Validation of a fractional model for erythrocyte sedimentation rate

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Abstract
We present the validation of a recent fractional mathematical model for erythrocyte sedimentation proposed by Sousa et al. (AIMS Math 2(4):692–705, 2017). The model uses a Caputo fractional derivative to build a time-fractional diffusion equation suitable to predict blood sedimentation rates. This validation was carried out by means of erythrocyte sedimentation tests in laboratory. Data on sedimentation rates (percentages) were analyzed and compared with the analytical solution of the time-fractional diffusion equation. The behavior of the analytical solution related to each blood sample sedimentation data was described and analyzed.

Keywords Clinical laboratory tests · Erythrocyte sedimentation rate · Fractional calculus · Time-fractional diffusion equation

Mathematics Subject Classification 26A06 · 26A33 · 33RXX · 34A30 · 35KXX · 92BXX · 92DXX

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1 Introduction

The study of differential equations with integer order has always proved important and useful in mathematics, in particular, for the formulation of mathematical models (Mishra and Saini 2007; Vaidya and Alexandro 1982; Chattopadhyay et al. 2002; Gourley et al. 2008; Villasana and Radunskaya 2003). Several such models are based on ordinary or partial differential equations. However, for systems with many variables, it is usually very difficult to build models that match reality.

On the other hand, one of the health problems that is critical to the humans is the hepatitis delta virus being the rarest form of viral hepatitis and until this moment. There are few models related to this type of problem. However, recently Zubik-Kowal (2018) published a nice paper on this type of problem. Through simulations involving differential equations, he clarified some questions about the hepatitis delta virus. In this sense, also recent, Tannenbaum et al. (2018), through numerical simulations of partial time-dependent and time-dependent differential equations, discussed the growth of human tumor cells and presented results that corroborated to the efficiency of the algorithm and thus obtained an efficient way for fast clinical applications. Since the growth of cases of people with cancer grows each year, the number of mathematical models involving cancer has been investigated and highlighted by the importance and relevance of the subject to human health (Oke et al. 2018; Matveev and Savkin 2002; Chu et al. 1991; Bratus et al. 2017; Samanta et al. 2017). Other important types of equations that support extremely important applications are differential equations such as convection, reaction–diffusion, and diffusion among others (Harris and Garra 2017; Mommer and Lebiedz 2009; Alvarado et al. 2012; Khanday et al. 2017; Wang et al. 2006).

With the expansion of the fractional calculation and consequently the vast number of important applications that have arisen and arise over time, to use fractional derivatives in the modeling of such systems complex systems by means of a differential equation of non-integer order presents some advantages as compared with mathematical models that use only classical, integer order operators. Indeed, it has been realized that the use of differential equations of fractional order to model certain complex phenomena usually provides better descriptions of their behavior, allowing us to obtain more accurate information about the underlying physical systems (Costa et al. 2015, 2017; Lenzi et al. 2009; Costa and Pereira 2017; Capelas de Oliveira et al. 2011, 2014). Thus, fractional calculus became popular because of its importance and relevance, specifically, due to its numerous applications in several fields of science and particularly in biology and medicine, in which the authors Sousa et al. (2017), using the Caputo fractional derivative, introduced a fractional mathematical model that describes the concentration of nutrients in blood, a parameter that affects erythrocyte sedimentation rate (ESR) and which contain, as a particular case, the result obtained in Sharma et al. (1996).

