Global Stability for Fractional Diffusion Equations in Biological Systems

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1. Introduction

In recent years, fractional differential equations (FDEs) are used to describe the temporal dynamics of various systems in many fields. These equations are the generalization of the classical ordinary differential equations (ODEs). However, fractional partial differential equations (FPDEs) are the generalization of the partial differential equations (PDEs) which can be an effective tool to describe the spatiotemporal dynamics of several phenomena with memory or have hereditary properties.

The construction of Lyapunov functionals to prove the global stability of fractional dynamic systems has attracted the attention of some authors. Aguila-Camacho et al. [1] established a new lemma for fractional derivative in Caputo sense with order \( \alpha \in (0, 1) \). They used this lemma to demonstrate the stability of some fractional-order systems by mean of quadratic Lyapunov functionals. Duarte-Mermoud et al. [2] extended the lemma of [1] to a vector of differentiable functions, and they used Lyapunov functionals containing general quadratic forms in order to analyze the stability of fractional-order model reference adaptive control (FOMRAC) schemes. Vargas-De-León [3] extended the Volterra-type Lyapunov function to fractional-order epidemic systems via an inequality to estimate the Caputo fractional derivative of this function. On the other hand, a study in [4] has been devoted to establish the global stability for some diffusion equations in biology by means of Lyapunov functionals.

The methods mentioned above are applied for particular Lyapunov functionals such as quadratic or Volterra-type. Likewise, the work in [4] is especially applicable for the models formulated by PDEs. Therefore, the main goal of this study is to develop a new mathematical method to construct the Lyapunov functionals for FDEs and FPDEs based on those of ODEs. To do this, the next section deals with the description of the method and the last section is devoted to the application of our method to investigate the global stability of some mathematical models in epidemiology as well as in virology.

2. Description of the Method

Consider the following FDE:

\[ D_{\alpha}^\alpha u = f(u), \] (1)

where \( D_{\alpha}^\alpha u \) is the fractional derivative in the Caputo sense of order \( \alpha \in (0, 1] \), the state variable \( u \) is a non-negative vector of concentrations \( u_1, \ldots, u_m \), and \( f: \mathbb{R}^m \rightarrow \mathbb{R}^m \) is a \( C^1 \)
function. It is obvious that if $\alpha = 1$, then (1) becomes the following ordinary differential equation:

$$u = f(u).$$

(2)

Let $\Omega$ be a bounded domain in $\mathbb{R}^n$ with smooth boundary $\partial \Omega$ and $\mathcal{D} = (d_1, \ldots, d_m)$ with $d_i \geq 0$. Assume that $u^*$ is a steady state of (1). Then, $u^*$ is also the steady state of the following fractional diffusion system with homogeneous Neumann boundary condition:

$$\begin{align*}
\frac{\partial^\alpha u}{\partial t^\alpha} &= \mathcal{D} u + f(u) \text{ in } \Omega \times (0, +\infty), \\
\frac{\partial u}{\partial \nu} &= 0 \text{ on } \partial \Omega \times (0, +\infty), \\
u(x, 0) &= u_0(x) \text{ in } \Omega,
\end{align*}$$

(3)

where $\Delta = \sum_{i=1}^n \frac{\partial^2}{\partial x_i^2}$ represents the Laplacian operator and $\partial u/\partial \nu$ denotes the outward normal derivative on the boundary $\partial \Omega$.

Let $V(u)$ be a $C^1$ function defined on some domain in $\mathbb{R}^m$ and $u(t)$ is a solution of (1). Further, we suppose that the range of $u(t)$ is contained in the domain of $V(u)$ and

$$D_\alpha^V (u(t)) \leq \nabla V(u) \cdot f(u),$$

(4)

whose equality holds if $\alpha = 1$.

We observe that the right-hand side of the above inequality is given by the scalar product of the gradient of the function $V(u)$ and the vector field $f(u)$. Hence, the right-hand side is defined without the fact that $u(t)$ is a solution of (1), which is very important for the construction of Lyapunov functionals.

