads to a coupled equations for rate of polymer formation, and the rate of disappearance of monomer from the solution phase into polymer.

Consequently, for mathematical simplicity, we used the well known phenomenological approach successfully applied in polymer dynamics [5, 6]; to obtain the differential equation governing the molecular dynamics of deoxy-HbS aggregation in simple shear flow. More precisely, the polymer formed during the time course of the aggregation process, is considered as a visco-elastic material. Then, the time evolution of stress/or deformation, can be readily described by a simple constitutive equation.

## 2.0 Theory

### 2.1 Phenomenological approach for the governing equation

The equation obtained by Dehardin & Olatunji [1] for the evolution of the absorbance measured in turbidity reads:

$$A(t) = A_{\infty}\left[1 + m\exp(-\mu t)\right]^{-1/p} \tag{2.1}$$

where

$$m = \left(\frac{A_{\infty}}{A_o}\right)^{1/p} \tag{2.2}$$

$A_o$ and $A_\infty$ respectively stand for the values of $A(t)$ at $t = 0$ and $t = \infty$, and $p$ a positive constant.
Starting from (1.1), we obtain after simple algebra, a second order non linear differential equation for the tine variation of the absorbance $A(t)$ vuz:

$$\ddot{A}(t) + \mu\dot{A}(t) - (p+1)\frac{\dot{A}^2}{A} = 0 \tag{2.3}$$

where the dots denote first and second differentiation with respect to time.

It is worthy to note that later Dejardin [7] performed a new theoretical model giving for the absorbance $A(t)$, a second order non linear differential equation written in the following form

$$\ddot{A}(t) + \Lambda_1\dot{A}(t) - \Lambda_2\frac{\dot{A}^2}{A} = 0 \tag{2.4}$$

Then identifying (2.3) and (2.4) the following correspondences are readily established.

$$\Lambda_1 = \mu;\ \Lambda_2 = p+1 \tag{2.5}$$

Now, if $Q(t)$ is the deformation of the deoxy-HbS molecule during the aggregation process, this new variable is closely related to the time-dependent absorbance measured in turbidity. More precisely, $Q(t)$ which is a ***dimensionless*** quantity and $A(t)$ are related by the phenomenological equation due to Wallace & Thompson [8]:

$$A(t) = kQ(t) \tag{2.6}$$

where $k$ is a positive constant.

Obviously, (2.6) is self-consistent. More precisely, according to Beer-Lambert's law [9] the absorbance $A(t)$ is also a dimensionless quantity defined by the following equation :

$$A(t) = \log\left[\frac{I(t)}{I_o}\right] \tag{2.7}$$

where $I_o$ is the light intensity at time $t = 0$ at the surface of the absorbing medium, while $I(t)$ is the intensity at time $t$ in the medium at a distance $d(t)$ from the surface. Consequently, (2.2) can be readily written in the following equivalent form:

$$\ddot{Q}(t) + \mu\dot{Q}(t) - (p+1)\frac{\dot{Q}^2}{Q} = 0 \tag{2.8}$$

Now, we introduce in (2.8) the efficient of inertia $\rho$ and we obtain:

$$\rho\ddot{Q}(t) + \eta\dot{Q}(t) - q\frac{\dot{Q}^2}{Q} = 0 \tag{2.9}$$

It is interesting to observe that (2.9) is more relevant for rheological study.

More precisely, if $M$,$L$ and $T$ denote the units of mass, length, and time respectively, the unit of a stress σ varies as $ML^{-1}T^{-2}$ : Hence, the unit of $\rho$ and q varied as $ML^{-1}$ (mass per unit length); that of $\eta$ varies $ML^{-1}T^{-1}$.

In rheology $\eta$ is the coefficient of viscosity and we can now give to (2.9) an important physical interpretation: Hence, (2.9) stands for the equilibrium condition of the total stress acting on a deoxy-HbS molecule during the aggregation process, namely Bauer [10] :

- the translational inertial stress $\sigma_{tr} = \rho\ddot{Q}$
- the rational inertial stress $\sigma_{inert} = q\frac{\dot{Q}^2}{Q}$
- the viscous stress $\sigma_{visc} = \eta\dot{Q}$

Obviously, from physico-biological point of view (2.9) is incomplete for correct description of the aggregation process. The reason for this is simple: Equation (2.9) not account for the elastic stress $\sigma_{elast} = GQ$ where $G$ is the coefficient of elasticity which varies as $ML^{-1}T^{-2}$.