The topic “health” is of great importance and has led several researchers to study mathematical models to obtain results that more accurately describe the evolution of certain diseases, in particular tumor growth. However, there are other types of health problems that are related to epidemics and that mathematicians have used fractional derivatives to propose mathematical models to obtain results that are more realistic. Pinto and Machado (2013) carried out work on the transmission of malaria using a fractional mathematical model and numerically studied the variation of the fractional derivative in relation with the order and obtained interesting results in the scope of malaria transmission. There are a large number of mathematical models formulated through fractional derivatives that provide more accurate and realistic results when compared to mathematical models proposed by means of whole-order derivatives (Vargas-De-León 2015; Pinto and Carvalho 2017; Wojtak et al. 2018).
Due to this popularity of fractional calculus, there are numerous recent works related to biology and medicine (Varalta et al. 2014; Ding and Ye 2009; Langlands et al. 2009; Tian 2015; Pahnehkolaei et al. 2017). The motivation for this work came from a mathematical model proposed by Sharma et al. (1996). First, Sousa et al. (2017), using the Caputo fractional derivative, proposed a fractional version of the model by Sharma et al. (1996), to generalize it and, possibly, make it more accurate. To obtain more accurate model information with respect to reality, the model must be tested and verified, that is, by ESR test, look at the data and compare with the analytical solution of the time-fractional diffusion equation.

This paper is organized as follows: in Sect. 2, we present a brief explanation about ESR, together with some tables showing analytical and clinical factors that affect erythrocyte sedimentation, increasing and decreasing ESR. A brief description of the erythrocyte sedimentation process and its three phases, rouleaux formation, precipitation, and packaging closes the section. In Sect. 3, we present our fractional mathematical model and the corresponding initial and boundary conditions. The analytical solution of the fractional model is presented and the solution of the mathematical model proposed by Sharma et al. is recovered. In Sect. 4, we present the experiments conducted to obtain experimental values (percentages) of ESR for eight blood samples from eight different individuals, which would be compared with the fractional mathematical model. The results are presented in two complete tables. In Sect. 5, the main result of this work, we validate the fractional mathematical model using data from the erythrocyte sedimentation tests of the eight samples. We present the respective graphs of each individual and carry out detailed discussions on the results obtained through the data collected and we demonstrated other possibilities of results if some changes were made in the process of data collection. Concluding remarks close the paper.

2 Erythrocyte sedimentation rate

ESR is a classic clinical test that measures how far erythrocytes settle into the bottom of a test tube over a 1 h period. The test was originally described in 1897 by Kucharz (1987, 1988) and Biernacki (1897a, b). It was introduced by Fahraeus and Westergren at the beginning of the nineteenth century (Westergren 1921, 1926; Fahraeus 1921, 1929).

ESR is in fact a very imprecise test due to the influence of analytical factors such as temperature, table slope and stability, and clinical factors like anemia, giant cells, diabetes, AIDS, smoking, drinking, weight, and even height, which can give rise to false-positive and false-negative results (Van den Broek and Letsky 2001; Olshaker and Jerrard 1997; Bedell and Bush 1985).

Among clinical factors, the erythrocytes themselves and influence of plasma proteins, associated with inflammation, are the ones that most influence ESR test results (Talstad et al. 1983; Whelan et al. 1971). Nevertheless, the role of ESR in clinical decision making under non-characteristic conditions has been reestablished in different settings, including rheumatology, hematology, and even orthopedics (Cheung et al. 2012; Choi et al. 2013; Greidanus et al. 2007; Hauser et al. 2012; Stojan et al. 2013; Tamhane et al. 2013; Ghanem et al. 2009).

The erythrocyte sedimentation test for red blood cells is performed within a vertical 200 mm blood test tube. The following two tables present the clinical factors that increase and decrease ESR. For the preparation of Table 1, we used the papers (Shusterman et al. 1985, 1986; Warner and George 1991; Pasulka et al. 1985; McPherson and Pincus 2017; Grace and Goldrick 1968; Fahraeus 1958; Shearn and Kang 1986; Bottiger and Svedberg
Table 1 Factors influencing erythrocyte sedimentation