Let $u(t, x)$ be a solution of (3). Denote

$$W = \int_\Omega V(u(t, x))dx.$$  

(5)

The fractional time derivative of $W$ along the positive solution of (3) satisfies

$$D_\alpha^V W \leq \int_\Omega \nabla V(u) \cdot (\mathcal{D} u + f(u))dx$$

$$= \int_\Omega \nabla V(u) \cdot f(u)dx + \int_\Omega \nabla V(u) \cdot \mathcal{D} u dx$$

$$= \int_\Omega \nabla V (u) \cdot f(u)dx + \sum_{i=1}^m d_i \int_\Omega \nabla V u_i dx.$$  

(6)

By applying Green’s formula, we find

$$\int_\Omega \frac{\partial V}{\partial u_i} \Delta u_i dx = \int_\Omega \frac{\partial V}{\partial u_i} \frac{\partial u_i}{\partial \nu} d\sigma - \int_\Omega \nabla u_i \cdot \left( \nabla \frac{\partial V}{\partial u_i} \right) dx.$$  

(7)

According to $(\partial u/\partial \nu) = 0$ on $\partial \Omega$, we have

$$\int_\Omega \frac{\partial V}{\partial u_i} \Delta u_i dx = - \int_\Omega \nabla u_i \cdot \left( \nabla \frac{\partial V}{\partial u_i} \right) dx.$$  

(8)

Therefore,

$$\frac{dW}{dt} \leq \int_\Omega \nabla V(u) \cdot f(u)dx - \sum_{i=1}^m d_i \int_\Omega \nabla u_i \cdot \left( \nabla \frac{\partial V}{\partial u_i} \right) dx.$$  

(9)

Additionally, we assume that the function $V$ satisfies the following condition:

$$d_i \int_\Omega \nabla u_i \cdot \left( \nabla \frac{\partial V}{\partial u_i} \right) dx \geq 0, \quad \text{for all } i = 1, \ldots, m.$$  

(10)

From the above, it is not difficult to obtain the following result.

**Theorem 1.** Let $V$ be a Lyapunov functional for the ordinary differential equation (2).

(i) If $V$ satisfies the condition (4), then $V$ is also a Lyapunov functional for fractional differential equation (1).

(ii) If $V$ satisfies the condition (4) and (10), then the function $W$ defined by (5) is a Lyapunov functional for fractional diffusion system (3).

In the literature, several researchers constructed the Lyapunov functional in the following form:

$$V = \sum_{i=1}^m a_i \left( u_i - u_i^* - u_i^* \ln \frac{u_i}{u_i^*} \right).$$  

(11)

**Corollary 2.** If $V$ is a Lyapunov functional for ordinary differential equation (2) of the form given in (11), then $V$ is a Lyapunov functional for fractional differential equation (1). Moreover, the function $W$ defined by (5) is a Lyapunov functional for fractional diffusion system (3).

**Proof.** We have

$$D_\alpha^V W = \sum_{i=1}^m a_i D_\alpha^V \left( u_i - u_i^* - u_i^* \ln \frac{u_i}{u_i^*} \right).$$  

(12)

By applying Lemma 3.1 in [3], we get

$$D_\alpha^V W \leq \sum_{i=1}^m a_i \left( 1 - \frac{u_i^*}{u_i} \right) D_\alpha^V u_i$$  

$$= \nabla V(u) \cdot f(u).$$  

(13)

Then, $V$ satisfies the condition (4). It follows from Theorem 1 (i) that $V$ is also a Lyapunov functional for fractional differential equation (1).

On the other hand, we have

$$\int_\Omega \nabla u_i \cdot \left( \nabla \frac{\partial V}{\partial u_i} \right) dx = a_i u_i^* \int_\Omega \frac{[\nabla u_i]^2}{u_i^2} dx \geq 0,$$  

(14)

which implies that $V$ satisfies the condition (10). According to Theorem 1 (ii), we deduce that the function $W$ given by (4) is also a Lyapunov functional for fractional diffusion system (3). This completes the proof. □
Remark 3. The method described above can be used to prove the stability of many fractional systems with and without diffusion. It is very important to recall that the steady state $u^*$ is stable if there exists a Lyapunov functional satisfying $D^n_{t}V(u) \leq 0$. Moreover, if $D^n_{t}V(u) < 0$ for all $u \neq u^*$, then $u^*$ is asymptotically stable. Additionally, according to [5], if $D^n_{t}V(u) \leq 0$ and the largest invariant set in $\{u | D^n_{t}V(u) = 0\}$ is the singleton $\{u^*\}$, then $u^*$ is asymptotically stable. This means that the solution of the system starting from any initial conditions converges to $u^*$.