More precisely, this equation is not in agreement with experimental results presented in [11, 12] clearly indicating that deoxy-HbS gels are visco-elastic and elasto-thixotropic. Gabriel et al [13] moreover established the following simple empirical law relating the elastic modulus $G$ to the concentration, viz :

$$G = \gamma[HbS]^n \, g/l. \tag{2.10}$$

where γ is a positive constant determined experimentally, and $n = 18$, for all concentration. Consequently, including the elastic stress in (2.9) we wet :

$$\rho\ddot{Q}(t) + \eta\dot{Q}(t) - q\frac{\dot{Q}^2}{Q} + GQ = 0 \tag{2.11}$$

**2.2 The general equation with a scalar structural parameter $\lambda = \lambda(t, x)$**

Drawing on the works of Quemada [3], we introduce in our nonlinear dynamic model, the scalar structural parameter $\lambda = \lambda(t, x)$ into (2.8). In addition to being time dependent, this parameter depends also on **a set of controlling factors** denoted $x$.

Thus, at a given time $t$, the system is assumed to exhibit a structural coefficient of viscosity $\eta(\lambda)$ and have a structural coefficient of elasticity $G(\lambda)$.

Furthermore, the set of controlling *factor x* can be limited to, say, the volume fraction $\phi$, a constant shear rate $\dot{\gamma}$, the deoxy-HbS concentration $c$, the temperature $T$, and other factors which influence the aggregation dynamics. Hence, equation (2.11) thus be generalized as follows :

$$\rho \ddot{Q}(t) + \eta(\lambda)\dot{Q}(t) - q\frac{\dot{Q}^2}{Q} + G(\lambda)Q = 0 \tag{2.12}$$

**2.3 Solving the governing equation.**

**2.3.1 Steady state conditions**

Let us assume that the rate equation of the structure variable $\lambda = \lambda(t,x)$, describing the dynamic equilibrium between the structure and unstructured states of the system can formally be written as follows

$$\frac{d\lambda}{dt} = F(\lambda) \tag{2.13}$$

where $F(\lambda)$ represents an analytical function in $\lambda$. Under steady conditions, we have $\frac{d\lambda}{dt} = 0$ when $\lambda$ reaches its equilibrium value $\lambda_{eq} = \lambda_{eq}(x)$. Then, only the introduction of the controller factor *x* allows the determination of the *structural steady coefficient of viscosity* $\eta(\lambda)$ and the *structural steady coefficient of stability* $G(\lambda)$. Equation (2.12) consequently reads as follows under steady conditions

$$\rho \ddot{Q}(t) + \eta(x)\dot{Q}(t) - q\frac{\dot{Q}^2}{Q} + G(x)Q(t) = 0 \tag{2.14}$$

Now, if we put : $$\omega_0^2 = \frac{G}{\rho}; \qquad s = \frac{q}{\rho}$$

we obtained for (2.14) the suitable form :

$$\ddot{Q}(t) + \mu(x)\dot{Q}(t) - s\frac{\dot{Q}^2}{Q} + \omega_0^2(x)Q(t) = 0 \tag{2.15}$$

