

AI-based data analysis method that improves cell assay results

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Abstract

A new data analysis method employing Artificial Intelligence software tools will improve cell assay and most other assay results. A type of pattern recognition measures the reproducibility of each well over multiple runs of a uniform plate-wide assay. Each well is scored based on the average value of the results and precision. The process develops a Gaussian distribution analysis of each well which can be used to adjust assay results that have been identified having a bias by AI pattern analysis.

Process Review

The process of analysis measures the location on the plate Gaussian curve over multiple assay runs and determines the movement of each well relative to the other wells. The measure is taken in 1/10ths of SD units so that the identical process can be used regardless of the absolute value of the results. This process measures small physical and surface chemical effects on the assay results. If there are other factors that produce repeating error on a well by well basis, like those of parallax or dispense head differences, they too are measured by this process. For some brands of microplates tested, same well position results between plate pairs have tighter precision than that well position does with the 8 wells surrounding it on the same plate. The difference we call Well Value Drift.

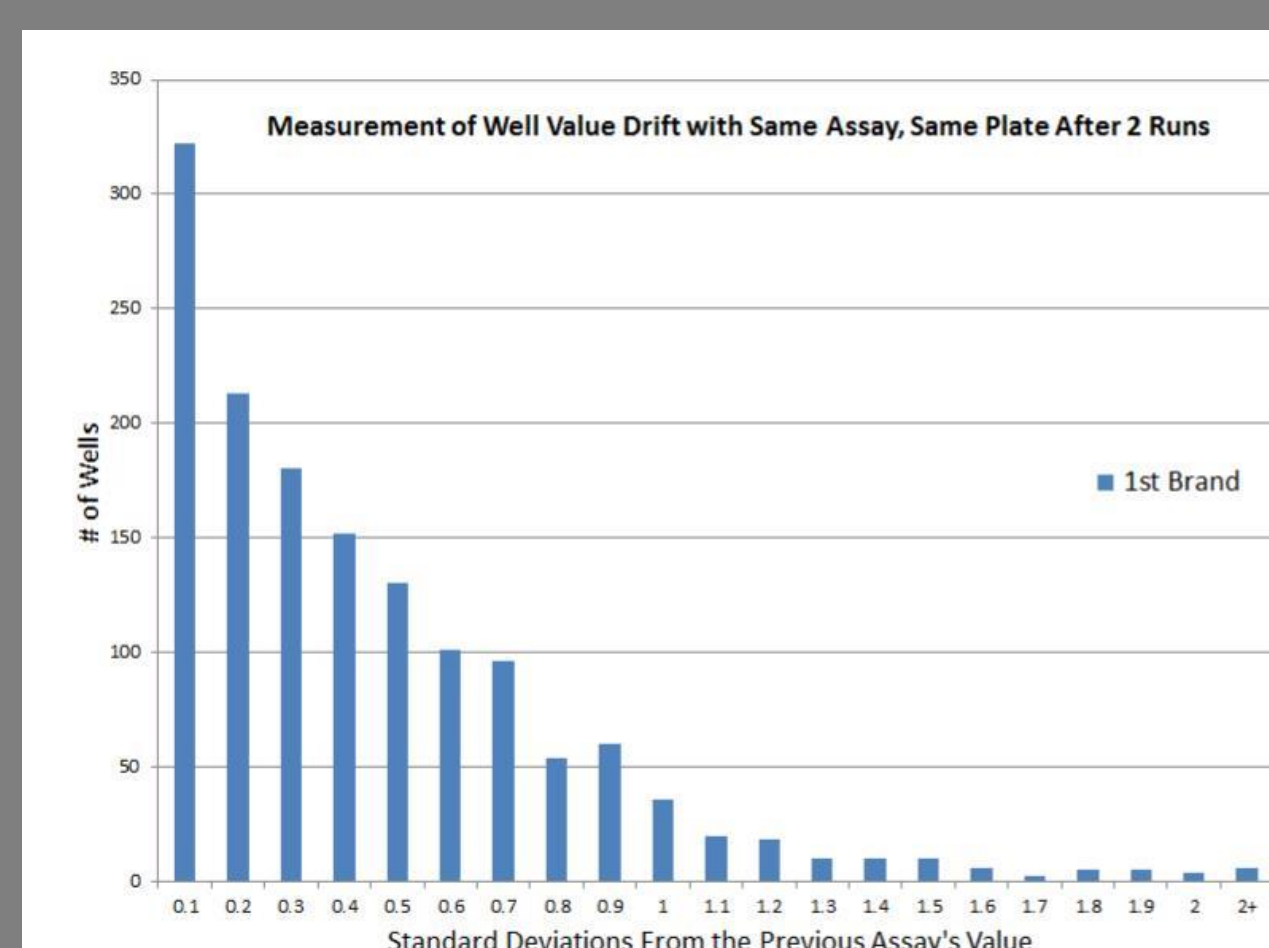


Figure 1. Example of Well Value Drift. Over 20% of wells repeated within 0.1 SD. 98% repeated within 1.0 SD.