| ESR increases                                                                 | ESR decreases                                                                                     |
|-------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Pregnancy                                                                     | Polycythemia                                                                                     |
| Old age                                                                       | Dysfibrinogenemia and afibrinogenemia                                                             |
| Anemia                                                                         | Intravascular diffuse coagulation                                                                  |
| High concentration of non-fibrogenic proteins                                 | Congestive heart failure                                                                          |
| Renal insufficiency                                                           | Valproic acid                                                                                    |
| Heparin                                                                        | Cachexia                                                                                         |
| Rheumatoid arthritis                                                          | Sickle cell disease                                                                               |
| Tuberculosis                                                                   | Hereditary spherocytosis                                                                          |
| Acute infections                                                               | Hyperglycemia                                                                                    |
| Kidney disease                                                                 | Acanthocytosis                                                                                    |
| Macrocytosis                                                                   | Microcytosis                                                                                      |
| Dextran                                                                        | Spherocytosis                                                                                    |
| Diabetes mellitus                                                              | Thalassemia                                                                                      |
| Gout                                                                           | Cortisone                                                                                        |
| Multiple myeloma                                                               | Quinine                                                                                         |
| Myocardial infarction                                                          |                                                                                                  |
| Rheumatic fever                                                                |                                                                                                  |
| Syphilis                                                                       |                                                                                                  |
| Temporal arteritis                                                             |                                                                                                  |

Table 2 Normal values of ESR

| Author  | Patient | Values in mm |
|---------|---------|--------------|
| Miller  | Children| 4–7          |
|         | Men     | 3–5          |
|         | Women   | 4–7          |
| Borges  | Children| 0–10         |
|         | Man     | 0–15         |
|         | Women   | 0–20         |

1967; Zauber and Zauber 1987; Jandl 1996; Bunting 1939; Glass 1971; Hutchinson et al. 1978; Murata and Secomb 1988; Zhang et al. 2008).

On the other hand, it is important to have in mind that ESR values are different for men, women, children, and elderly people. Table 2 presents the reference values of ESR for each type of individual. For the preparation of Table 2, we used references (Brigden 1999; Solberg and Olson 2014; Collares and Vidigal 2014; McPherson and Pincus 2017; Hameed and Waqas 2006).

Erythrocytes usually form aggregates, called rouleaux, which resemble piles of coins. However, the formation of rouleaux does not occur in the blood flow of a healthy human.

The erythrocyte sedimentation process can be divided into three phases: rouleaux formation, precipitation, and packaging. Rouleaux formation is the most influential phase in determining the test result. Normally, red blood cells have negative charges on their surfaces and repel each other, while many plasma proteins have positive charges and neutralize the
surface charges of erythrocytes, promoting aggregation. Thus, an increase in plasma proteins will be associated with higher ESR. Precipitation is the second phase of the erythrocyte sedimentation process; it occurs over a period of 40 min. Aggregates of erythrocytes fall under the influence of gravity at a constant rate. Large aggregates fall faster than small aggregates and isolated cells. The falling aggregates induce an upward plasma current that delays sedimentation. Finally, the packaging stage takes place during 10 min. The sedimentation rate decreases and cells begin to pack at the bottom of the tube. In this way, the erythrocyte sedimentation process is terminated (Hashemi et al. 2015; Cha et al. 2009).

3 Fractional mathematical model

In this section, we describe, as a review, the fractional mathematical model by means of the Caputo fractional derivative (Sousa et al. 2017). In addition, the corresponding analytical solution for the mathematical model, as proposed by Sharma et al. (1996), is recovered as a particular case of our fractional mathematical model.

The concentration of nutrients in blood is a function $C(x, t)$ twice continuously differentiable that satisfies the following non-homogeneous time-fractional partial differential equation (PDE):

$$D_L \partial_x^2 C(x, t) - \partial_t^\mu C(x, t) = \phi(x, t),$$  \hspace{1cm} (1)

where $\partial_t^\mu = \frac{\partial^\mu}{\partial t^\mu}$ is the Caputo fractional derivative, with $0 < \mu \leq 1$, $D_L$ is a positive constant, and $\phi(x, t)$ is a function twice continuously differentiable describing the nutrient transfer rate and which satisfies the PDE

$$D \partial_x^2 \phi(x, t) - k \phi(x, t) - \partial_t \phi(x, t) = 0,$$  \hspace{1cm} (2)

with $D$ and $k$ both positive constants.