3. Applications

This section focuses on the application of the method described in the above section in order to establish the global stability of some fractional diffusion biological models by constructing Lyapunov functionals from those of the corresponding systems which are formulated by ODEs. Example 1. Consider the SIR epidemic model described by the following nonlinear system of FDEs:

$$
\begin{align*}
D^n_{t}S &= A - \mu S - \frac{\beta SI}{\alpha_0 + \alpha_1 S + \alpha_2 I + \alpha_3 SI}, \\
D^n_{t}I &= \frac{\beta SI}{\alpha_0 + \alpha_1 S + \alpha_2 I + \alpha_3 SI} - (\mu + d + r)I, \\
D^n_{t}R &= rI - \mu R,
\end{align*}
$$

where $S, I,$ and $R$ are the populations of susceptible, infected, and recovered individuals, respectively. The parameters $A, \mu,$ $d,$ and $r$ are, respectively, the recruitment rate, the natural death rate, the death rate due to disease, and the recovery rate. The incidence function of system (15) is described by Hattaf–Yousfi functional response [6] of the form $\beta S/I + \alpha_1 S + \alpha_2 I + \alpha_3 SI,$ where the non-negative constants $\alpha_1, \alpha_2, \alpha_3,$ measure the saturation, inhibitory, or psychological effects, and the positive constant $\beta$ is the infection rate. This functional response covers the most famous forms existing in the literature such as the classical bilinear incidence, the saturated incidence, the Beddington–DeAngelis functional response [7], the Crowley–Martin functional response [8], and the specific functional response introduced in [9]. Further, the fractional models proposed in [10, 11] are particular cases of model (15); it suffices to take $\alpha_0 = 1$ and $\alpha_1 = \alpha_2 = \alpha_3 = 0$ for [10] and $\alpha_0 = 1$ for [11].

Since the state variable $R$ does not appear in the two first equations of fractional model (15), we can reduce (15) to the following system:

$$
\begin{align*}
D^n_{t}S &= A - \mu S - \frac{\beta SI}{\alpha_0 + \alpha_1 S + \alpha_2 I + \alpha_3 SI}, \\
D^n_{t}I &= \frac{\beta SI}{\alpha_0 + \alpha_1 S + \alpha_2 I + \alpha_3 SI} - (\mu + d + r)I.
\end{align*}
$$

(16)

Due to the great mobility of individuals inside or outside a country or region, we consider the following fractional model:

$$
\begin{align*}
D^n_{t}S &= d_3 \Delta S + A - \psi(S(x,t), I(x,t))I(x,t), \\
D^n_{t}I &= d_3 \Delta I + \psi(S(x,t), I(x,t))I(x,t) - \eta I(x,t),
\end{align*}
$$

(17)

where $\psi(S,I) = (\beta S/\alpha_0 + \alpha_1 S + \alpha_2 I + \alpha_3 SI)$ and $\eta = \mu + d + r$. The parameters $d_3$ and $d_4$ are the diffusion coefficients for the susceptible and infected populations, respectively. Also, we consider model (17) with homogeneous Neumann boundary conditions:

$$
\frac{\partial S}{\partial y} = \frac{\partial I}{\partial y} = 0, \text{ on } \partial \Omega \times (0 + \infty),
$$

(18)

and initial conditions:

$$
S(x,0) = S_0(x) \geq 0, \\
I(x,0) = I_0(x) \geq 0,
$$

(19)

$$
x \in \Omega.
$$

For $\alpha = 1$, model (16) becomes the following nonlinear system of ODEs:

$$
\begin{align*}
\dot{S} &= A - \mu S - \psi(S,I)I, \\
\dot{I} &= \psi(S,I)I - \eta I.
\end{align*}
$$

(20)