Analytics Experiment 1

Using this process, a number of experiments were run to assess the utility of the well drift data for reanalyzing data. The first experiment with good results adjusted the average well value to the mean of the assay, effectively overlaying each well's Gaussian curve to form a plate-wide roll up of each well.

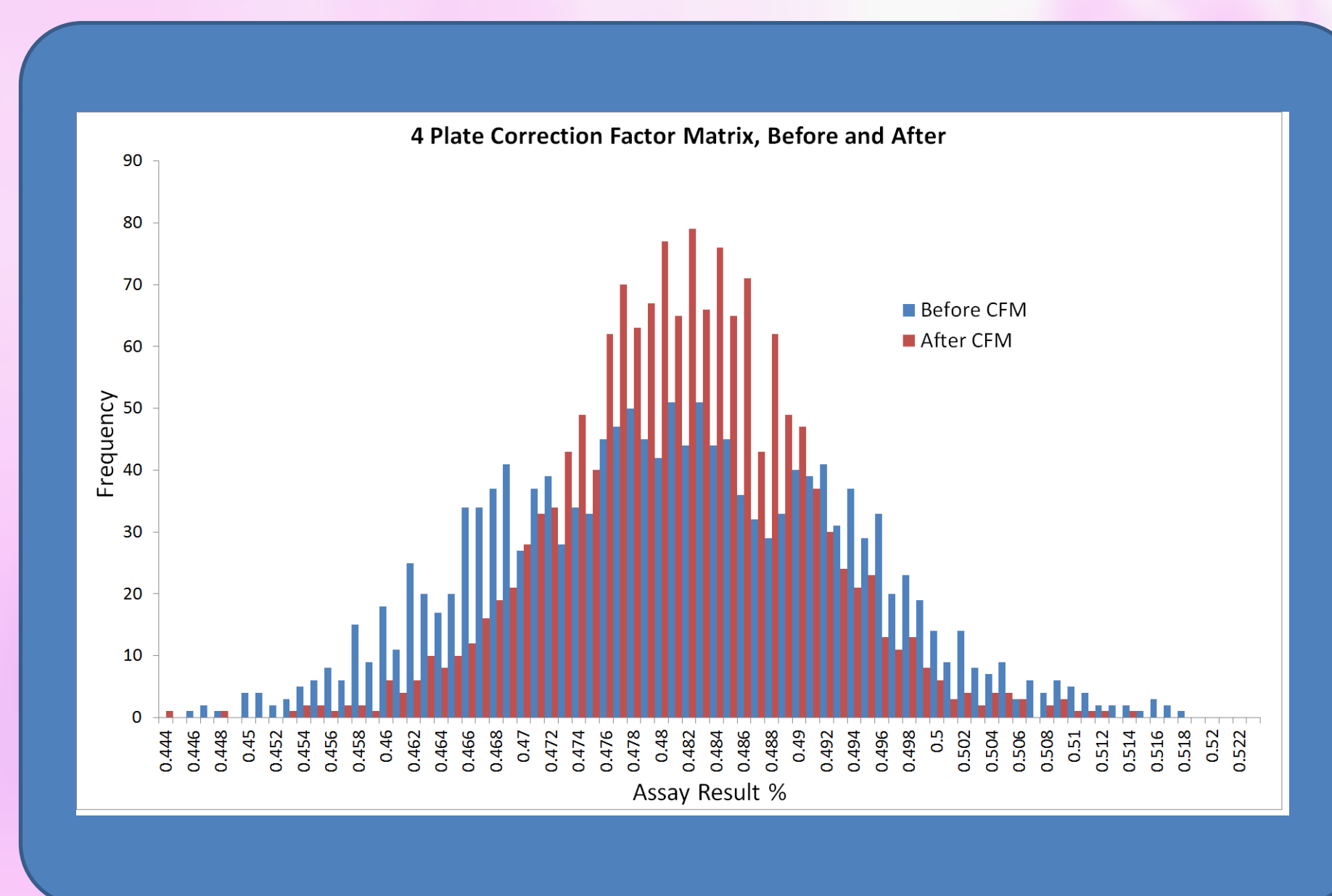


Figure 2. Overlay of before/after Ave Centering for a homogeneous assay

The assay results in Fig 2 are from a homogeneous assay and the number of learning cycles was 4. The reduction in SD was just under 30%. The CV for this assay was 2%.