The initial and boundary conditions imposed here are given by

$$\begin{cases} 
\phi(x, 0) = \exp \left( -\sqrt{\frac{k-a}{D}} x \right), & k \geq a, D > 0, \\
\phi(0, t) = \exp (-at), & t > 0, \\
\phi(\infty, t) = 0, & t > 0. 
\end{cases}$$

The solutions of Eq. (2) can be written as

$$\phi(x, t) = \exp \left( -(at + bx) \right),$$

where $b^2 = \frac{(k-a)}{D} > 0$ and $a$ is a constant to be adequately chosen from a known value of $\phi(x, t)$.

Furthermore, we must impose the initial and boundary conditions for Eq. (1):

$$\begin{cases} 
C(x, 0) = 0, & x \geq 0 \\
C(0, t) = 1, & t > 0 \\
C(\infty, t) = 0, & t > 0, 
\end{cases}$$  \hspace{1cm} (3)

with $C(x, t) \in C^2[0, b]$.

Thus, from these considerations, it follows that the time-fractional mathematical model to be addressed is composed of a non-homogeneous fractional PDE

$$D_L \partial_x^2 C(x, t) - \partial_t^\mu C(x, t) = \exp \left( -(at + bx) \right), \hspace{1cm} a, b \in \mathbb{R},$$  \hspace{1cm} (4)
with initial and boundary conditions given by Eq. (3) and $0 < \mu \leq 1$.

In this paper, we do not take into account the dimensionless of the time-fractional diffusion equation (4). However, it is possible to leave in a dimensionless form for a reading of some works related to this topic that we suggest (He 1990).

We solve this problem, employing the methodology of Laplace transform to convert the non-homogeneous fractional PDE into a non-homogeneous linear ordinary differential equation.

Thus, the solution associated with our problem, i.e., a solution of Eq. (4) satisfying the conditions given by Eq. (3), is (Sousa et al. 2017)

$$C(x, t) = t^\mu \sum_{m=0}^{\infty} \frac{(-\alpha x - \mu/2)^m}{m!} \sum_{k=0}^{\infty} (-at)^k \mathcal{E}_{\mu, \mu+k+1}^{\mu, \mu} \left( \beta^2 t^{\mu} \right)$$

$$+ \mathcal{W} \left( -\mu/2, 1; -\alpha x t^{\mu/2} \right) - \exp \left( -bx t^{\mu} \right) \sum_{k=0}^{\infty} (-at)^k \mathcal{E}_{\mu, \mu+k+1}^{\mu} \left( \beta^2 t^{\mu} \right), \quad (5)$$

where $\mathcal{E}_{\mu, \nu} (\cdot)$ is the two-parameter Mittag–Leffler function, $\mathcal{W}(a, b; \cdot)$ is the Wright function (Gorenflo et al. 2014), and the parameters are given by $\alpha^2 = 1/D_L$, $\beta^2 = b^2 D_L$, and $0 < \mu \leq 1$. The solution given by Eq. (5) is AC$^\alpha[0, b]$ and class $C^2$, then substituting it in Eq. (4) and evaluating the calculation we verify that it satisfies the initial value problem (Sousa 2018).

Note that the solution of the fractional PDE in the limit $\mu \to 1$ recovers the result by Sharma et al. (1996).

4 Experimental
4.1 Materials and methods

The ESR tests were conducted at the Hematology Laboratory of the Clinical Hospital, State University of Campinas, state of São Paulo, southeast Brazil. For the erythrocyte sedimentation test, the (Westergren 1921, 1926; Fahraeus 1921, 1929) method was adopted as the reference method for ESR measurement by the international council of ICSH (1973, 1993). We used a test tube of length 200 mm, but for evaluation purposes, we consider up to 120 mm height with an ambient temperature of 22 °C and the angle between the tube and the table is 90° (8 samples were collected, 4 males and 4 females).

