ASSAY SYSTEM CALIBRATION SYSTEMS AND METHODS

Field of the Invention

[0001] The present disclosure is related to methods of calibrating and employing assay systems and devices. In particular, the present disclosure relates to methods and systems employing improved calibration models.

Background

[0002] A wide variety of assay devices and formats are available for conducting assays and assay measurements. Generating quantitative sample assay results based on assay signals may be obtained by calibrating the assay using appropriate calibrations standards. Embodiments described herein provide improved calibration models and techniques to generate sample assay results having improved accuracy.

Summary

[0003] In embodiments, an assay system calibration method is provided. The method includes performing, on an assay system, a plurality of calibration assays on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte to obtain a plurality of calibration assay signal values; generating, by at least one processing unit, a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples; selecting, by the at least one processing unit, a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of the quantity value, identifying, by the at least one processing unit, fitting parameters that fit the calibration model equation to the calibration data set, generating, by the at least one processing unit, a calibration model including the calibration model equation and the fitting parameters; performing, on the assay system, at least one sample assay on at least one test sample to obtain at least one sample assay signal value; generating, by the at least one processing unit, a sample assay data set including the at least one sample assay signal value; and obtaining, by the at least one processing unit, a sample quantity value determined according to the calibration model and the at least one sample assay signal value.

[0004] In further embodiments, an assay system is provided. The assay system includes at least one memory unit; at least one processing unit programmed according to instructions on the at least one memory unit; and at least one assay system component configured to be controlled by the at least one processing unit. The at least one processing unit is configured to: control the at least one assay system component to perform a plurality of calibration assays on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte to obtain a plurality of calibration assay signal values; generate a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples; select a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of the quantity value; identify fitting parameters that fit the calibration model equation to the calibration data set; generate a calibration model including the calibration model equation and the fitting parameters; control the at least one assay system component to perform at least one sample assay on at least one test sample to obtain at least one sample assay signal value; generate a sample assay data set including the at least one sample assay signal value; and obtain a sample quantity value determined according to the calibration model and the at least one sample assay signal value.

[0005] In still further embodiments, one or more non-transitory computer-readable media are provided. The one or more non-transitory computer-readable media have instructions stored thereon that, when executed by at least one processing unit, cause the at least one processing unit to: perform, via control of an assay system, a plurality of calibration assays on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte to obtain a plurality of calibration assay signal values; generate a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples; select a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of the quantity value; identify fitting parameters that fit the calibration model equation to the calibration data set; generate a calibration model including the calibration model equation and

the fitting parameters; perform, via control of the assay system, at least one sample assay on at least one test sample to obtain at least one sample assay signal value; generate a sample assay data set including the at least one sample assay signal value; and obtain a sample quantity value determined according to the calibration model and the at least one sample assay signal value.

[0006] In yet further embodiments, an assay system calibration method is provided. The assay calibration method includes performing, on an assay system, a plurality of calibration assays on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte to obtain a plurality of calibration assay signal values; generating, by at least one processing unit, a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples; selecting, by the at least one processing unit, a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of the quantity value; identifying, by the at least one processing unit, fitting parameters that fit the calibration model equation to the calibration data set; generating, by the at least one processing unit, a calibration model including the calibration model equation and the fitting parameters; and storing, by the at least one processing unit, the calibration model.

[0007] In still further embodiments, an assay system calibration method is provided. The assay calibration method includes obtaining, by at least one processing unit: a calibration model including a calibration model equation and fitting parameters, wherein the calibration model equation relates the defined quantities to the plurality of calibration assay signal values and is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of the quantity value, and the fitting parameters fit the calibration model equation to a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples; performing, on an assay system, at least one sample assay on at least one test sample to obtain a sample assay signal value; generating, by the at least one processing unit, a sample assay data set including the at least one sample assay signal value; and determining, by the at least one processing unit, a sample quantity value determined according to the calibration model and the at least one sample assay signal value.

[0008] In yet further embodiments, one or more non-transitory computer-readable media are provided. The one or more non-transitory computer-readable media have instructions stored thereon that, when executed by at least one processing unit, cause the at least one processing unit to obtain a calibration data set including the results of assay measurements on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte, the calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples; select a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of the quantity value; identify fitting parameters that fit the calibration model equation to the calibration data set; generate a calibration model including the calibration model equation and the fitting parameters; obtain a sample assay data set including the results of assay measurements on at least one test sample, the test data set including at least one sample assay signal value corresponding to the at least one test sample; and determine a sample quantity value according to the calibration model and the at least one sample assay signal value.

