Comment to the Reply 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 may not have been the “main scientific purpose” but the title of the 2009 paper mentioned ANN and argued it is “useful for examining complex systems such as mass calibration.” That message is incorrect and the paper illustrates a (mis)use of

ANN that masked a “small mistake.” The size of the mistake may be “small” in practical terms but it was “statistically” significant. If the purpose of the calibration was to find a calibration function then the ANN function, when overfit, will cause biased measurements and, in fact, it did lead to underestimation of variance. It is good that the mistake was discovered and now the calculations can be corrected to provide more accurate calibration function and estimate of measurement error.

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