from a sample, and the normalized reads from are used to determine the titer of one or more target organisms in a sample.

[0018] In one aspect, provided herein are multi-analyte controls comprising a mixture of at least three different species of organisms, wherein the organisms have been inactivated. In some embodiments, the multi-analyte controls comprise at least ten different species of organisms.

[0019] In another aspect, provided herein are methods of quantifying at least one target sequence in a sample, wherein the sample comprises a multi-analyte control comprising a mixture of at least three different species of organisms, wherein the organisms have been inactivated.

[0020] In another aspect, provided herein are methods of quantifying at least one target sequence in a sample, the methods comprising mixing a known amount of a multi-analyte control with the sample, wherein the multi-analyte control comprises a mixture of at least three different species of organisms, and wherein the organisms have been inactivated.

[0021] In another aspect, provided herein are methods quantifying a titer of a target organism in a sample, comprising: (a) providing a sample comprising the target organism, wherein the target organism comprises at least one target sequence; (b) providing a multi-analyte control comprising known titers of at least three species of organisms, wherein the organisms have been inactivated; (c) mixing a known amount of the normalization controls of the disclosure with the sample and with the multi-analyte control; (d) preparing high throughput sequencing libraries from the sample and the multi-analyte control; (e) sequencing said libraries to produce a collection of sample reads and a collection of multi-analyte control reads; (f) normalizing the collection of sample reads and the collection of multi-analyte control reads from (e) using the normalization controls; (g) determining a relationship between normalized reads and the known titers of organisms from the at least three species of organisms in the multi-analyte control; and (h) calculating a titer of the target organism in the sample using the relationship determined in (g).

[0021a] In another aspect, provided herein are method of quantifying a titer of a target organism in a sample, comprising: (a) providing a sample comprising the target organism, wherein the target organism comprises at least one target sequence, (b) providing a multi-analyte control comprising known titers of at least three species of

organisms, wherein the organisms have been inactivated, (c) mixing a known amount of a normalization control with the sample and with the multi-analyte control, (d) preparing high throughput sequencing libraries from the sample and the multi-analyte control, (e) sequencing said libraries to produce a collection of sample reads and a collection of multi-analyte control reads, (f) normalizing the collection of sample reads and the collection of multi-analyte control reads from (e) using the normalization controls, (g) determining a relationship between normalized reads and the known titers of the at least three species of organisms in the multi-analyte control; and (h) calculating the titer of the target organism in the sample using the relationship determined in (g).

[0022] In some embodiments, normalizing at step (f) comprises: (i) mapping reads from the collection of sample reads to the sample or the normalization control; (ii) mapping reads from the collection of multi-analyte control reads to the multi-analyte control or the normalization control; (iii) determining the number of reads produced by each of the

CLAIMS

What is claimed is:

1. A method of quantifying a titer of a target organism in a sample, comprising:
    a. providing a sample comprising the target organism, wherein the target organism comprises at least one target sequence;
    b. providing a multi-analyte control comprising known titers of at least three species of organisms, wherein the organisms have been inactivated;
    c. mixing a known amount of a normalization control with the sample and with the multi-analyte control;
    d. preparing high throughput sequencing libraries from the sample and the multi-analyte control;
    e. sequencing said libraries to produce a collection of sample reads and a collection of multi-analyte control reads;
    f. normalizing the collection of sample reads and the collection of multi-analyte control reads from (e) using the normalization controls;
    g. determining a relationship between normalized reads and the known titers of the at least three species of organisms in the multi-analyte control; and
    h. calculating the titer of the target organism in the sample using the relationship determined in (g).
2. The method of claim 1, wherein the normalization control comprises at least three groups of polynucleotides, wherein the polynucleotides within each group are of the same length.
3. The method of claim 2, wherein the lengths of all of the polynucleotides in the normalization control are the same.
4. The method of claim 2, wherein the polynucleotides within each group are of a different length when compared to the polynucleotides within any other group.
5. The method of claim 4, wherein the lengths of the groups of polynucleotides are distributed in a linear sequence or a geometric sequence.
6. The method of any one of claims 2-5, wherein the lengths of the polynucleotides in the at least three groups are between about 15 bp and about 50,000 bp.

7. The method of any one of claims 2-5, wherein the lengths of the polynucleotides in the at least three groups are between about 500 bp and about 1500 bp, about 100 and 1200 bp, or about 150 and about 600 bp.

8. The method of any one of claims 2-7, wherein the polynucleotides within each group comprise the same sequence.

9. The method of any one of claims 2-8, wherein the polynucleotides within each group do not comprise the same sequence.

10. The method of claim 9, wherein each group of polynucleotides comprises at least three subgroups of polynucleotides,

wherein the polynucleotides within each subgroup comprise the same sequence, and wherein the polynucleotides within each subgroup do not comprise the same sequence as any other subgroup.

11. The method of any one of claims 8-10, wherein at least one sequence in at least one group of polynucleotides comprises a component sequence.

12. The method of any one of claims 8-10, wherein every sequence in every group of polynucleotides comprises a component sequence.

13. The method of any one of claims 8-11, wherein the sequence of at least one group of polynucleotides comprises an isolated sequence.

14. The method of any one of claims 8-10, wherein the sequence of every group of polynucleotides comprises an isolated sequence.

15. The method of claims 10 or 11, wherein the sequence of at least one subgroup of at least one group of polynucleotides comprises an isolated sequence.

16. The method of claim 10 or 11, wherein the sequence of every subgroup of at least one group comprises an isolated sequence.

17. The method of claim 10, wherein the sequence of every subgroup of every group comprises an isolated sequence.

18. The method of claim 16 or 17, wherein the isolated sequence of each subgroup is not the same as the isolated sequence of any other subgroup.

19. The method of any one of claims 13-18, wherein the isolated sequence comprises a sequence of between about 6 bp and about 200,000 bp, between about 15 bp and about

50,000 bp, between about 500 bp and about 1500 bp, between about 100 bp and about 1200 bp, or between about 150 bp and about 600 bp.

20. The method of any one of claims 13-19, wherein the isolated sequence is isolated or derived from a virus, a bacterium, a fungus or a eukaryotic parasite.

21. The method of any one of claims 13-20, wherein the isolated sequence is not the same as at least one target sequence in a sequencing sample.