Reply to the Comment on:
"Utilizing Artificial Neural Networks in MATLAB to Achieve Parts-Per-Billion Mass Measurement Accuracy with a Fourier Transform Ion Cyclotron Resonance Mass Spectrometer" by D. Keith Williams Jr., Alexander L. Kovach, David C. Muddiman, and Kenneth W. Hanck. *J. Am. Soc. Mass Spectrom.* 20, 1303–1310 (2009)

It is unfortunate that there was an honest mistake in two of the theoretical *m*/*z* values used in our previous study [1], which propagated into this study. It is important to clearly state that we only learned of this after publication of this research and, even more importantly, because it did not change the conclusions in the least and that the actual numbers were not published for the theoretical *m*/*z* values (hence, no one could propagate that error in future work), we decided it was not necessary to correct.

Regarding the scientific criticism by Proctor, several "laws" have been proposed and tested to better define the relationship between *m*/*z* and f_{obs} in Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR) [1, 2]. Each of these "laws" relies on linear relationships, which are based on the basic physical models believed to be at work in FT-ICR. We agree with Proctor that MLR methods are the preferable fitting method provided they are well supported by the underlying physical models. ANN does not require an explicit mathematical or physical model and is, hence, useful for examining complex systems such as mass calibration in FT-ICR. Our purpose in conducting the ANN experiments described in the paper was to determine how well ANN performed (with no explicit physical model) relative to MLR models. Thus, it seems that Proctor, given his emphasis on the small error, missed the main scientific purpose of our contribution.

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References

1. Williams, D.K., Muddiman, D.C.: Parts-per-billion mass measurement accuracy achieved through the combination of multiple linear regression and automatic gain control in a Fourier transform ion cyclotron resonance mass spectrometer. Anal. Chem. ***79***, 5058–5063 (2007)
2. Muddiman, D.C., Oberg, A.L.: Statistical evaluation of internal and external mass calibration laws utilized in Fourier transform ion cyclotron resonance mass spectrometry. Anal. Chem. *77*, 2406–2414 (2005)

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