

We Claim:

1. A method executed by one or more computing devices for adaptive normalization of analyte levels in one or more samples, the method comprising:

receiving, by at least one of the one or more computing devices, one or more analyte levels corresponding to one or more analytes detected in the one or more samples, each analyte level corresponding to a detected quantity of that analyte in the one or more samples; and

normalizing the one or more analyte levels over one or more iterations by, for each iteration, removing any outlier analyte levels in the one or more analyte levels, computing a scale factor based at least in part on at least one remaining analyte level in the one or more analyte levels, and applying the scale factor to the one or more analyte levels;

wherein outlier analyte levels in the one or more analyte levels are determined based at least in part on an outlier analysis between each analyte level and a corresponding reference distribution of that analyte in a reference data set.

2. The method of claim 1, wherein the outlier analysis comprises a distance based outlier analysis.

3. The method of claim 1, wherein the outlier analysis comprises a density based outlier analysis.

4. The method of any one of claims 1-3, wherein normalizing the one or more analyte levels over one or more iterations comprises performing additional iterations until a change in the scale factor between consecutive iterations is less than or equal to a predetermined change threshold or until a quantity of the one or more iterations exceeds a maximum iteration value.

5. A computer-executed method for adaptive normalization of analyte levels in one or more samples, the method comprising:

receiving one or more analyte levels corresponding to one or more analytes detected in the one or more samples, each analyte level corresponding to a detected quantity of that analyte in the one or more samples; and

iteratively applying a scale factor to the one or more analyte levels over one or more iterations until a change in the scale factor between consecutive iterations is less than or equal to a predetermined change threshold or until a quantity of the one or more iterations exceeds a maximum iteration value, each iteration in the one or more iterations comprising:

determining a distance between each analyte level in the one or more analyte levels and a corresponding reference distribution of that analyte in a reference data set;

determining the scale factor based at least in part on analyte levels that are within a predetermined distance of their corresponding reference distributions; and

normalizing the one or more analyte levels by applying the scale factor.

6. The method of claim 5, wherein determining a distance between each analyte level in the one or more analyte levels and a corresponding reference distribution of that analyte in a reference data set comprises:

determining an absolute value of a Mahalanobis distance between each analyte level and the corresponding reference distribution of that analyte in the reference data set.

7. The method of claim 5, wherein determining a distance between each analyte level in the one or more analyte levels and a corresponding reference distribution of that analyte in a reference data set comprises:

determining a quantity of standard deviations between each analyte level and a mean or a median of the corresponding reference distribution of that analyte in the reference data set.

8. The method of any one of claims 5-7, wherein the predetermined distance comprises a value in a range between 0.5 to 6, inclusive.

9. The method of any one of claims 5-8, wherein the predetermined distance comprises a value in a range between 1 to 4, inclusive.

10. The method of any one of claims 5-9, wherein the predetermined distance comprises a value in a range between 1.5 to 3.5, inclusive.

11. The method of any one of claims 5-10, wherein the predetermined distance comprises a value in a range between 1.5 to 2.5, inclusive.

12. The method of any one of claims 5-11, wherein the predetermined distance comprises a value in a range between 2.0 to 2.5, inclusive.

13. The method of any one of claims 5-12, wherein determining the scale factor based at least in part on analyte levels that are within a predetermined distance of their corresponding reference distributions comprises:

determining an analyte scale factor for each analyte level that is within the predetermined distance of the corresponding reference distribution, the analyte scale factor being determined based at least in part on the analyte level and a mean or median value of the corresponding reference distribution;

determining the scale factor by computing either an average or a median of analyte scale factors corresponding to analyte levels that are within the predetermined distance of their corresponding reference distributions.

14. The method of any one of claims 5-12, wherein determining the scale factor based at least in part on analyte levels that are within a predetermined distance of their corresponding reference distributions comprises:

determining a value of the scale factor that maximizes a probability that analyte levels that are within the predetermined distance of their corresponding reference distributions are part of their corresponding reference distributions.

15. The method of claim 14, wherein the probability that each analyte level is part of the corresponding reference distribution is determined based at least in part on the scale factor, the analyte level, a standard deviation of the corresponding reference distribution, and a median of the corresponding reference distribution.

16. The method of any one of claims 4-15, wherein the change in the scale factor between subsequent iterations is measured as a percentage change and wherein the predetermined change threshold comprises a value between 0 and 40 percent, inclusive.

17. The method of any one of claims 4-16, wherein the predetermined change threshold comprises a value between 0 and 20 percent, inclusive.

18. The method of any one of claims 4-17, wherein the predetermined change threshold comprises a value between 0 and 10 percent, inclusive.

19. The method of any one of claims 4-18, wherein the predetermined change threshold comprises a value between 0 and 5 percent, inclusive.

20. The method of any one of claims 4-19, wherein the predetermined change threshold comprises a value between 0 and 2 percent, inclusive.

21. The method of any one of claims 4-20, wherein the predetermined change threshold comprises a value between 0 and 1 percent, inclusive.

22. The method of any one of claims 4-21, wherein the predetermined change threshold comprises 0 percent.

23. The method of any one of claims 4-22, wherein the maximum iteration value comprises one of: 10 iterations, 20 iterations, 30 iterations, 40 iterations, 50 iterations, 100 iterations, or 200 iterations.

24. The method of any one of claims 1-4, wherein the scale factor is computed by normalizing the at least one remaining analyte level to median or mean values of their corresponding reference distributions.

25. The method of any one of claims 1-4, wherein the scale factor is computed by maximizing a probability that the remaining analyte levels are part of their corresponding reference distributions.

26. The method of any one of claims 1-25, wherein the one or more samples comprise a biological sample.

27. The method of claim 26, wherein the biological sample comprises one or more of: a blood sample, a plasma sample, a serum sample, a cerebral spinal fluid sample, a cell lysates sample, or a urine sample.

28. The method of any one of claims 1-27, wherein the one or more analyte levels corresponding to the one or more analytes detected in the one or more samples comprise a plurality of analyte levels corresponding to a plurality of analytes detected in the one or more samples.

29. The method of any one of claims 1-28, wherein the one or more analytes comprise one or more of: a protein analyte, a peptide analyte, a sugar analyte, or a lipid analyte

30. The method of any one of claims 1-29, wherein each analyte level is determined based on applying a binding partner of the analyte to the one or more samples, wherein the binding of the binding partner to the analyte results in a measurable signal, and wherein the measurable signal yields the analyte level.

31. The method of claim 30, wherein the binding partner is an antibody or an aptamer.

32. The method of any one of claims 1-31, wherein each analyte level is determined based on mass spectrometry of the one or more samples.

33. The method of any one of claims 1-32, wherein the one or more samples comprise a plurality of samples, wherein the one or more analyte levels corresponding to the one or more analytes comprise a plurality of analyte levels corresponding to each analyte, and wherein

determining a distance between each analyte level in the one or more analyte levels and a corresponding reference distribution of that analyte in a reference data set comprises:

determining a Student's T-test, Kolmogorov-Smirnov test, or a Cohen's D statistic between the plurality of analyte levels corresponding to each analyte and the corresponding reference distribution of each analyte in the reference data set.

34. A computer program which, when executed by one or more processors, causes the one or more processors to carry out a method according to any one of the preceding claims.

35. An apparatus arranged to carry out a method according to any one of claims 1-33.