Obviously, model (20) has always one disease-free equilibrium $E_f((A/\mu),0)$. By a simple computation, the basic reproduction number is given by

$$
R_0 = \frac{\beta A}{(\alpha_0 \mu + \alpha_1 A)(\mu + d + r)}.
$$

(21)

When $R_0 > 1$, model (20) has another equilibrium named endemic equilibrium $E^*(S^*, I^*)$, where

$$
S^* = \frac{2(\eta \alpha_1 + \alpha_2 A)}{\beta - \alpha_1 \eta + \alpha_2 \mu - \alpha_1 A + \sqrt{\delta}},
$$

$$
I^* = \frac{\Lambda - \mu S^*}{\eta},
$$

(22)

with $\delta = (\beta - \alpha_1 \eta + \alpha_2 \mu - \alpha_1 A)^2 + 4\alpha_2 \mu (\eta \alpha_1 + \alpha_2 A)$.

System (20) is a special case of the mathematical model presented in [12]. Thus, the disease-free equilibrium $E_f$ is globally asymptotically stable when $R_0 < 1$. However, $E_f$ becomes unstable and the endemic equilibrium $E^*$ is globally asymptotically stable if $R_0 > 1$.

Let $S_0 = A/\mu$ and $\Phi(z) = z - 1 - \ln(z)$ for $z > 0$. From [12], the function

$$
V_1(u) = \frac{\alpha_0 S^0}{\alpha_0 + \alpha_1 S^0} \Phi \left( \frac{S}{S^0} \right) + I
$$

(23)

is a Lyapunov functional for ODE model (20) at $E_f$. Moreover, we have

$$
\begin{align*}
\nabla V_1(u) \cdot f(u) &= \frac{\alpha_0}{\alpha_0 + \alpha_1 S^0} (1 - \frac{S}{S^0}) (A - \mu S - \psi(S,I)I) \\
&\quad + \psi(S,I)I - \eta I \\
&\quad - \alpha_1 \psi(S,S^0) + \eta I \left( \frac{\psi(S,I)}{\psi(S,0)} \right) - 1
\end{align*}
$$

(24)

$$
\leq -\frac{\alpha_0 (S - S^0)^2}{(\alpha_0 + \alpha_1 S^0)^2} + \eta I (R_0 - 1).
$$
Additionally, we have
\[ D^\alpha_t V_1(u) \leq \nabla V_1(u) \cdot f(u). \] (25)

Then, \( V_1 \) satisfies the condition (4). By applying Theorem 1 (i), we deduce that \( V_1 \) is also a Lyapunov functional for FDE model (16) at \( E^*_f \).

Now, we construct the Lyapunov functional for fractional diffusion model (17) at \( E^*_f \) as follows:
\[ W_1 = \int_\Omega V_1(u(x,t))dx. \] (26)

In this case, we have
\[ d_i \int_\Omega \nabla u_i \cdot \nabla \frac{\partial V_1}{\partial u_i} dx \geq 0, \quad \text{for all } i = 1, 2. \] (27)

In fact,
\[ d_s \int_\Omega \nabla S \cdot \left( \frac{\partial V_1}{\partial S} \right) dx = \frac{\alpha_0 d_S S^0}{\alpha_0 + \alpha_1 S^0} \int_\Omega \frac{\nabla S^2}{S^2} dx \geq 0, \]
\[ d_i \int_\Omega \nabla I \cdot \left( \frac{\partial V_1}{\partial I} \right) dx = 0. \] (28)

This implies that \( V_1 \) satisfies the condition (10). It follows from Theorem 1 (ii) that \( W_1 \) is a Lyapunov functional for fractional diffusion systems (17)–(19) at \( E^*_f \) when \( R_0 \leq 1 \).

For the global stability of the endemic equilibrium \( E^* \), we consider the following function:
\[ V_2(u) = S - S^* - \int_S^\infty \frac{\psi(S', I')}{\psi(S, I')} dS + I^* \Phi \left( \frac{I}{I^*} \right), \] (29)

which is a Lyapunov functional for ODE model (20) at \( E^* \). On the other hand, we have
\[ \nabla V_2(u) \cdot f(u) = \left( 1 - \frac{\psi(S', I')}{\psi(S, I')} \right) (A - \mu S - \psi(S, I)'I) + \left( 1 - \frac{I'}{I} \right) (\psi(S, I)'I - \eta I), \]
\[ D^\alpha_t V_1(u) \leq \nabla V_1(u) \cdot f(u). \] (30)

Thus, \( V_2 \) obeys the condition (4) and then \( V_2 \) is a Lyapunov functional for FDE model (8) at \( E^* \).