Patient blood samples were placed in test tubes containing no anticoagulant in the eight samples. The height of the erythrocyte column in the test tube, in millimeters, was recorded at a 5 min interval for 1 h, and was subsequently converted to sedimentation rate (percentage) according to the decreased proportion in height. The following tables indicate the values of ESR and clinical factors of the tests carried out on the 8 samples collected. Table 3 (1–2), below, describes the sedimentation rate of each individual as time progresses. A detailed description of some information from the individuals in whom erythrocyte sedimentation tests were performed are shown in Table 4. An important observation related to Table 4 is the fact that besides presenting the ESR values (manual sedimentation), we also present the sedimentation performed in the automated system.

The reason for presenting these two versions, made manually and by device, is that the version via apparatus changes the properties of the blood and consequently the sedimenta-
Table 3  Sedimentation rate in the time intervals

| Time/pipe | 0   | 5   | 10  | 15  | 20  | 25  | 30  |
|-----------|-----|-----|-----|-----|-----|-----|-----|
| Pipe 1-F  | 0.83| 0.83| 0.83| 1.66| 3.32| 6.64|
| Pipe 2-F  | 0.83| 0.83| 0.83| 1.66| 2.49| 3.32|
| Pipe 3-F  | 0.83| 0.83| 0.83| 2.49| 4.98| 9.96|
| Pipe 4-F  | 1.66| 1.66| 2.49| 3.32| 3.32| 8.30|
| Pipe 1-M  | 0   | 0   | 0.83| 0.83| 1.66| 1.66|
| Pipe 2-M  | 0   | 0   | 0.83| 0.83| 0.83| 1.66|
| Pipe 3-M  | 0.83| 1.66| 2.49| 4.15| 7.47| 12.45|
| Pipe 4-M  | 0   | 0   | 0   | 0.83| 0.83| 0.83|

| Time/pipe | 35  | 40  | 45  | 50  | 55  | 60  |
|-----------|-----|-----|-----|-----|-----|-----|
| Pipe 1-F  | 9.96| 13.28| 16.60| 19.09| 24.07| 25.73|
| Pipe 2-F  | 4.15| 5.81 | 7.47 | 9.96 | 11.62| 14.11|
| Pipe 3-F  | 14.11| 20.75| 29.05| 34.86| 40.67| 45.65|
| Pipe 4-F  | 19.09| 30.71| 41.50| 51.46| 59.76| 65.57|
| Pipe 1-M  | 2.49| 4.15 | 5.81 | 7.47 | 9.96 | 12.45|
| Pipe 2-M  | 1.66| 2.49 | 3.32 | 4.98 | 5.91 | 6.64|
| Pipe 3-M  | 18.26| 23.24| 29.88| 35.69| 40.67| 45.65|
| Pipe 4-M  | 0.83| 0.83 | 1.66 | 1.66 | 1.66 | 2.49|

In this sense, it is necessary and important to present the difference between the two corresponding rates.

Remark 1  – For individuals 1, 2, and 3: unlikely to influence ESR;
  – For individuals 4 and 7: may influence ESR;
  – For individuals 5, 6, and 8: do influence ESR.

5 Results and discussion

In this section, we will present the graphs of the results obtained in the ESR realization and make some analysis and comparisons with the solution of the fractional diffusion equation (1). Discussions involving the sedimentation rate of erythrocytes, the data collected and the solution of the fractional diffusion equation conclude the section.

We start with the analysis of graphs 1–4, which represent the sedimentation rate of four males.

Rheumatoid arthritis is a rheumatic disorder that is also known to be consistent with ESR alterations, sometimes increasing it manyfold. As shown in Fig. 1, the male individual with rheumatoid arthritis presented a slight evolution, although the pathology is autonomous for ESR raise. In this sense, many factors (pathological, external, and clinical) can change ESR and thus the behavior of the graph.

