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### A fractional-order model for Ebola virus infection with delayed immune response on heterogeneous complex networks



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#### ABSTRACT

Most of the biological systems have long-range temporal memory and modeling of such systems by fractional-order differential equations has more advantages than classical models with integer-orders. In this paper, we provide a fractional-order Ebola virus epidemic model with delayed immune response on heterogeneous complex networks. The time-delay is introduced in the cytotoxic T-lymphocyte (CTLs) term. Based on fractional Laplace transform, some conditions on stability are derived for the model. The analysis shows that the fractional-order time-delay can effectively enrich the dynamics and strengthen the stability condition of fractional-order infection model. Finally, the derived theoretical results are justified by some numerical simulations.

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#### 1. Introduction

Over the past decades, several infectious diseases have increased in incidence and expanded into new geographical areas. The infectious disease remains a major cause of death, disability, social and economic disorders throughout the world. It is difficult to understand the transmission of diseases and also the control strategies. Mathematical modeling acts as an effective way to identify spread of epidemics, and has been widely used to study the control of infectious disease [1–3]. It is a powerful tool for controlling the disease such as dengue, yellow fever, Ebola virus and so on. Ebola is one of the highly lethal virus, which has caused at least 18 outbreaks in African countries. There exist five known Ebola viruses, according to the International Committee on Taxonomy of Viruses currently: Ebola virus (EBOV), Sudan virus (SUDV), Reston virus (RESTV), Tai Forest virus (TAFV), and Bundibugyo virus (BDBV). Four species of these viruses (except RESTV) are known to cause Ebola virus disease in humans [4,5]. Ebola is transmitted by physical contact with body fluids, secretions, tissues or semen from infected persons. The incubation period, or the time interval from infection to onset of symptoms, is from 2 to 21 days. The onset of Ebola is characterized by severe headaches, fever, vomiting, bloody diarrhea and rashes. The mortality rate of Ebola varies from 50% to 90% [6].

Introduction to epidemic modeling is usually made through one of the first epidemic models proposed by Kermack and McKendrick in 1927, a model known as the SIR epidemic model [7] to study the transmission of black death. Based on this model, several other models are proposed in the literature [8–12]. Fundamentally, the compartmental modeling is used to study the spread and behavior of diseases when the population is small and has homogeneous contacts. Whereas, the development of society, behaviors of human being and disease spreading become heterogeneous. In order to overcome

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this problem, we adopt the idea of complex networks on compartmental epidemic modeling, in which the individuals are modeled as nodes and possible contacts between individuals by edges.

Most of the epidemic models on complex networks, which are based on the common SIR, SIS and SIRS compartmental models, have been first described in 1980s, then attracting many researchers [13–15]. However, most of the existing epidemic models on complex networks in the literature are described by integer-order; see, e.g., [16–18]. The authors in [17] studied an SIR epidemic model with demographics and time-delay on networks. In [18], the epidemic model has been considered with birth and death rate on networks, where the basic reproductive threshold parameter  $\mathcal{R}_0$  is given to show the dynamics of epidemic. In [16], the authors studied epidemic dynamics in finite size scale-free networks. They concluded that the epidemic threshold is very small even at a relatively small cut-off, showing that the neglection of connectivity fluctuations in bounded scale-free networks leads to a strong over-estimation of the epidemic threshold.

In recent decades, there is a growing interest in applying fractional calculus to mathematical epidemiology. Applications of fractional-order differential equations have been widely examined due to their extensive use in the fields of science and engineering such as physics, chemistry, biology and so on [19–23]. The representation of memory and hereditary properties [24–26] has made the fractional-order as an excellent tool in epidemiology compared to integer-order systems. The study of qualitative properties of fractional-order epidemic-models has been discussed in [27–29]. The authors in [30] have discussed fractional SIRC model associated with the evolution of influenza. The local stability of the fractional-order dengue model has been discussed in [31]. Many researchers studied the spread of Ebola virus with integer-order for population levels [32–37]. In [36], the authors analyzed Ebola virus by considering the SIR model to provide useful prediction of transmission of virus. The authors in [33,35] presented the SEIR model in order to describe the spread of Ebola virus, to control the propagation of the virus and to predict the impact of vaccine programmes. Recently, fractional-order models have been used to study Ebola epidemic; see [38–41]. In [42], the authors have discussed Ebola epidemic model with nonlinear transmission and conditions for existence and stability of a unique endemic equilibrium to the Ebola system have been derived.

Up to best of our knowledge, the study of fractional-order epidemic models has been restricted to the compartmental model with small-size of population. A very few works have been done on the epidemics of fractional-order with complex networks, [43], where the network is applied to the basic fractional SIR model with birth and death on heterogeneous population where time-delay has not been considered. Most of the research works carried for analyzing stability of fractional-order are restricted without delay. The existence of a delay is mandatory in the model, in the real life, the activation of immune response is due to the time-lag for occurring sequence of events [44,45]. This made the time-delay mandatory in the model. In [41], the authors provided a fractional-order delay differential model for Ebola infection and CD8+ T-cells response and widely studied the stability and Hopf bifurcation of the addressed model.

Based on the above discussion, in this paper, we propose and analyze an Ebola virus epidemic model on heterogeneous complex networks with delayed immune response, to gain further insights and understanding of viral dynamics during the course of infection. The qualitative study of the model is discussed. Numerical simulations are also presented to demonstrate the analytical results.

#### 1.1. Preliminaries

Herein, we provide some basic definitions and properties of integration and differentiation with fractional-order (free-order)  $\alpha$  (see [46]).

**Definition 1.** Let  $\alpha \in (0, \infty)$ , the operator  $I_a^{\alpha}$  on  $L_1[a, b]$  is defined by

$$I_a^{\alpha}f(t) = \frac{1}{\Gamma(\alpha)} \int_a^t (t-s)^{\alpha-1}f(s)ds \quad (f \in L_1[a,b], \ t \in [a,b]),$$

which is called the fractional-integral (or Riemann–Liouville integral) of order  $\alpha$ , where  $I_a^0 = \text{Id}$ , is the identity operator.

**Definition 2.** Let  $\alpha \in [0, \infty)$  and  $n = \lceil \alpha \rceil$  where  $\lceil x \rceil = \min\{k \in \mathbb{Z} : k \ge x\}$ , the operator  $_{RL}D_a^{\alpha}$  is defined for  $f \in L_1[a, b]$  by

$$_{RL}D_a^{\alpha}f(t) = \frac{1}{\Gamma(n-\alpha)} \left(\frac{d}{dt}\right)^n \int_a^t (t-s)^{n-\alpha-1}f(s)ds,$$

which is called the Riemann–Liouville fractional derivative of order  $\alpha$ .

**Definition 3.** Let  $\alpha \in [0, \infty)$  and f be such that  $I_a^{n-\alpha}f^{(n)}$  exists, where  $n = \lceil \alpha \rceil$ ,  $f \in A^n[a, b]$  (the set of all functions  $f : [a, b] \to \mathbb{R}$  provided that  $f^{(n-1)}$  be absolutely continuous), then we define the operator  ${}_C D_a^{\alpha}$  by

$$_{C}D_{a}^{\alpha}f(t)=\frac{1}{\Gamma(n-\alpha)}\int_{a}^{t}(t-s)^{n-\alpha-1}f^{(n)}(s)ds,$$

which exists for almost every  $x \in [a, b]$ . The operator  ${}_{C}D_{\alpha}^{\alpha}f(t)$  is called the Caputo fractional derivative of order  $\alpha$ .

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