Let defines a new dynamic variable *f(t)* as :

$$f(t) = \frac{\dot{Q}(t)}{Q(t)} \tag{2.16}$$

As we can see, results obtained in this work allow us to give to the function *f(t)*, a physical interpretation as a time-dependent aggregation frequency which governs the molecular dynamics.
Using equation (2.16) in equation (2.15) yields :

$$\dot{f} + \left[(1-s)f^2 + \mu(x)f + \omega_0^2(x)\right] = 0 \tag{2.17}$$

which is obviously a Riccati type of ordinary differential equation. For the aggregation frequency *f(t)*. Such an equation can be solved analytically. Using a suitable dynamic boundary conditions we in fact obtain the following explicit analytic expression for the aggregation frequency *f(t)* :

$$f(t) = \frac{(\alpha l/\nu)\exp(-\alpha t)}{1 + l\exp(-\alpha t)} \tag{2.18}$$

where $(\alpha, l, \nu)$ are the coupling parameters of the dynamical coefficient $\mu(x)$ and $\omega_0^2(x)$. here,

$$\alpha = \mu\delta \;\; ; \quad \delta = \left[1 + \frac{4p\omega_0^2}{\mu^2}\right]^{1/2} \tag{2.19}$$

$$\nu = \frac{2p\delta}{1+\delta};\ l = \frac{f_0}{(\alpha/\nu) - f_0} \tag{2.20}$$

$p = s - 1$ designates a positive constant and $f_0$ the value of $f(t)$ at $t = 0$.
It follows from (2.14) that

$$\frac{dQ}{Q} = f(t)dt \tag{2.21}$$

Integration yields for the dynamic variable $Q(t)$ the following functional form :

$$Q(t) = Q_\infty [1 + l\exp(-\alpha t)]^{-1/\nu} \tag{2.22}$$

Hence, from (2.4) we readily obtain the time dependent absorbance $A(t)$, viz :

$$A(t) = A_\infty [1 + l\exp(-\alpha t)]^{-1/\nu} \tag{2.23}$$

where

$$l = \left(\frac{A_\infty}{A_0}\right)^{\nu} - 1 \tag{2.24}$$

$A_0$ and $A_\infty$ respectively stand for the value of $A(t)$ at $t = \theta$ and $t = \infty$.

It is useful putting the governing equations in a form which directly accounts for the coupling parameters $(\alpha, l, \nu)$. Start from (2.22), it takes little algebra to obtain the following three governing equations :

(a) a nonlinear second order differential equation:

$$\ddot{Q} + \alpha\dot{Q} - (\nu + 1)\frac{\dot{Q}^2}{Q} = 0 \tag{2.25}$$

(b) a first order deterministic differential equation:

$$\frac{\dot{Q}}{Q} = \frac{\alpha}{\nu}\left[1 - \left(\frac{Q}{Q_\infty}\right)^{\nu}\right] \tag{2.26}$$

(c) a Riccati type of ordinary differential equation for $f(t)$ :

$$\dot{f} - \nu f^2 + \alpha f = 0 \tag{2.27}$$

## 3.0 Validity of the theoretical model

Several theoretical studies have been devoted to the modeling of cooperative phenomena in biology. Various deterministic equations are used in population dynamics to describe the well known Verhulst logistic curve [13], a man characteristic of all cooperative phenomena. For an excellent review of the subject, the interested reader is referred to the reent article by Hallam, [14].

To describe the growth dynamics in a population of a single species, most deterministic differential models based attempt use some appropriately prescribed unit growth

$$\frac{\dot{Q}}{Q} = kW\left(\frac{Q}{\theta}\right) \tag{3.1}$$

rate as in [11], where $Q(t)$ measures the size or density of a single species as a function of time. $W(Q/\theta)$ is an *arbitrary saturation inducing function* such that:

$$W(Q/\theta) \to 1 \ as \ Q \to \theta$$

As can be seen, model (2.28) depends on two parameters $k$ and $\theta$ respectively termed *intrinsic growth rate and carrying capacity*. The classical logistic equation derived by (Verhulst [12] is an example of a saturation inducing function. It is given by

$$W\left(\frac{Q}{\theta}\right) = \left[1 - \frac{Q}{\theta}\right] \tag{3.2}$$

Other examples of population saturation functions exist in the literature; Hallam [14]. A simple example can be constructed with $k > 0$ and by choosing the density term $W(Q/\theta)$, to be function of the ratio $(Q/\theta)$ as in the case of the classical logistic curve. The Verhulst generalized saturation inducing function provides a simple example of a function meeting these requirements. This function can be put in the form of a deterministic differential equation as follows

$$\frac{\dot{Q}}{Q} = k\left[1 - \left(\frac{Q}{\theta}\right)^{1/n}\right] \tag{3.3}$$