Lupus is a systemic disorder affecting connective tissue throughout the body and is also capable of increasing ESR manyfold. Nevertheless, as shown in Fig. 2, the behavior of the experimental data is very distant from the analytical solution of the fractional diffusion equation (5). However, supposing that this individual has other pathologies besides lupus,
| Label | Sex | Height (m) | Weight (kg) | BMI  | Man. Sed. (%) | Apa. Sed. (%) | Disorder                                  | Diff. (%) |
|-------|-----|------------|-------------|------|---------------|---------------|-------------------------------------------|-----------|
| 1     | F   | 1.60       | 72.00       | 28.1 | 25.73         | 27.00         | Bursitis trochanterica                     | 4.94      |
| 2     | F   | 1.58       | 65.00       | 26.0 | 14.11         | 33.00         | Spondylarthrosis                          | 133.88    |
| 3     | F   | 1.52       | 42.70       | 18.5 | 45.65         | 50.00         | Control                                   | 9.53      |
| 4     | F   | 1.58       | 81.00       | 32.4 | 65.57         | 68.00         | Polyarthritis                              | 3.71      |
| 5     | M   | 1.67       | 78.50       | 28.1 | 12.45         | 19.00         | Rheumatoid arthritis                      | 52.61     |
| 6     | M   | 1.90       | 105.0       | 29.1 | 6.64          | 3.00          | Lupus                                     | -54.82    |
| 7     | M   | 1.69       | 74.00       | 25.9 | 45.65         | 39.00         | Retinopathy                               | -14.57    |
| 8     | M   | 1.87       | 73.00       | 20.9 | 2.49          | 3.00          | Vasculitis lupus erythematosus disseminated | 20.48     |
e.g., renal insufficiency, it may be that these factors greatly accelerate the increase in ESR and experimental data will fit better the analytical solution. However, these factors are very unpredictable, since several internal and external factors alter ESR.

Retinopathy is a very common disease which comes with many systemic disorders, thus making it likely to promote some altered values in ESR. Note that, particularly in this case, if the individual with retinopathy ingested drugs that diminish ESR, e.g., cortisone and quinine, this would certainly increase the chances of better fitting the data, as shown in Fig. 3.

The condition of this patient is exactly the same as that of individual 3 and the same hypotheses apply to this case.
With the purpose to look at the data of individuals, and plot their respective graphs, for a particular choice of the parameter $0 < \mu \leq 1$, we tried to approach the analytic solution of the fractional diffusion equation and obtain more precise information on erythrocyte sedimentation behavior in that interval. Then, graphs 1–4 allow to carry out an analysis of the sedimentation of erythrocytes. The graphs were plotted using the software MALTAB 6.10.

To look at the data and validate the fractional mathematical model, recently introduced by Sousa et al. (2017), the graphs present an expected behavior in the sense that each individual has a certain clinical problem. The erythrocyte sedimentation behavior via a graphical analysis varies from individual to individual. Note that from the graph of male 1, the erythrocyte sedimentation behavior presents a characteristic similar to the solution of the fractional diffusion equation, that is, as it moves away from the border ($x \neq 0$), the concentration of nutrients decreases. On the other hand, the graphs of individuals 2 and 4, the characteristic of the sedimentation curve does not present a good behavior, this is due to the characteristics of each individual, from clinical factors among them, the age. However, if we perform other experiments, we could obtain better results, and consequently, the behavior of the ESR graph is somehow best viewed by the analytical solution given by Eq. (5). On the other hand, it is possible to note that the behavior of the analytical solution of Eq. (5) better approach the erythrocyte sedimentation of individual. In fact, it is possible to choose $n$ individuals and to study the graph that describes the ESR and thus to make the model more accurate.

The next graphs 5–8 refer to the behavior of erythrocytes sedimentation for the other four individuals in the case of females.

Bursitis trochanterica is a traumatic condition. Although the lesions are inflammatory in nature, it is not known as a disorder capable of altering ESR and is unlikely to influence it. However, the experimental data collected present a good behavior, as shown in the graph of Fig. 5. Note that it is very unlikely to get a sample from a particular individual that would fit the analytical solution (5), since several factors, whether analytical, external, or pathogenic, influence the ESR. Thus, what we expect is that the behavior of the graph plotted with the data collected resemble that of the solution of Eq. (5).
Spondylarthritis is also a traumatic condition, in fact, an osteoarthritis that affects the spine at different levels. Due to its traumatic nature, it is also unlikely that this disorder will alter ESR.

