Proceedings of the International Conference on Biomedical Engineering and Systems
Prague, Czech Republic, August 14-15, 2014
Paper No. 34

A Preliminary Fractional Calculus Model of the Aortic Pressure Flow Relationship during Systole

Glen Atlas[1,2]
[1]Rutgers New Jersey Medical School, Dept. of Anesthesiology
Newark, New Jersey, USA
[2]Stevens Institute of Technology
Dept. of Chemistry, Chemical Biology, and Biomedical Engineering
Hoboken, New Jersey, USA
atlasgm@njms.rutgers.edu

Sunil Dhar
New Jersey Institute of Technology Dept. of Mathematical Sciences
Newark, New Jersey, USA

Abstract **-**The aortic pressure flow relationship is typically described using traditional integer calculus. This paper uses fractional calculus to relate the velocity of aortic blood flow to aortic pressure. The basis for this research is a Taylor series model of the velocity of aortic blood flow with subsequent term-by-term fractional integration as well as fractional differentiation. Fractional calculus may be a useful mathematical tool in hemodynamic modelling.

Keywords**:** Fractional calculus, Aortic blood flow, Esophageal Doppler monitor, Differintegral, Differintegration

1. Introduction

Traditional hemodynamic modelling is typically based upon a second-order system utilizing the acceleration, velocity, and displacement of blood flow (Atlas, 2008). By convention, acceleration is defined as the first derivative of velocity, with respect to time, whereas displacement is its indefinite integral. In contradistinction, fractional calculus (FC) is based upon both non-integer differentiation as well as non-integer integration (Dalir and Bashour, 2010; David et al., 2011). The purpose of this paper is to illustrate how FC may be utilized in understanding the aortic pressure flow relationship during systole.

To cognize this application of FC, traditional integer differentiation is first examined for a power function of time:

$$f(t) = t^m \tag{1}$$

$$f'(t) = mt^{(m-1)} \tag{2}$$

$$f''(t) = m(m-1)t^{(m-2)} \tag{3}$$

$$f'''(t) = m(m-1)(m-2)t^{(m-3)} \tag{4}$$

The n^{th} repetitive integer differentiation process can therefore be summarized as:

$$\frac{d^n f}{dt^n} = \frac{(m!)t^{(m-n)}}{(m-n)!} \tag{5}$$

In a likewise manner, the n^{th} repetitive integer integration process can also be examined for a power function of time:

$$f(t) = t^m \tag{6}$$

$$\int f(t)dt = \frac{t^{(m+1)}}{m+1} \tag{7}$$

$$\int\int f(t)dtdt = \frac{t^{(m+2)}}{(m+1)(m+2)} \tag{8}$$

$$\int\int\int f(t)dtdtdt = \frac{t^{(m+3)}}{(m+1)(m+2)(m+3)} \tag{9}$$

$$\underbrace{\int \ldots \int f(t)dt \ldots dt}_{n} = \frac{d^{-n}f}{dt^{-n}} = \frac{(m!)t^{(m+n)}}{(m+n)!} \tag{10}$$

Note that a constant of integration can be utilized ***after*** *the completion of the repetitive integration process.* Thus, using either (5) or (10), repetitive differentiation or repetitive integration can be similarly accomplished using either positive or negative values for *n* respectively.

The gamma function $\Gamma(x)$ can be defined as (Bonnar, 2013):

$$\Gamma(x) = \lim_{\mu\to\infty} \frac{\mu^x}{x}\left(\frac{1}{x+1}\right)\left(\frac{2}{x+2}\right)\ldots\left(\frac{\mu}{x+\mu}\right) = \lim_{\mu\to\infty} \frac{1}{x}\mu^x \prod_{j=1}^{\mu}\left(1+\frac{x}{j}\right)^{-1} \tag{11}$$

Note that the gamma function is not defined for values of *x* equal to either zero or negative integer values. Furthermore, when *x* is a positive integer, the gamma function has the following property:

$$\Gamma(x) = (x-1)! \tag{12}$$

Additionally, $\Gamma(x)$ "smoothly connects" the integer values of the factorial function. *It is therefore suitable for defining non-integer factorial values.* The gamma function is illustrated in Figure 1.