$n$ denotes a positive constant with $n = 1$ corresponding to the Verhulst case [12]. It is interesting to observe that the aggregation frequency expression $f = Q/Q$ of (2.26) has exactly the same functional form as the generalized type of Verhulst deterministic differential equation given in (3.3). Hence, as we have hitherto indicated, this important result clearly attests the validity of the function *f(t)* (2.16) as the aggregation frequency which governs the molecular dynamics. Moreover, the present nonlinear dynamic model is suitable for describing the cooperative phenomenon of deoxy-HbS molecules aggregation.

The remarkable aspect of (2.26) resides in the physical interpretation that can be assigned to its parameters as regarded the description of both the rheological properties and the aggregation kinetics of deoxy-HbS.

Finally, direct comparison of (2.26) yields the following correspondence

$$k = \frac{\alpha}{v} \quad \theta = Q_\infty; \; 1/n = v = \frac{2p\delta}{1+\delta} \tag{3.4}$$

We close this section with our remark on (2.9).

Referring to (2.9) and letting $G = \theta$, we get immediately from equations (2.19) and (2.20):

$$\delta = 1; \; \alpha = \mu; \; v = p; \; l = m = \frac{f_0}{(\mu/v) - f_0} \tag{3.5}$$

Then, our previous results, (2.1) and (2.3) are readily obtained.

## 4.0 Analytical solution of the dynamic equation

### 4.1 Solving the Riccati equation (2.15) for *f(t)*

The Riccati ordinary differential equation obtained for the aggregation frequency *f(t)* reads:

$$\frac{df}{dt} = -\left[(1-s)f^2 + \mu f + \omega_0^2\right] \tag{A1}$$

This equation can be readily solved using suitable boundary conditions. For this purpose, one observe that at the initial time $t = \theta$, all the deoxy-HbS molecules are in the solution phase (*disaggregated state)*, and the aggregation frequency or the *probability of polymer formation* has a maximum value $f(0) = f_0$.

During the time course of the kinetic process, the deoxu-HbS molecules aggregate and the intermolecular space reduced progressively giving rise to a steric effect. At the last stage of the kinetic process for $t \to \infty$, all the deoxy-HbS molecules are in the polymer or solid phase (*aggregated state*), and the aggregation frequency has a minimum value.

Consequently, so solve (A1), we process as follows:

#### 4.1.1 1°- Equilibrium solution $\varsigma_1$ and $\varsigma_2$

From the steady state condition $df/dt = 0$, we obtain a second order equation in $f$:

$$(1-s)f^2 + \mu f + \omega_0^2 = 0 \tag{A2}$$

The discriminant of (A2) is given by

$$\Delta = \mu^2 - 4(1-s)\omega_0^2 \tag{A3}$$

Provided that $\Delta \geq 0$, we can write $\sqrt{\Delta} = \pm \mu\delta$

where $$\delta = \left[1 - \frac{4(1-s)\,\omega_0^2}{\mu^2}\right]^{1/2} \quad \text{(A4)}$$

As can be seen from (A4), the necessary and sufficient condition $\Delta \geq 0$ comes to

$$\delta \geq 0 \Leftrightarrow \frac{4(1-s)\,\omega_0^2}{\mu^2} \leq 1$$

Under these conditions, we obtain the two equilibrium solutions :

$$\begin{cases} \zeta_1 = \dfrac{-\mu}{2(1-s)}(1-\delta) \\ \zeta_2 = \dfrac{-\mu}{2(1-s)}(1-\delta) \end{cases} \quad \text{(A5, A6)}$$