Denote
\[ W_2 = \int_\Omega V_2(u(x,t))dx. \] (31)

It is not hard to show that
\[ d_s \int_\Omega \nabla S \cdot \left( \frac{\partial V_2}{\partial S} \right) dx = \frac{(\alpha_0 + \alpha_1 I^*) d_S S^*}{\alpha_0 + \alpha_1 S^* + \alpha_2 I^* + \alpha_3 S^* I^*} \int_\Omega \frac{\nabla S^2}{S^2} dx \geq 0, \]
\[ d_i \int_\Omega \nabla I \cdot \left( \frac{\partial V_2}{\partial I} \right) dx = d_i I^* \int_\Omega \frac{\nabla I^2}{I^2} dx \geq 0. \] (32)

Then, condition (10) holds. Therefore, \( W_2 \) is a Lyapunov functional for fractional diffusion systems (17)–(19) at \( E^*_f \) when \( R_0 > 1 \).

Consequently, we have the following:
(i) When \( R_0 \leq 1 \), the disease-free equilibrium \( E^*_f \) of (17)–(19) is globally asymptotically stable.
(ii) When \( R_0 > 1 \), the endemic equilibrium \( E^* \) of (17)–(19) is globally asymptotically stable.

Example 2. Consider the following fractional viral infection model:
\[
\begin{align*}
D^\alpha_t H &= \lambda - \mu H - \beta_1 HV - \beta_2 HI, \\
D^\alpha_t I &= \beta_1 HV + \beta_2 HI - \delta I, \\
D^\alpha_t V &= pI - cV,
\end{align*}
\] (33)

where healthy cells \( (H) \) are produced at rate \( \lambda \), die at rate \( \mu H \), and become infected by contact with virus at rate \( \beta_1 HV \) and by contact with infected cells at rate \( \beta_2 HI \). Infected cells \( (I) \) die at rate \( \delta I \). Free viral particles \( (V) \) are released from infected cells at rate \( pI \) and decay at rate \( cV \). Note that when \( \alpha = 1 \) and \( \beta_1 = 0 \), we obtain the basic model which was used to study some viral infections such as HIV, HBV, and HCV [13–16].

Now, we extend the above fractional model (33) by taking into account the mobility of the virus as well as the cells. Then, model (33) becomes
\[
\begin{align*}
\partial_t H &= d_H \Delta H + \mu - \mu H(x,t) - \beta_1 H(x,t)V(x,t) - \beta_2 H(x,t)I(x,t), \\
\partial_t I &= d_I \Delta I + \beta_1 H(x,t)V(x,t) + \beta_2 H(x,t)I(x,t) - \delta I(x,t), \\
\partial_t V &= d_V \Delta V + pI(x,t) - cV(x,t),
\end{align*}
\] (34)

where \( H(x,t), I(x,t), \) and \( V(x,t) \) denote the concentrations of healthy cells, infected cells, and free viral particles at position \( x \) and time \( t \), respectively. The parameters \( d_H, d_I, \) and \( d_V \) represent, respectively, the diffusion coefficients of healthy cells, infected cells, and free viral particles.

The cells and virus are biological quantities which should be non-negative, and they also should not cross the boundary of the domain. Then, we consider system (34) with the homogeneous Neumann boundary conditions:
\[ \frac{\partial H}{\partial v} = \frac{\partial I}{\partial v} = \frac{\partial V}{\partial v} = 0, \text{ on } \partial \Omega \times (0, +\infty), \] (35)

and initial conditions:
\[
\begin{align*}
H(x,0) &= H_0(x) \geq 0, \\
I(x,0) &= I_0(x) \geq 0, \\
V(x,0) &= V_0(x) \geq 0, \quad \forall x \in \Omega.
\end{align*}
\] (36)