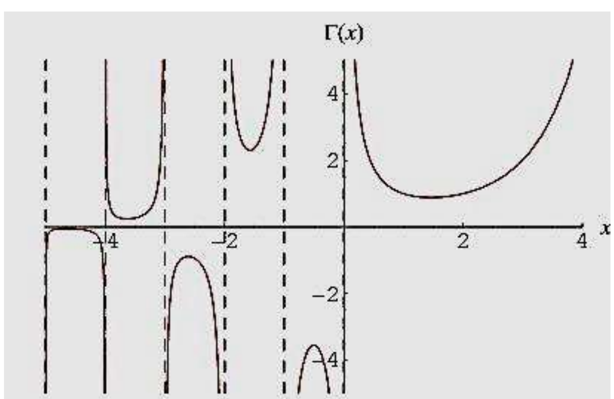

Fig. 1. The gamma function is useful in determining non-integer values of the factorial function. It is not defined for zero and negative integer values (Web-1).

Equations (5) and (10) can then be modified to utilize the gamma function:

$$\frac{d^q f}{dt^q} = \frac{\Gamma(m+1)t^{(m-q)}}{\Gamma(m-q+1)} \tag{13}$$

Equation (13) can be used as the definition of the differintegral (Das, 2011). Where q can have a positive value; either integer or non-integer.[*] Note that q can also take on integer or non-integer negative values:[†]

$$\underbrace{\int \dots \int f(t)dt \dots dt}_{q} = \frac{d^{-q} f}{dt^{-q}} = \frac{\Gamma(m+1)t^{(m+q)}}{\Gamma(m+q+1)} \tag{14}$$

The term q is referred to as the *order of differintegration* (Campos, 1989). Additionally, $f(t) = \left.\frac{d^q f}{dt^q}\right|_{q=0}$. As previously stated, Γ(0) is not defined. The gamma function is also not defined for negative integer values. Thus, specific fractional derivatives, or fractional integrals, may be unattainable.

Owing to either the positive or negative value of q in (13), the differintegral can therefore be utilized for the fractional differentiation, or fractional integration, of power functions. Furthermore, using FC, differentiation and integration may possibly be represented as a continuous process rather than discrete processes.

2. Fractional Calculus and the Taylor Series of an Exponential Function

The Taylor series for an exponential function is:

$$e^{-g \cdot t} = \sum_{n=0}^{N} \frac{(-g \cdot t)^n}{n!} = \frac{(-g \cdot t)^0}{0!} + \frac{(-g \cdot t)^1}{1!} + \frac{(-g \cdot t)^2}{2!} \dots + \frac{(-g \cdot t)^N}{N!} \tag{15}$$

Thus, for a sufficiently large N, an exponential function can be accurately approximated as a summation of power functions. Using the above methodology, the Taylor series for an exponential can therefore be term-by-term fractionally differentiated or fractionally integrated:

$$\frac{d^q(e^{-g \cdot t})}{dt^q} = \sum_{n=0}^{N} \left\{ \frac{(-g)^n}{n!} \cdot \left[\frac{\Gamma(n+1)t^{(n-q)}}{\Gamma(n-q+1)} \right] \right\} \tag{16}$$

For mathematical purposes, t cannot equal zero and be raised to a negative power. However, t can take on positive near-zero values. Negative values of t can also yield complex results. To further reiterate, care must be used when selecting integer values of q to prevent undefined values of the gamma function from occurring.

3. Methods: Examining the Velocity of Aortic Blood Flow

The esophageal Doppler monitor (EDM) is frequently utilized to assess the velocity of aortic blood flow during systole. The EDM allows clinicians to accurately assess patients' cardiac output and stroke volume during anesthesia and critical care conditions (Atlas et al., 2012). Figure 2 illustrates this waveform.

This velocity, $v(t)$, can be modelled as (Atlas, 2008):

---

[*] Imaginary and complex values of q can also be utilized. However, these will not be addressed in this introductory paper.

