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A fractional calculus approach to the dynamic optimization of biological reactive systems. Part I: Fractional models for biological reactions

Rasiel Toledo-Hernandez [a], Vicente Rico-Ramirez [a,*], Gustavo A. Iglesias-Silva [a], Urmila M. Diwekar [b]

[a] Instituto Tecnologico de Celaya, Departamento de Ingenieria Quimica, Av. Tecnologico y Garcia Cubas S/N, Celaya, Guanajuato 38010, Mexico
[b] Vishwamitra Research Institute, 368 56th Street, Clarendon Hills, IL 60514, USA

HIGHLIGHTS

- The dynamics of reactive systems with atypical behavior are represented by FDE.
- Different fermentation processes were represented by the same fractional model.
- A formal fractionalization approach was used to obtain the model of hydrolysis.
- Results show the capabilities of fractional calculus for modeling dynamic systems.

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ABSTRACT

This series of two papers is concerned with both the modeling and the optimization of systems whose governing equations contain fractional derivative operators. In this first work, we show that the dynamics of some reactive systems displaying atypical behavior can be represented by fractional order differential equations. We consider three different instances of fermentation processes and one case of a thermal hydrolysis process. We propose a fractional fermentation model and, based on experimental data, a non-linear fitting approach that includes fractional integration is used to obtain the fractional orders and kinetics parameters. On the other hand, since the ordinary thermal hydrolysis model used as a reference was derived from fundamental principles, a formal fractionalization approach was used in this work to obtain the corresponding fractional model. Results show the feasibility and capabilities of fractional calculus as a tool for modeling dynamic systems in the area of process systems engineering.

1. Introduction: fractional calculus and its modeling capabilities

Fractional calculus is a generalization of ordinary calculus which introduces derivatives and integrals of fractional order. Major reviews on the concepts and history of fractional calculus can be found in the books of Samko et al. (1993), Oldham and Spanier (1974), Miller and Ross (1993) and Podlubny (1999). Reports of successful modeling applications of fractional calculus are as old as the works developed by Caputo (1967) and Caputo and Mainardi (1971), related to the modeling of viscoelastic fluids; however, it has not been until the last two decades when the use of fractional order operators and operations has become more popular among many research areas.

Several authors have recently shown that fractional calculus is a powerful modeling tool to represent the behavior of a number of mechanical and electrical dynamic systems (Magin, 2006; Sabatier et al., 2007). In addition, many works describe and/or study the non-locality property and the memory effect of fractional calculus operators (Magin, 2006; Herrmann, 2011; Sun et al., 2011; Constantinescu and Stoicescu, 2011; Du et al., 2013). In particular, Magin (2006) provides a simple but illustrative example of the memory effect of a fractional derivative. It is therefore generally accepted that physical considerations, such as memory and hereditary effects, favor the use of fractional derivative-based models. Theoretical developments are also in progress (Diethelm, 2010; Ortigueira, 2011) in order to consolidate the fundamentals and provide the basis for a more extensive use of this tool in science and engineering.

* Corresponding author. Tel.: +52 461 611 7575x156; fax: +52 461 611 7744.
E-mail address: vicente@iqcelaya.itc.mx (V. Rico-Ramirez).

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Of particular interest in this work are the applications of fractional calculus to diffusion and anomalous kinetics. Literature suggests that diffusion processes are accurately represented by fractional differential equations (FDE) (Sokolov et al., 2002; San Jose Martinez et al., 2007). Further, diffusion is one of the main mechanisms of various processes in living organisms and gives rise to kinetics that are referred to as anomalous, to indicate the fact that deviate from the classic description. Anomalous kinetics can also result from reaction-limited processes and long-time trapping. It is thought that anomalous kinetics introduces memory effects in the process that need to be accounted for to correctly describe it (Dokoumetzidis and Macheras, 2009). Literature reports several approaches to describe anomalous kinetics including empirical power-laws, gamma functions or fractal kinetics. Nevertheless, anomalous kinetics have recently been modeled by using fractional calculus (Dokoumetzidis and Macheras, 2009; Dokoumetzidis et al., 2010a, 2010b). Dokoumetzidis and Macheras (2009) study the drug release/dissolution processes (pharmacokinetics) as a fractional model. Due to the heterogeneous structure and function of the GI tract, the dissolution or release of drug takes place in a disordered under stirred medium. Since diffusion is the principal transport mechanism, fractional derivatives can be used to describe this anomalous kinetics under the heterogeneous in vivo conditions.

In other fields, the applications of fractional calculus are developed as extensions of well established mathematical models that are based upon ordinary differential equations. Therefore, in those cases it is important to understand how to properly fractionalize these classic models (Dokoumetzidis et al., 2010a, 2010b).

