# Response to 'Comment on "A critical understanding of the fractal model of metabolic scaling"'

I identify the following claims in the comments of Savage, Enquist and West (hereafter referred to as SEW) (Savage et al., 2007) about my manuscript (Chaui-Berlinck, 2006):

(1) that the first term in parentheses in equation 5a is not 0/0 and, therefore, the correct limit corroborates their results;

(2) that I have performed an analysis '*in a regime where the equation does not hold*';

(3) that a geometric constant is absorbed into the Lagrange multiplier $\lambda_k$, and, therefore, the distinction between a cube or a sphere is irrelevant;

(4) that I have rehashed mistaken ideas from other authors and ignored the answers given to these authors.

In relation to (1), I agree with SEW that I have mistranscribed the first term in the equation, and I apologize for this. Therefore, that term is not 0/0, only the other two are, and the limit that SEW present is correct.

However, these were not the problems I addressed in my manuscript. In their original paper (West et al., 1997), the authors state that: '*Although the result $\beta_k=n^{-1/3}$ is independent of k, it is not area-preserving and therefore does not give a=3/4 when used in Eq. 5; instead, it gives a=1.*' Thus, the authors are discussing a general case of $\beta=n^{-1/3}$, not the specific one related to two distinct rules for this ratio (i.e. equation 5a in Chaui-Berlinck, 2006). If one analyses the general case and, as I state in my manuscript, '*take into account the possibility that the product $n\gamma\beta^2$ could be equal to 1*', then applying the sum of a power series to obtain $V_b$ from equation 4 of West et al. (West et al., 1997), the net result is $V_b=V_c n^N(N+1)$, as shown below:

$$r_k = \frac{r_{k+1}}{\beta} \Leftrightarrow r_{N-j} = \frac{r_N}{\beta^j}\,, \quad (1a)$$

$$l_k = \frac{l_{k+1}}{\gamma} \Leftrightarrow l_{N-j} = \frac{l_N}{\gamma^j}\,, \quad (1b)$$

where $r_N$ and $l_N$ are the radius and the length of a capillary, respectively, and $j$ is a counter from the capillaries ($j$=0) towards the great vessels. Inserting $r$ and $l$ into equation 4 from West et al. (West et al., 1997) gives:

$$V_b = \underbrace{\sum_{k=0}^{N} \pi r_k^2 l_k n^k}_{\text{(West et al., 1997)}} = \sum_{j=0}^{N} \pi \left(\frac{r_N}{\beta^j}\right)^2 \frac{l_N}{\gamma^j}\, n^{(N-j)} = \sum_{j=0}^{N} \frac{\pi\, r_N^2\, l_N\, n^N}{(\beta^2\gamma\, n)^j}\,. \quad (2)$$

As given by West et al. (West et al., 1997), the volume $V_c$ of a capillary is $\pi r_N^2 l_N$ and, by the assumption of the case $n\gamma\beta^2$=1, the result is the one presented above: $V_b=V_c n^N(N+1)$. This prevents West et al. from obtaining a linear relationship of $V_b$ with body mass in a general case. It has nothing to do with applying or not applying L'hospital's rule. Moreover, in contrast to what SEW state in their comments, this computation of $V_b$ is not '*the most critical claim made by Chaui-Berlinck*'. This is, simply, another source of inconsistency in the West et al. (West et al., 1997) model.

In relation to (2), all I can say is that in my manuscript (Chaui-Berlinck, 2006) I present a step-by-step reasoning based on what West et al. stated in their paper (West et al., 1997). Every step in the analysis can be easily tracked by means of figure 1 in the manuscript (Chaui-Berlinck, 2006). The impedance for each type of flow was analyzed by the equations put forward by West et al. themselves (West et al., 1997). For example, in my section 'Impedances and resistances to flow' (Chaui-Berlinck, 2006), it is clearly demonstrated that West et al. cannot obtain the necessary ratio between radii, $\beta=n^{-1/2}$, a conclusion that other authors, in a much deeper analysis, have drawn as well (e.g. Painter et al., 2006).

Item (3) is related to the energy minimization procedure taken by West et al. (West et al., 1997). On the one hand, SEW are correct in that a constant term ($3\pi/2$) could or could not be incorporated in a given Lagrange multiplier, just because it is a constant. On the other hand, West et al. directly assert that: '*For a fixed mass M, the auxiliary Lagrange function F, <u>which incorporates the constraints</u>, must be minimized with respect to <u>all variables for the entire system ($r_k$, $l_k$, and n)</u>.*' (underlines have been added by me); then, they put their augmented function $F$:

$$F(r_k,l_k,n) = W(r_k,l_k,n_k,M) + \lambda V_b(r_k,l_k,n_k,M) + \sum_{k=0}^{N} \lambda_k N_k l_k^3 + \lambda_M M\,. \quad (3)$$

Therefore, up to this point, one should understand that body mass $M$ is to be taken as a constraint in the model, which has, as variables, the radius $r$, the length $l$ and the branching ratio $n$. So, the question is not whether we are dealing with spheres or cubes. The question concerns how West et al. *constructed* a way to obtain their desired results: '*Now varying M and minimizing F in Eq. 7 ($\partial F/\partial M = 0$) leads to $V_b \propto M$, which is just the relation needed to derive Eq. 5.*' (West et al., 1997). Therefore, they took the derivative of the augmented function $F$ in relation to body mass, i.e. the derivative in relation to a constraint of their model, a completely heterodox/unexplained step in optimization *via* Lagrange multipliers.

In relation to (4), *mea culpa*. I agree with the criticism that I did not cite their response to other authors. The following explanation to the 'service volume' issue can be found in Savage et al. (Savage et al., 2004): '*As pointed out in the quotations below, <u>WBE clearly state that only the characteristics of the capillaries themselves are assumed to be invariant.</u> Nevertheless, K & K <u>incorrectly interpreted this size-invariance to mean that each capillary must supply a constant</u> **<u>volume of tissue</u>**' (underlines have been added by me).

However, West et al. (West et al., 1997) state: '*The network must branch so that a group of cells, referred to here as a "service volume," is supplied by each capillary. Because* $r_k \ll l_k$ *and the total number of branchings N is large, the volume supplied by the total network can be approximated by the sum of spheres whose diameters are that of a typical kth-level vessel, namely* $4/3\pi(l_k/2)^3 N_k$.' (underlines have been added by me). Thus, what the authors didn't realize is that when they concluded that '*the volume serviced by each capillary must scale as* $M^{1/4}$…' (West et al., 1997), they made themselves free from their own assumptions. Simply, they have two non-coincident explanations for 'service volume'.

As I show here, the problem is not with my mathematical literacy. And it is not with my geometric skills. It is also not with those who reviewed my manuscript. The problem lies in a model that was, and still is, presented to the audience as a complete and general structure for dealing with almost all topics related to biological scaling. Such a model is fully discussed in my manuscript, which presents a number of fundamental issues that have been avoided more than answered by SEW.

In conclusion, the request for the retraction of 'A critical understanding of the fractal model of metabolic scaling' (Chaui-Berlinck, 2006) is, at least, delusional.

10.1242/jeb.006858

## References

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