[0009] In still further embodiments, a computer-implemented method to be carried out by a system including at least one memory unit and at least one processing unit programmed according to instructions on the at least one memory unit is provided. The method includes obtaining, by at least one processing unit: a calibration model including a calibration model equation and fitting parameters, wherein the calibration model equation relates the defined quantities to the plurality of calibration assay signal values and is modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of the quantity value, and the fitting parameters fit the calibration model equation to a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples; obtaining, by the at least one processing unit, a sample assay data set including the results of sample assay measurements on at least one test sample, the sample assay data set including at least one sample assay signal value corresponding to the at least one test sample; and determining, by the at least one processing unit, a sample quantity value according to the calibration model and the at least one sample assay signal value.

Claims:

1. An assay system calibration method comprising:

performing, on an assay system, a plurality of calibration assays on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte to obtain a plurality of calibration assay signal values;

generating, by at least one processing unit, a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples;

selecting, by the at least one processing unit, a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation with a modified Hill's slope that is dependent on a function of a quantity value;

identifying, by the at least one processing unit, respective values for fitting parameters that fit the calibration model equation to the calibration data set;

generating, by the at least one processing unit, a calibration model including the calibration model equation and the respective values for the fitting parameters;

performing, on the assay system, at least one sample assay on at least one test sample to obtain at least one sample assay signal value;

generating, by the at least one processing unit, a sample assay data set including the at least one sample assay signal value; and

obtaining, by the at least one processing unit, a sample quantity value determined according to the calibration model and the at least one sample assay signal value.

2. An assay system including:

at least one memory unit;

at least one processing unit programmed according to instructions on the at least one memory unit; and

at least one assay system component configured to be controlled by the at least one processing unit, wherein the at least one processing unit is configured to:

control the at least one assay system component to perform a plurality of calibration assays on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte to obtain a plurality of calibration assay signal values;

generate a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples;

select a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of a quantity value;

identify respective values for fitting parameters that fit the calibration model equation to the calibration data set;

generate a calibration model including the calibration model equation and the respective values for the fitting parameters;

control the at least one assay system component to perform at least one sample assay on at least one test sample to obtain at least one sample assay signal value;

generate a sample assay data set including the at least one sample assay signal value; and

obtain a sample quantity value determined according to the calibration model and the at least one sample assay signal value.

3. The assay system of claim 2, wherein, in the calibration model equation, the modified Hill's slope is dependent on a function of an inverse of the quantity value.

4. The assay system of claim 3, wherein the calibration model equation is defined as:

$$y = A + \frac{B - A}{1 + \left({}^{C}/_{x}\right)^{D+E\left(\frac{C}{x}\right)}}$$

wherein, x represents a quantity value, y represents an assay signal value, and A, B, C, D, and E are fitting parameters.

5. The assay system of claim 2, wherein, in the calibration model equation, the modified Hill's slope is dependent on a function of a natural logarithm of an inverse of the quantity value.

6. The assay system of claim 5, wherein the calibration model equation is defined as:

$$y = A + \frac{B - A}{1 + \left({}^{C}/_{x}\right)^{D+E\ln {}^{C}/_{x}}}$$

wherein, x represents the quantity value, y represents an assay signal value, and A, B, C, D, and E are fitting parameters.

7. The assay system of claim 6, wherein obtaining the sample quantity value according to the calibration model is performed using an equation

$$x = C * e^{\left[\frac{D-\sqrt{D^2+4E\ln\left(\frac{B-A}{y-A}-1\right)}}{2E}\right]}.$$

8. The assay system of claim 2, wherein the calibration model equation is defined as:

$$y = A + B(x/C)^{D+E\,ln(\frac{x}{C})}$$

wherein, x represents the quantity value, y represents an assay signal value, C represents a selected constant, and A, B, D, and E are fitting parameters.

9. The assay system of claim 2, wherein the calibration model equation is defined as:

$$y = A + B(x/C)^{D+E\left(\frac{x}{C}\right)}$$

wherein, x represents the quantity value, y represents an assay signal value, C represents a selected constant, and A, B, D, and E are fitting parameters.