**4.1.2 $2^o$– Dynamic solution *f(t)***

From (A1), we obtain after simple sequence of transformations

$$\left[\frac{1}{f-\zeta_1} - \frac{1}{f-\zeta_2}\right] df = -(\zeta_1 - \zeta_2)(1-s)\,dt \quad \text{(A7)}$$

where $\zeta_1$ *and* $\zeta_2$ are the equilibrium solutions given by (A5) and (A6). Integrating (A7) yields:

$$\frac{f-\zeta_1}{f-\zeta_2} = C\exp(-\alpha t) \quad \text{(A8)}$$

where $\alpha = \mu\delta$ and *C* is an arbitrary constant. From the initial condition *f(0)* = $f_0$ we obtain:

$$C = \frac{f_0 - \zeta_1}{f_0 - \zeta_2} \quad \text{(A9)}$$

Hence, using. (A9), (A8) reads:

$$\frac{f-\zeta_1}{f-\zeta_2} = \frac{f_0-\zeta_1}{f_0-\zeta_2}\exp(-\alpha t) \quad \text{(A10)}$$

Obviously, the equilibrium solutions $\zeta_1$ and $\zeta_2$ have the dimension of a frequency. More precisely, they must be real and positive quantities. Consequently, the basic compatibility condition in (A5) and (A6) comes to: *s* = *p* + 1 with ***p a real positive constant***

$$\begin{cases} \zeta_1 = \dfrac{+\mu}{2p}(1-\delta) \\ \zeta_2 = \dfrac{+\mu}{2p}(1+\delta) \end{cases} \quad \text{(A11 and A12)}$$

Now with the well defined expression for the parameter $\delta$ viz.

$$\delta = \left[1 + \frac{4p\,\omega_0^2}{\mu^2}\right] > 1 \quad \text{(A13)}$$

However, as we can be seen from (A11), the necessary and sufficient condition (A13) $\delta > 1$ comes to

$$\zeta_1 = 0 \quad \text{(A14)}$$

Consequently, the analytical solution *f(t)* which satisfies the suitable boundary conditions is defined by the following reduced form of (A10)

$$\frac{f}{f-\zeta_2} \quad \frac{f_0}{f_0-\zeta_2}\exp(+\alpha t) \tag{A15}$$

Solving for *f(t)* in (A15) yields

$$f(t)=\frac{\zeta_2 l\exp(-\alpha t)}{1+l\ \exp\ (-\alpha t)} \tag{A16}$$

where *l* is a ***positive constant*** defined by $$l=\frac{f_0}{\zeta_2-f_0} \tag{A17}$$

More precisely, solving for $f_0$ in .(A17) we obtain the following relationship:

$$f_0=\frac{\zeta_2 l}{1+l}<\zeta_2 \tag{A18}$$

For all values of the parameter *l* $$v=\frac{2p\delta}{1+\delta} \tag{A19}$$

Now, letting (2.26). Then from (A12) we get the value of $\zeta_2$ in terms of the model parameters.

$$\zeta_2=\frac{\alpha}{v} \tag{A20}$$

α and *v* viz :

Finally, using (A16) and (A20), the analytical solution *f(t)* reads

$$f(\ )=\frac{(\alpha l/v)\exp(-\alpha t)}{1+l\exp(-\alpha t)} \tag{A21}$$

Thus establishing the result of the main text.

**4.2 Transformation of the dynamic equation (2.15) of second order as a two systems of differential equations of first order**

Let $\dot{x}=Q$ and $xy=Q\dot{}$. Then we have:

$$\begin{cases}\dot{x}=y\\ \dot{y}=-\mu y+s\dfrac{y^2}{x}-\omega^2 x\end{cases} \tag{B1}$$

where the dot stands for differentiation with respect to time.

From equations (B1) we get: $$\frac{dx}{dy}=\frac{xy}{sy^2-\mu xy-\omega^2x^2} \tag{B2}$$