The corresponding ordinary system of the above models is given by
This system admits a unique infection-free equilibrium $Q_f (H^0, 0, 0)$, where $H^0 = (\lambda/\mu)$. Further, the basic reproduction number is given by

$$R_0 = \frac{\lambda (p\beta_1 + c\beta_2)}{c \mu}. \tag{38}$$

This basic reproduction number is the sum of two basic reproduction numbers due to virus-to-cell and cell-to-cell transmissions. If $R_0 > 1$, ODE model (37) has another biologically steady state called the infection chronic which is labeled by $Q^* (H^*, I^*, V^*)$, where

$$H^* = \frac{\lambda}{d R_0}, \quad I^* = \frac{c \mu (R_0 - 1)}{pp_1 + c \beta_2}, \quad V^* = \frac{pc \mu (R_0 - 1)}{c (p\beta_1 + c\beta_2)} \tag{39}$$

These two equilibria are also steady states of both models (33) and (34). First, we consider a Lyapunov functional for ODE model (37) at $Q_f$ as follows:

$$L_1 (u) = H^0 \Phi \left( \frac{H}{H^0} \right) + I + \frac{\beta_1 H^0}{c} \cdot V. \tag{40}$$

Calculating the time derivative of $L_1$ along the solution of (37), we get

$$\frac{dL_1}{dt} = \nabla L_1 (u) \cdot f (u) = \left( 1 - \frac{H^0}{H} \right) (\lambda - \mu H - \beta_1 HV - \beta_2 HI) + \beta_1 HV + \beta_2 HI - \delta I$$

$$+ \frac{\beta_1 H^0}{c} (pI - cV)$$

$$= -H \frac{(H - H^0)^2}{H} + \delta I (R_0 - 1).$$

If $R_0 \leq 1$, then $(dL_1/ dt) \leq 0$ with equality if and only if $H = H^0$, $I = 0$ and $V = 0$. Therefore, the infection-free equilibrium $Q_f$ is globally asymptotically stable when $R_0 \leq 1$. Since

$$D^*_1 L_1 (u) \leq \nabla L_1 (u) \cdot f (u), \tag{42}$$

it follows from Theorem 1 (i) that $L_1$ is also a Lyapunov functional for FDE model (33) at $Q_f$.

Next, we construct a Lyapunov functional for fractional diffusion model (34) at $Q_f$ as follows:

$$\mathcal{L}_1 = \int_{\Omega} L_1 (u (x,t)) dx. \tag{43}$$

We have

$$d_I \int_{\Omega} \nabla H \cdot \left( \frac{\partial L_1}{\partial H} \right) dx = d_I H \int_{\Omega} \frac{\partial H^2}{H} dx \geq 0,$$

$$d_I \int_{\Omega} \nabla I \cdot \left( \frac{\partial L_1}{\partial I} \right) dx = 0,$$

$$d_I \int_{\Omega} \nabla V \cdot \left( \frac{\partial L_1}{\partial V} \right) dx = 0.$$ (44)

Then, $L_1$ satisfies the condition (10). Using Theorem 1 (ii), we deduce that $\mathcal{L}_1$ is a Lyapunov functional for fractional diffusion systems (34)–(36) at $Q_f$ if $R_0 \leq 1$.

Based on the results in [17], the function

$$L_2 (u) = H - H^* - H^* \ln \frac{T}{T^*} + I - I^* - I^* \ln \frac{I}{I^*}$$

$$+ \frac{\beta_1 H^*}{c} \left( V - V^* - V^* \ln \frac{V}{V^*} \right) \tag{45}$$

is a Lyapunov functional for ODE model (37) at $Q^*$ when $R_0 > 1$. Let

$$\mathcal{L}_2 = \int_{\Omega} L_2 (u (x,t)) dx. \tag{46}$$

Since $L_2$ has the form given in (11), we conclude, by applying Corollary 2, that $L_2$ is a Lyapunov functional for FDE model (33) and $\mathcal{L}_2$ is a Lyapunov functional for fractional diffusion systems (34)–(36) at $Q^*$ when $R_0 > 1$.

**Data Availability**

The data used to support the findings of this study are available from the corresponding author upon request.

**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

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