10. The assay system of claim 2, wherein the at least one processing unit is further configured to identify the respective values for the fitting parameters by determining the respective values of the fitting parameters that minimize a mean square error between the calibration data set and one or more estimates or predictions obtained from the calibration model.

11. The assay system of claim 10, wherein the mean square error is calculated using a $1/y^2$ model.

12. One or more non-transitory computer-readable media having instructions stored thereon that, when executed by at least one processing unit, cause the at least one processing unit to:

perform, via control of an assay system, a plurality of calibration assays on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte to obtain a plurality of calibration assay signal values;

generate a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples;

select a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of a quantity value;

identify respective values for fitting parameters that fit the calibration model equation to the calibration data set;

generate a calibration model including the calibration model equation and the respective values for the fitting parameters;

perform, via control of the assay system, at least one sample assay on at least one test sample to obtain at least one sample assay signal value;

generate a sample assay data set including the at least one sample assay signal value; and

obtain a sample quantity value determined according to the calibration model and the at least one sample assay signal value.

13. An assay system calibration method comprising:

performing, on an assay system, a plurality of calibration assays on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte to obtain a plurality of calibration assay signal values;

generating, by at least one processing unit, a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to the plurality of calibration samples;

selecting, by the at least one processing unit, a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of a quantity value;

identifying, by the at least one processing unit, respective values for fitting parameters that fit the calibration model equation to the calibration data set;

generating, by the at least one processing unit, a calibration model including the calibration model equation and the fitting parameters; and

storing, by the at least one processing unit, the calibration model.

14. An assay system calibration method comprising:

obtaining, by at least one processing unit: a calibration model including a calibration model equation and respective values for fitting parameters, wherein

the calibration model equation relates defined quantities to a plurality of calibration assay signal values and is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of a quantity value, and

the respective values for the fitting parameters fit the calibration model equation to a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to a plurality of calibration samples;

performing, on an assay system, at least one sample assay on at least one test sample to obtain a sample assay signal value;

generating, by the at least one processing unit, a sample assay data set including the at least one sample assay signal value; and

determining, by the at least one processing unit, a sample quantity value determined according to the calibration model and the at least one sample assay signal value.

15. One or more non-transitory computer-readable media having instructions stored thereon that, when executed by at least one processing unit, cause the processing unit to:

obtain a calibration data set including results of assay measurements on a plurality of calibration samples having defined quantities of an analyte and including calibration samples having different quantities of the analyte, the calibration data set including a plurality of a quantity values according to defined quantities and a plurality of calibration assay signal values corresponding to the plurality of calibration samples;

select a calibration model equation relating the defined quantities to the plurality of calibration assay signal values, wherein the calibration model equation is a modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of quantity value;

identify respective values of fitting parameters that fit the calibration model equation to the calibration data set;

generate a calibration model including the calibration model equation and the respective values of the fitting parameters;

obtain a sample assay data set including results of assay measurements on at least one test sample, a test data set including at least one sample assay signal value corresponding to the at least one test sample; and

determine a sample quantity value according to the calibration model and the at least one sample assay signal value.

16. The one or more non-transitory computer-readable media of claim 12 or 15, wherein, in the calibration model equation, the modified Hill's slope is dependent on a function of an inverse of the quantity value.

17. The one or more non-transitory computer-readable media of claim 16, wherein the calibration model equation is defined as:

$$y = A + \frac{B - A}{1 + \left({}^{C}/_{x}\right)^{D+E\left(\frac{C}{x}\right)}}$$

wherein, x represents a quantity value, y represents an assay signal value, and A, B, C, D, and E are fitting parameters.

18. The one or more non-transitory computer-readable media of claim 12 or 15, wherein, in the calibration model equation, the modified Hill's slope is dependent on a function of a natural logarithm of an inverse of the quantity value.

19. The one or more non-transitory computer-readable media of claim 18, wherein the calibration model equation is defined as:

$$y = A + \frac{B - A}{1 + \left({}^{C}/_{x}\right)^{D + E \ln {}^{C}/_{x}}}$$

wherein, x represents the quantity value, y represents an assay signal value, and A, B, C, D, and E are fitting parameters.