Motivated by the use of fractional calculus in pharmacokinetics, in this work we intend to extend the modeling capabilities of fractional calculus to the areas of chemical and biochemical engineering. In our opinion, it is reasonable to think that the physicochemical nature of biological processes (fermentations, enzymatic reactions, cell growth, etc.) will result in a dynamic behavior with memory. Therefore, we focus on biological reactive systems as the main illustrative cases of our approach. It is interesting that, in spite of the extensive existing literature on fractional calculus applications, literature related to reaction kinetics of chemical and biochemical processes is limited.

1.1. The fractional derivative

Fractional derivatives can be introduced trough successive differentiation of integer powers of x (notice that the expression introduces the differentiation operator D)

$$D^0x^p = x^p;\ \ Dx^p = px^{p-1}\ ;\ \ D^2x^p = p(p-1)x^{p-2};\\ D^mx^p = p(p-1)(p-2)\ldots(p-m+1)x^{p-m} \tag{1}$$

Multiplying and dividing Eq. (1) by $(p-m)!$

$$D^mx^p = \frac{p(p-1)(p-2)\ldots(p-m+1)(p-m)!\,x^{p-m}}{(p-m)!}$$

$$D^mx^p = \frac{p!}{(p-m)!}x^{p-m} \tag{2}$$

where m is a positive integer number. To derive an expression for fractional differentiation (m is generalized to fractional values), the factorial function is substituted by the Gamma function

$$\Gamma(z) = \int_0^\infty e^{-u}u^{z-1}\,du$$

Since it can be proved that $\Gamma(z+1) = z!$ for all $z \in \mathbb{R}$. Then, Eq. (2) can be re-written as follows:

$$D^\alpha x^p = \frac{\Gamma(p+1)}{\Gamma(p-\alpha+1)}x^{p-\alpha} \tag{3}$$

where $\alpha \in \mathbb{R}.\ \ \alpha \geq 0$.

Eq. (3) is one of the definitions of the Riemann–Liouville fractional derivative (Oldham and Spanier, 1974; Miller and Ross 1993). A more elegant and general methodology (Magin, 2006) uses Laplace transformation and the definition of the Cauchy integral to obtain expressions for the Riemann–Liouville fractional integration

$${}_0D_t^{-\alpha}f(t) = \frac{1}{\Gamma(\alpha)}\int_0^t \frac{f(\tau)}{(t-\tau)^{1-\alpha}}d\tau \qquad 0<\alpha<1 \tag{4}$$

and two alternative definitions of fractional derivative, the Riemann–Liouville definition

$$f(t) = {}_0D_t^\alpha Y(t) = \frac{d}{dt}[{}_0D_t^{-(1-\alpha)}Y(t)]$$

and the Caputo definition

$$f(t) = {}_0D_t^\alpha Y(t) = {}_0D_t^{-(1-\alpha)}[Y'(t)] + \frac{Y(0)t^{-\alpha}}{\Gamma(1-\alpha)}$$

The fractional derivative definitions differ in the initial condition considered in each case. The order of the derivative can be extended to values of $\alpha>1$. Then, for $-1<\alpha<m$, where m is the smallest positive integer larger than α, the definitions are as follow:

$${}_0D_t^\alpha Y(t) \equiv \frac{d^m}{dt^m}\left[\frac{1}{\Gamma(m-\alpha)}\int_0^t \frac{Y(\tau)}{(t-\tau)^{\alpha+1-m}}d\tau\right] \tag{5}$$

and

$${}_0^CD_t^\alpha Y(t) \equiv \frac{1}{\Gamma(m-\alpha)}\int_0^t \frac{Y^{(m)}(\tau)}{(t-\tau)^{\alpha+1-m}}d\tau \tag{6}$$

Eq. (5) is the Riemann–Liouville fractional derivative definition and Eq. (6) is the Caputo definition, which is generally expresses as ${}_0^CD_t^\alpha f(x)$. Eqs. (5) and (6) are extensively used in most of the theoretical and practical applications of fractional calculus.

2. Anomalous kinetics and reactive biological systems

Typical simulation and optimization models for reactive biological systems, which exhibit anomalous kinetics that do not necessary follow the classical mass-action form, include equations involving empirical or semi-empirical expressions. Anticipating a potential memory effect on the dynamics of such systems, one of our goals is to show that, as an alternative, the kinetics of those reactive systems, such as fermentation, enzymatic reaction and biomass growth processes, can also be accurately represented by using fractional calculus without the need for empirical considerations.

To illustrate the approach, here we consider three instances of a fermentation process; two of them produce bioethanol with different substrate and microorganisms and the third one is for the production of *Tequila*. In addition, we also analyze the case of the thermal hydrolysis of *Agave salmiana* to produce *Mezcal* under two different temperature conditions.

2.1. Fermentation processes

In general, the models reported in the literature for fermentation are based on empirically driven kinetics. However, many times these models are not the best fit for the experimental data.