Comment on "Asymptotic time dependence in the fractal pharmacokinetics of a two-compartment model"

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A clarification is due about the paper by Chelminiak *et al.* [Phys. Rev. E **72**, 031903 (2005)]. In changing notation at the beginning, the authors incur an unfortunate error that significantly impacts the rest of the paper.

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Chelminiak *et al.* [1] correctly derived their Eq. (6) as

$$\ddot{C}_1 + (k_{12} + k_{20} + k_{21})\dot{C}_1 + k_{12}k_{20}C_1 = \frac{f}{V_d}(k_{21} + k_{20}) \quad (1)$$

for the compartmental model of Fig. 1. However, they later change notation substituting C_1 with ϕ in deriving their Eq. (10) as the homogeneous case equivalent to Eq. (1) for $f=0$ when $t>0$,

$$\ddot{\phi} + (a + b + kt^{-\alpha})\dot{\phi} + akt^{-\alpha}\phi = 0, \quad (2)$$

where $a=k_{21}$, $b=k_{12}$, and $kt^{-\alpha}=k_{20}$. Obviously, this equation should instead read

$$\ddot{\phi} + (a + b + kt^{-\alpha})\dot{\phi} + bkt^{-\alpha}\phi = 0.$$

This simple typographic error impacts significantly the entire rest of the paper, since the authors go about investigating several special cases for fixed parameter values and all the subsequent analytical expressions are mistaken. Particularly for case 3, where the authors assume "$b=0$, corresponding to fast clearance," stating

$$\ddot{\phi} + (a + kt^{-\alpha})\dot{\phi} + akt^{-\alpha}\phi = 0 \quad (3)$$

[their Eq. (18)], they really mean $a=0$, i.e., $k_{21}=0$, and therefore

$$\ddot{\phi} + (b + kt^{-\alpha})\dot{\phi} + bkt^{-\alpha}\phi = 0.$$

Subsequent derivations and discussion are unfortunately entangled in error, in spite of their theoretical and scientific interest.

Apparently, the root cause for all these problems stemmed from the stated intention of the authors about further investigating the previous work of Fuite *et al.* [2]. In this paper, the same compartment model with fractal elimination is presented but using the more common convention in physics for the designation of rate constants, rather than the pharmacokinetics one (Fig. 2).

In the Introduction, Fuite *et al.* explicitly say "The indices denote the direction of transfer, so k_{21} indicates flow into the second compartment from the first …," while Chelminiak *et al.* adopted the pharmacokinetic convention. In their words, also in the Introduction, "The coefficient k_{ij} represents the fractional transfer rate from compartment i to compartment j." Unfortunately they just missed updating the corresponding equations.

In summary, both these papers are extremely relevant in the field of pharmacokinetics and pharmacometrics, and whatever effort may be made to correct Chelminiak *et al.*'s communication will be worthwhile.

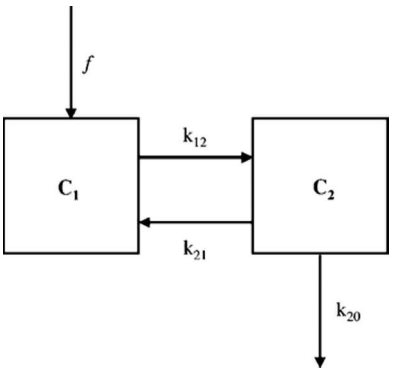

FIG. 1. The model of Ref. [1].

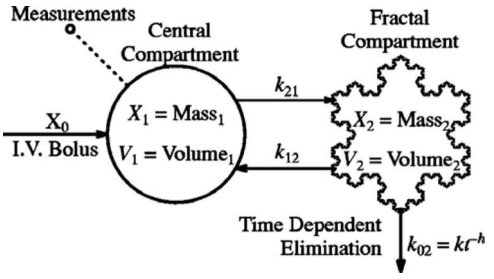

FIG. 2. The model of Ref. [2].

[1] P. Chelminiak, R. E. Marsh, J. A. Tuszynski, J. M. Dixon, and K. J. E. Vo, Phys. Rev. E **72**, 031903 (2005).

[2] J. Fuite, R. Marsh, and J. Tuszynski, Phys. Rev. E **66**, 021904 (2002).