20. The one or more non-transitory computer-readable media of claim 19, wherein obtaining the sample quantity value according to the calibration model is performed using an equation

$$x = C * e^{\left[\frac{D - \sqrt{D^2 + 4E \ln\left(\frac{B-A}{y-A} - 1\right)}}{2E}\right]}.$$

21. The one or more non-transitory computer-readable media of claim 12 or 15, wherein the calibration model equation is defined as:

$$y = A + B(x/C)^{D + E\, ln(\frac{x}{C})}$$

wherein, x represents the quantity value, y represents an assay signal value, C represents a selected constant, and A, B, D, and E are fitting parameters.

22. The one or more non-transitory computer-readable media of claim 12 or 15, wherein the calibration model equation is defined as:

$$y = A + B(x/C)^{D + E\left(\frac{x}{C}\right)}$$

wherein, x represents the quantity value, y represents an assay signal value, C represents a selected constant, and A, B, D, and E are fitting parameters.

23. The one or more non-transitory computer-readable media of claim 12 or 15, wherein the at least one processing unit is caused to identify the respective values of the fitting parameters by determining the respective values of the fitting parameters that minimize a mean square error between the calibration data set and one or more estimates or predictions obtained from the calibration model.

24. The one or more non-transitory computer-readable media of claim 23, wherein the mean square error is calculated using a $1/y^2$ model.

25. A computer-implemented method to be carried out by a system including at least one memory unit and at least one processing unit programmed according to instructions on the at least one memory unit, the method comprising:

obtaining, by at least one processing unit: a calibration model including a calibration model equation and respective values for fitting parameters, wherein

the calibration model equation relates defined quantities to a plurality of calibration assay signal values and is modified four parameter logistic regression fit equation where a modified Hill's slope is dependent on a function of a quantity value, and

the respective values for the fitting parameters fit the calibration model equation to a calibration data set including a plurality of quantity values according to the defined quantities and the plurality of calibration assay signal values corresponding to a plurality of calibration samples;

obtaining, by the at least one processing unit, a sample assay data set including results of sample assay measurements on at least one test sample, the sample assay data set including at least one sample assay signal value corresponding to the at least one test sample; and

determining, by the at least one processing unit, a sample quantity value according to the calibration model and the at least one sample assay signal value.

26. The method of any one of claims 1, 13, 14, and 25, wherein, in the calibration model equation, the modified Hill's slope is dependent on a function of an inverse of the quantity value.

27. The method of claim 26, wherein the calibration model equation is defined as:

$$y = A + \frac{B - A}{1 + \left(C/x\right)^{D+E\left(\frac{C}{x}\right)}}$$

wherein, x represents a quantity value, y represents an assay signal value, and A, B, C, D, and E are fitting parameters.

28. The method of any one of claims 1, 13, 14 and 25, wherein, in the calibration model equation, the modified Hill's slope is dependent on a function of a natural logarithm of an inverse of the quantity value.

29. The method of claim 28, wherein the calibration model equation is defined as:

$$y = A + \frac{B - A}{1 + \left(C/x\right)^{D+E\ln C/x}}$$

wherein, x represents the quantity value, y represents an assay signal value, and A, B, C, D, and E are fitting parameters.

30. The method of claim 29, wherein obtaining the sample quantity value according to the calibration model is performed using an equation

$$x = C * e^{\left[\frac{D-\sqrt{D^2+4E\ln\left(\frac{B-A}{y-A}-1\right)}}{2E}\right]}.$$

31. The method of any one of claims 1, 13, 14, and 25, wherein the calibration model equation is defined as:

$$y = A + B(x/C)^{D+E\,ln\left(\frac{x}{C}\right)}$$

wherein, x represents the quantity value, y represents an assay signal value, C represents a selected constant, and A, B, D, and E are fitting parameters.

32. The method of any one of claims 1, 13, 14 and 25, wherein the calibration model equation is defined as:

$$y = A + B(x/C)^{D+E\left(\frac{x}{C}\right)}$$

wherein, x represents the quantity value, y represents an assay signal value, C represents a selected constant, and A, B, D, and E are fitting parameters.

33. The method of any of claims 1, 13, 14 and 25, wherein identifying the respective values of the fitting parameters includes determining the respective values of the fitting parameters that minimize a mean square error between the calibration data set and one or more estimates or predictions obtained from the calibration model.

34. The method of claim 33, wherein the mean square error is calculated using a $1/y^2$ model.