This is labeled as a control, which means that there is a known malfunction, and it is highly unlikely that any ESR changes will be expected in this case. Here, we can apply the same considerations, as presented in Fig. 5.

Although there was no further information about the cause of polyartralgia, the existence of pain that affects many joints at the same time is consistent with a systemic disorder of the kind that allows one to expect some influence on ESR.
An important observation must be made about the difference in the graphs obtained for males and females. Note that sex actually influences the ESR, and even more, the best agreement between experimental results and the solution of the fractional mathematical model were obtained for the female subjects. Of course, since it is possible to carry out numerous tests and obtain your samples with a variety of pathologies, it may be that, for certain males, experimental data will present a good behavior when compared to the fractional mathematical model.

At first, it can be noted that the behavior of ESR of four female individuals presented in the four graphs above is in fact better and the solution of the fractional diffusion equation, the data tape better. However, in the same way that we can perform $n$ tests of female individuals and
find others in which the solution Eq. (5) tape the data more efficiently, making the fractional mathematical model able to offer information closer to reality in regards to erythrocyte sedimentation.

In addition, it is worth noting that, as observed in graphs 1–8, the fractional mathematical model proposed by Sousa et al. (2017) via a Caputo fractional derivative allows a variation in the order of the derivative, and consequently in the analytical solution of Eq. (1), making it possible to look better at the data. On the other hand, the mathematical model as proposed by Sharma et al. (1996) does not allow this freedom to look at the data in the same way as our model. Thus, our fractional mathematical model allows a better reading of the data, that is, the concentration of nutrients in the blood, in relation with the model proposed by Sharma et al. (1996).

It is important to note that as parameter $0 < \mu \leq 1$, we have chosen the values of $\mu = 0.10$, $\mu = 0.30$, $\mu = 0.50$, $\mu = 0.70$, $\mu = 0.90$, and $\mu = 1.00$, for the graphs in Figs. 1, 2, 3, 4, 5, 6, 7 and 8 presented, to plot the numerical solutions of the fractional diffusion equation (5) and compare them with the data collected to validate the fractional mathematical model. However, as there are many factors that can change the ESR, it is unpredictable to know which combination of pathological, physiological, clinical, and external factors would look the best possible with respect to the choice of parameter $\mu$. In this sense, as can be seen, the graphs in Figs. 5, 6, 7 and 8 of the female subjects showed a better correspondence with the data, and the sex can also change the ESR. It is possible to combine several diseases and generate a sample to look at the data and compare it with the solution graph of the fractional diffusion equation. However, we do not know what would be the best combination, since we would have a wide class of possible factors: pathological, clinical, external, and physiological.

6 Concluding remarks

After a brief introduction to a fractional mathematical model used to describe the blood concentration of nutrients that influence the sedimentation rate of blood cells, we present...
the results of laboratory ESR tests with eight samples, four males and four females, used to validate that mathematical model. For this sake, the results of sedimentation tests were compared, through graphical analysis, with the analytical solution of the mathematical model. Only eight samples were enough to carry out this comparison and discuss the model. However, more tests, providing new data, would surely allow a better comprehension of the fractional mathematical model, making it more appropriate to describe reality.

A remarkable advantage of the fractional mathematical model is the freedom to choose the order of the derivative in it and, consequently, the analytical solution of the problem.

With the freedom given to parameter $0 < \alpha \leq 1$, we were able to analyze the concentration of nutrients on certain intervals and regions in which the mathematical model proposed by Sharma et al. (1996) cannot be used. Our model can thus provide information on the blood concentration of nutrients closer to reality.

In a future work, we intend to consider another type of fractional derivative (Sousa and de Oliveira 2017, 2018a, b, c), namely, a general problem of fractional space diffusion. After that, we shall carry out the same sedimentation tests and shall use their results to analyze the capabilities of that new model for describing real living systems.

Another possibility that was proposed during the experiments is to perform the tests with healthy individuals and apply to them the same procedure used here, to compare the results obtained with the results presented here.

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