The equation (B2) suppresses the singularity for x = 0 in equation (B1). However, from (B2) it would be understand that $\frac{dx}{dt}=\dot{x}=xy$ which is not exact. Hence, if we take a new independent variable $\tau$ defined

such that $$\tau=\int_0^t\frac{dt}{x} \tag{B3}$$

the system (B2) becomes $\begin{cases}\dot{x}(\tau)=xy\\ \dot{y}(\tau)=-\mu xy+sy^2-\omega^2x^2\end{cases}$, where the dot stands now for differentiation with respect to $\tau$. Now we consider the transformation $(x,y)\to(x,f=y/x)$. We get $\frac{df}{dx}=\frac{xdy-ydx}{x^2dx}$

which leads to the following equation $$\frac{dx}{df} = \frac{xX_m(x,y)}{Y(x,y\ ))- fX_m(x,y)} \tag{B4}$$

where $\begin{cases} X(x,y) = x^2 X_m(1,f) \\ Y_m(x,y) = x^2 Y_m(1,f) \end{cases}$. With the following definitions: $X_m(1,f) = f$ and $Y_m(1,f) = -sf^2 - \mu f - \omega^2$

Now, if we write (B4) as : $\frac{dx}{df} = xZ(f)$. We obtain: $Log[x(f)] = \int_0^f Z(u)du + cste$. Let

$$I = \int_0^f Z(u)du = \int_0^f \frac{u}{pu^2 - \eta u - G} = \int_0^f \left[\frac{a_1}{(u-\zeta_1)} + \frac{a_2}{(u-\zeta_2)}\right]du \tag{B5}$$

where $\boldsymbol{p = s - 1}$ is a real and positive constant. We obtain for the parameters $\boldsymbol{a_1}$ and $\boldsymbol{a_2}$ the following relationships: $a_1 = \frac{\delta - 1}{2p\delta} = \frac{1}{\xi}$, $a_2 = \frac{\delta + 1}{2p\delta} = \frac{1}{\nu}$. We have $\zeta_1 = \frac{\alpha}{\xi}$ and $\zeta_2 = \frac{\alpha}{\nu}$. The integral in equation (B5) can be easily calculated, and we obtain: $I = Log\left[C(f-\zeta_1)^{1/\xi}(f-\zeta_2)^{1/\nu}\right]$.

As $I = Log[x(f)]$, the solution desired reads in the following parametric form, viz:

$$\begin{cases} x(f) = K\left(1 - \frac{f}{\zeta_2}\right)^{1/\xi}\left(1 - \frac{f}{\zeta_2}\right)^{1/\nu} \\ y(f) = fx(f) \end{cases} \tag{B6}$$

These results indicate that only the solution which is finite for $\delta = 1$. Have physical significance. This correspond to the frequency $\zeta_2$: For $t \to \infty$, *we have* $f = f_\infty$ *and* $x(f_\infty) = K = x_\infty$. Hence equation (B6) reduces to:

$$\begin{cases} x(f) = x_\infty\left(1 - \frac{f}{\zeta_2}\right)^{1/\nu} \\ y(f) = fx(f) \end{cases} \tag{B7}$$

Finally, equation (B7) can be resolves for *f* and we obtain the desired result:

$$f = \frac{\dot{Q}}{Q} = \frac{\alpha}{\nu}\left[1 - \left(\frac{Q}{Q_\infty}\right)^{\nu}\right] \tag{B8}$$

## 5.0 Conclusion

In a previous work Dejardin and Olatunji [1] derived a mathematical model for the kinetics of deoxyhemoglobin S (doxy-HbS) aggregation. The function $A(t)$ for the time evolution of the absorbance satisfactoryily fit the experimental data:

In the present work, starting with the function $A(t)$ we used a new phenomenological approach to derive a general non linear dynamic for the aggression of deoxy-HbS. More precisely, we introduced in the parameters base, a scalar structural ammeter $\lambda = \lambda(t,x)$.

We develop the solution of the non linear governing equation under steady state conditions. For this purpose, we used two different mathematical methods which lead to two equivalent analytical function $f(t)$ for the aggression frequency governing the molecular dynamics.

The present work opens interesting perspectives fro kinetic and rheological studies on sickle cell heamoglobin. More precisely, the pioneering works of Hofrichter et al [4], Gabriel et al [12], harris et al [16],

and Damish et al [9] have emphasized the effects of others factors such as the volume fraction $\phi$, a constant shear rate $\dot{\gamma}$, the initial deoxy-HbS concentration *c*, the temperature *T*, and other factors which influence the aggregation dynamics. The major advantage of the present non linear governing equation, resides ability to take into account these controlling factors.

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