A second assay using a cancer cell line was processed similarly. The raw data when graphed showed a significant skew due to a parallax effect of the plate reader instrument. Fig 3 shows that the average of the raw data from results with a should not be used as a centering point. The overlay graph shown in Fig 4 below shows that the skew is eliminated. The alignment is centered on the average of the three highest peaks.

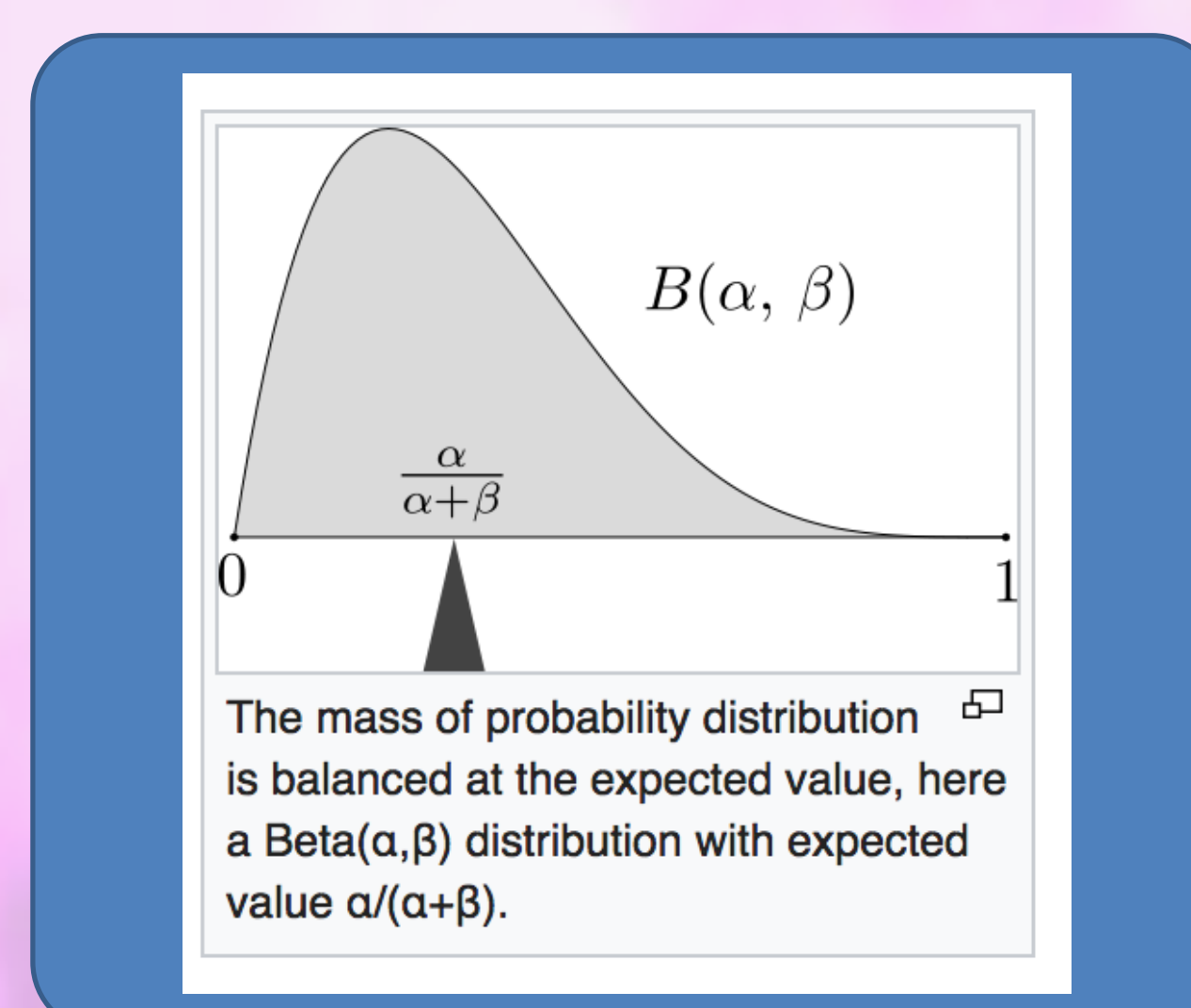


Figure 3. Skew effect on average

The peak alignment was found to near perfectly align the high value curves while pulling up the skew into a normal Gaussian shaped curve. The software is being configured so that the end user can define curve adjustment for each assay.