[†] Note that an alternative terminology could be that of *fractional* *derivatives* and *fractional* *antiderivatives*.

$$v(t) = \alpha\beta e^{-\gamma t}\left(1 - \frac{t}{FT}\right)t \qquad 0 < t < FT \tag{17}$$

Where α represents an acceleration term and β is a dimensionless gain. The time spent in systole is referred to as flow time, *FT*. It should be noted that γ can be determined (Atlas, 2008):

$$\gamma = \frac{2 - \left(\frac{FT}{FT_p}\right)}{\left(FT_p - FT\right)} \qquad 0 < FT_p < FT \tag{18}$$

Note that *FTp* represents the time at which peak velocity (PV) occurs. This is illustrated in Figure 2. Using a Taylor series, $v(t)$ can subsequently be approximated as a time-based power function:

$$v(t) = \alpha\beta\left[\sum_{n=0}^{N}\frac{(-\gamma)^n \cdot (t)^{(n+1)}}{n!} - \frac{1}{FT}\sum_{n=0}^{N}\frac{(-\gamma)^n \cdot (t)^{(n+2)}}{n!}\right] \qquad 0 < t < FT \tag{19}$$

By means of the aforementioned technique, fractional derivatives and fractional integrals of $v(t)$ can then be determined:

$$\frac{d^q v}{dt^q} = \alpha\beta\left[\sum_{n=0}^{N}\frac{(-\gamma)^n \cdot \Gamma(n+2) \cdot (t)^{(n+1-q)}}{n! \cdot \Gamma(n+2-q)} - \frac{1}{FT}\sum_{n=0}^{N}\frac{(-\gamma)^n \cdot \Gamma(n+3) \cdot (t)^{(n+2-q)}}{n! \cdot \Gamma(n+3-q)}\right] \qquad 0 < t < FT \tag{20}$$

Figure 3 demonstrates the *continuous* differintegral (20) over the range: $-1 \leq q \leq 1$.

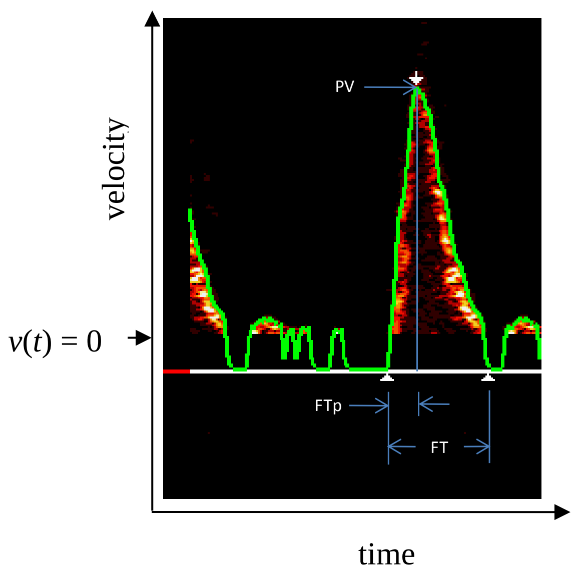

Fig. 2. The velocity of aortic blood flow as measured by an EDM. Note that *PV* represents peak velocity whereas *FT* signifies the time spent in systole. The time at which *PV* occurs is referred to as *FTp* (Atlas, 2008).

