# Letters to the Editor

## Prion Kinetics

In a recent article, Pöschel et al. (2003) point out what they believe to be a mistake in our model of prion kinetics (Masel et al., 1999) and claim to present a corrected version. In fact, it is their version that is in error.

Both articles consider linear polymers breaking into two fragments. Polymer fragments less than a minimum size $n$ convert instantaneously into monomers. Let the concentration of polymers of size $i$ be $y_{\mathrm{i}}$ and let the rate of breaking at each of the points along the polymer length be $b$. Pöschel et al. (2003) calculate the rate at which monomers are formed through polymer breakage as

$$2b\sum_{\mathrm{j=1}}^{\mathrm{n-1}}\sum_{\mathrm{i=n+j}}^{\infty} jy_{\mathrm{i}} + 2b\sum_{\mathrm{j=1}}^{\mathrm{n-1}}\sum_{\mathrm{i=n}}^{\mathrm{n+j-1}} iy_{\mathrm{i}}.$$

The factor 2 in their first term reflects the fact that a piece of size $j$ can break off from two sides of a linear polymer. The second term, however, should not have the factor 2 as this term accounts for polymers converted by a single break in two pieces smaller than size $n$. By multiplying this term with a factor 2, they have in effect double-counted this term. By changing the order of summation it can be shown that

$$b\sum_{\mathrm{j=1}}^{\mathrm{n-1}}\sum_{\mathrm{i=n}}^{\mathrm{n+j-1}} iy_{\mathrm{i}} = b\sum_{\mathrm{i=n}}^{\mathrm{2n-2}} i(2n-i-1)y_{\mathrm{i}} = 2b\sum_{\mathrm{j=1}}^{\mathrm{n-1}}\sum_{\mathrm{i=n}}^{\mathrm{n+j-1}} jy_{\mathrm{i}}.$$

Adding this to their first term, we obtain

$$2b\sum_{\mathrm{j=1}}^{\mathrm{n-1}}\sum_{\mathrm{i=n+j}}^{\infty} jy_{\mathrm{i}} + 2b\sum_{\mathrm{j=1}}^{\mathrm{n-1}}\sum_{\mathrm{i=n}}^{\mathrm{n+j-1}} jy_{\mathrm{i}} = 2b\sum_{\mathrm{j=1}}^{\mathrm{n-1}}\sum_{\mathrm{i=n}}^{\infty} jy_{\mathrm{i}},$$

which sums exactly to the term for the production of monomers by breakage of polymers of all sizes in Masel et al., (1999). A further indication that the reasoning used to arrive at the differential equation model in Pöschel et al. (2003) is incorrect is that their results violate the conservation of matter. The gain of free monomers through breakage (last two terms in Eq. 1) does not match the loss through breakage of monomers contained in polymers (last term of Eq. 10) in Pöschel et al. (2003). In our 1999 article, we arrived at our results directly and did not give a detailed justification of how we summed, but hope to have remedied this here.

The simulations in Pöschel et al. (2003) are performed from first principles and so do not reflect this mistake, and the results from the simulation therefore compare to the differential equation model as presented in Masel et al. (1999). Their solution of the final steady state is identical to that which can be trivially derived from our system. Their claim that a constant concentration of monomers was ''a basic hypothesis'' of our theory, in contrast to theirs, is not true, however. We presented a full set of differential equations, including that for the change in the monomer concentration. Based on the vast majority of in vivo kinetic studies, we concentrated the details of our analysis on the initial stages of the kinetics during which monomer concentration is approximately constant and prion growth is exponential. An extension of the detailed analysis to describe later kinetics is not in conflict with our model. Their work represents an interesting extension of ours, without refuting it.

### REFERENCES

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Joanna Masel

*University of Arizona*
*Ecology and Evolutionary Biology*
*Tucson, AZ 85721 USA*

Vincent A. A. Jansen

*School of Biological Sciences*
*Royal Holloway, University of London*
*Egham TW20 0EX, United Kingdom*

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Address reprint requests to Dr. Joanna Masel, Dept. of Ecology and Evolutionary Biology, University of Arizona, PO Box 210088, Tucson, AZ 85721 USA. Tel.: 303-449-5686; E-mail: masel@charles.stanford.edu.



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