The assay data in Fig 4 showed a reduction in SD of 60%. The CV for the original assay data was 6%. The number of learning cycles was only 2. If more learning cycle plates were available, it is anticipated the SD reduction would improve. The improvement with just two cycles is a significant improvement in precision.

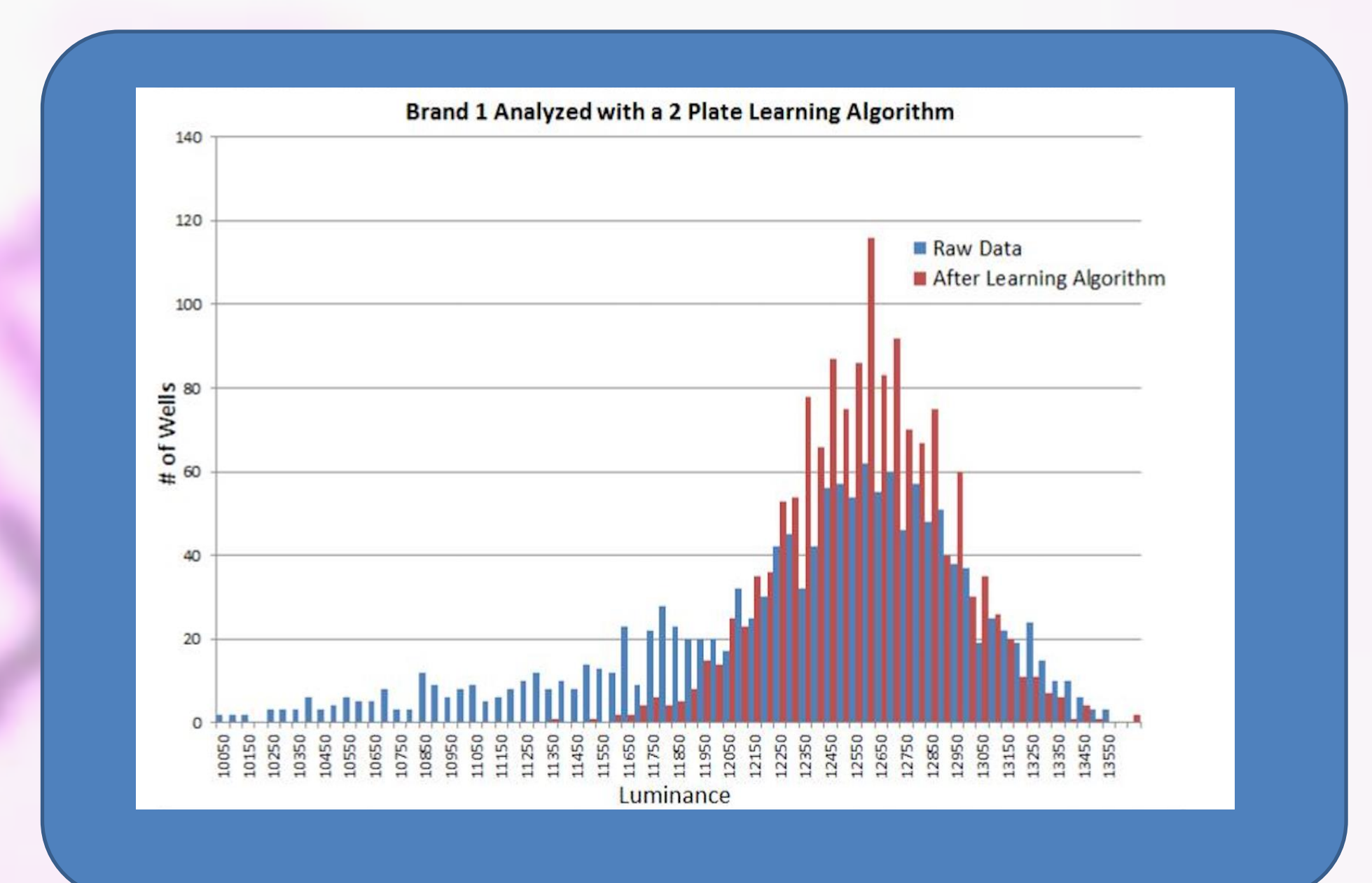


Figure 4. Overlay of before/after Peak Centering for a cell assay

Conclusions

- AI-base analysis of individual well patterns is a powerful to identify differences between microplate wells.
- The process of identifying differences also provides statistical data to adjust results based on measured performance.
- Improvements in assay precision demonstrate that 30% reduction in SD is to be expected if there are no other factors.
- The AI process is shown to be similarly effective measuring other patterns that repeat on a plate by plate basis or assay wide basis.
- The overall process is highly adaptable by the user to the assay, measurement modality and instrumentation limitations.