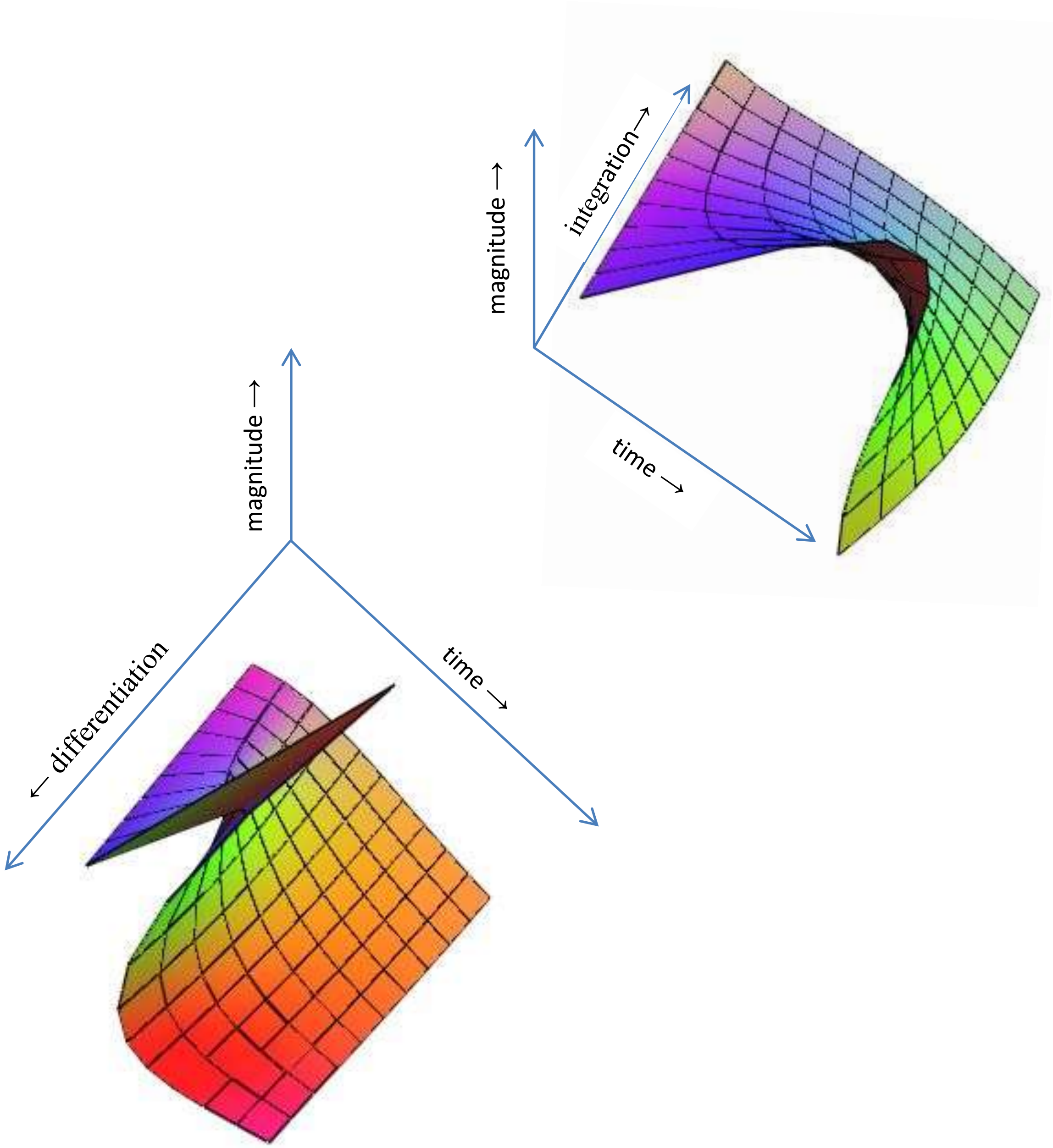

Fig. 3. Equation (20), the velocity of aortic blood flow during systole, $v(t)$, represented as a continuous differintegral. Note that fractional integration is associated with $-1 < q < 0$ whereas fractional differentiation is associated with $0 < q < 1$. Furthermore, $v(t) = \left.\frac{d^q v}{dt^q}\right|_{q=0}$.

4. Methods: Numerical Assessment

Using MATHCAD (PTC Corp., Needham, MA, USA) $v(t)$ can be calculated utilizing the numerical values from Table 1. Subsequently, its differintegrals of order −0.7 and 0.1 can both be determined. These functions are illustrated in Figure 4.

Note that the dimension associated with $v(t)$ is m/s whereas that of $\frac{d^{(-0.7)}v}{dt^{(-0.7)}}$ is m/s$^{(-0.7)}$.‡ Furthermore, the dimension of $\frac{d^{(0.1)}v}{dt^{(0.1)}}$ is m/s$^{0.1}$.

Table 1. Numerical values used for initial computational purposes.

Term	Value	Units	Notes
α	7.25	m/s^2	acceleration
β	3.00	dimensionless	gain
γ	6.154	s^{-1}	exponential decay
FT	0.36	s	flow time
FTp	0.1	s	time to peak flow
a	−0.7	dimensionless	order of fractional differintegration
b	0.1	dimensionless	order of fractional differintegration

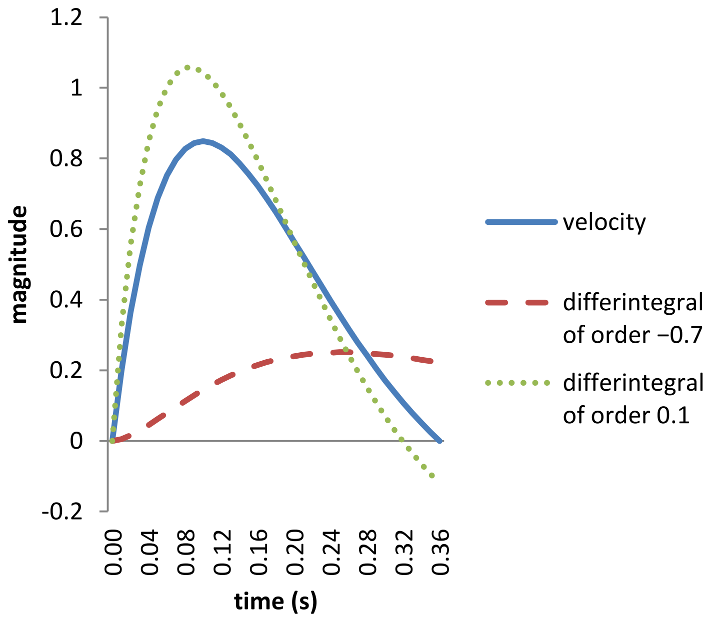

Fig. 4. Velocity as a function of time, $v(t)$, and both its associated differintegrals of order −0.7 and 0.1 are displayed.

5. Results: The Systolic Pressure Flow Relationship in the Aorta

Using (20), a straightforward model of aortic blood pressure, $P(t)$, as a function of the velocity of aortic blood flow during systole is:

$$P(t) = \frac{d^0 P}{dt^0} = k\pi r^2 \left(Z_a \frac{d^a v}{dt^a} + Z_b \frac{d^b v}{dt^b} \right) + C \qquad (21)$$

‡This dimension is equivalent to m·s$^{0.7}$.

Where r represents the radius of the aorta, and a and b are both velocity-based differintegrals of order −0.7 and 0.1 respectively. The term Z_a is "reactance-like" and would be analogous to a combination of elastance and resistance. Whereas Z_b would be analogous to a combination of inertia and resistance. Furthermore, C is a constant of integration and k converts units of Pascals to mmHg. In addition:

$$\left.\frac{d^a v}{dt^a}\right|_{t=0} = \left.\frac{d^b v}{dt^b}\right|_{t=0} = 0 \tag{22}$$

So that C also functions as an initial condition. Moreover, for the purposes of this preliminary assessment, a "trial and error" technique was employed to determine numerical values for a, b and Z_a and Z_b. These are displayed in Table 2. Note that Z_a and Z_b have magnitudes which are "ballpark approximate" to those of traditionally-derived resistance, elastance, and inertia.

The above model can also be utilized to assess $\frac{dP}{dt}$ during systole:

$$\frac{dP}{dt} = k\pi r^2 \left(Z_a \frac{d^{(a+1)} v}{dt^{(a+1)}} + Z_b \frac{d^{(b+1)} v}{dt^{(b+1)}} \right) \tag{23}$$

Both $P(t)$ and $\frac{dP}{dt}$ are illustrated in Figure 5. Note that a positive near-zero initial value for t, instead of zero, has to be used in (23) to prevent a "division by zero" singularity error from occurring.

Table 2. Numerical values used for final computational purposes.

Term	Value	Units	Notes
C	80	mmHg	constant of integration
k	0.0075	mmHg/Pascal	unit conversion
r	0.011	m	aortic radius
Z_a	$3.157 \cdot 10^7$	$N \cdot s^a/m^5$	"reactance-like" term
Z_b	$7.015 \cdot 10^6$	$N \cdot s^b/m^5$	"reactance-like" term

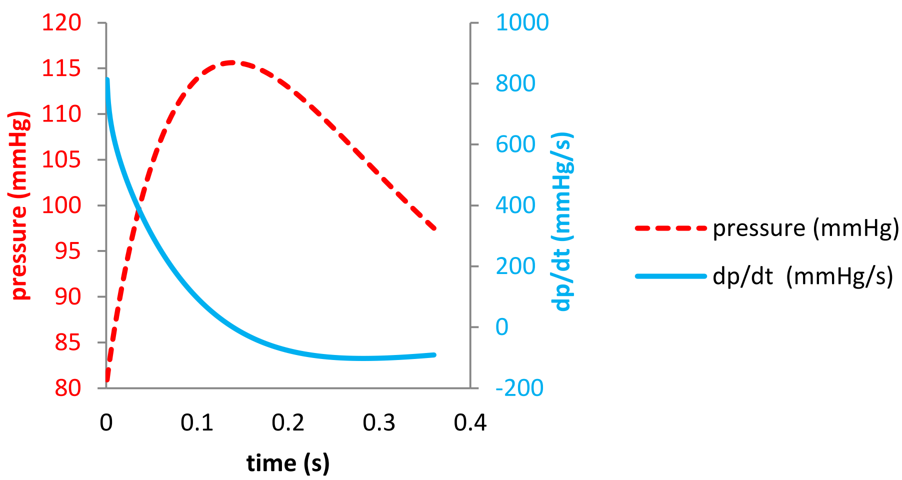

Fig. 5. Using fractional calculus, $P(t)$ is modelled using differintegrals which are based upon the velocity of aortic blood flow during systole. Note that $\frac{dP}{dt}$ is also displayed.

6. Discussion and Conclusion

The combination of both Taylor's series and computer-based mathematical tools allow for relatively simple numerical assessment of FC in hemodynamic modelling. Future research could focus on more refined utilization of this mathematical technique.

In addition, the use of Fourier series may also be readily applied to hemodynamic-based FC research. Specifically, each sine and cosine term can be fractionally integrated or differentiated with the inclusion of an appropriate "phase shift."

Thus, the utilization of a truncated convergent infinite series allows for relatively straightforward fractional integration and fractional differentiation to be performed with the aid of numerical analysis software. Furthermore, FC allows integration and differentiation to be thought of as a continuous progression rather than discrete processes.

References

Atlas G. (2008). Development and application of a logistic-based systolic model for hemodynamic measurements using the esophageal Doppler monitor. Cardiovasc. Eng., 8(3), 159-173.

Atlas G., Brealey D., Dhar S., Dikta G., Singer M. (2012). Additional hemodynamic measurements with an esophageal Doppler monitor: a preliminary report of compliance, force, kinetic energy, and afterload in the clinical setting. J. Clin. Monitor. Comp., 26(6), 473-482.

Bonnar J. (2013). "The Gamma Function" Applied Research Press.

Campos, LMBC. (1989). On a generalized Mittag-Leffler theorem and implicit differintegration. SIAM J. Math. Anal., 20(2), 454-467.

Dalir M., Bashour, M. (2010). Applications of fractional calculus. Appl. Math. Sci., 4(21), 1021-1032.

Das S. (2011). "Functional Fractional Calculus" Springer-Verlag.

David SA, Linares J.L., Pallone, EMJA. (2011). Fractional order calculus: historical apologia, basic concepts and some applications. Rev. Bras. Ensino Fis., 33(4), 4302-1−4302-7.

Web sites:

Web-1: http://mathworld.wolfram.com/GammaFunction.html