processors, using the genetic data to produce an adjusted test result in a characterization of the genetic information of the subject; and (d) outputting the adjusted test result into computer memory.

[0005a] In an aspect, the present disclosure provides a method for analyzing a disease state of a subject, comprising:

(a) using a genetic analyzer to generate genetic data from cell-free nucleic acid molecules in a plurality of biological samples of the subject obtained at (i) two or more time points or (ii) substantially the same time point, wherein the genetic data comprises sequence information corresponding to said cell-free nucleic acid molecules;

(b) receiving the genetic data from the genetic analyzer;

(c) with one or more programmed computer processors, using the genetic data to produce an adjusted test result by processing the sequence information of the subject to identify one or more genetic variations associated with a disease state,

wherein the adjusted test result comprises a reduction of noise compared to a test result produced from genetic data generated from only one biological sample of said plurality of biological samples,

wherein the genetic data comprises current sequence reads and prior sequence reads, and a first co-variate variation is detected in said genetic data,

wherein the processing comprises comparing the current sequence reads with the prior sequence reads, and updating a diagnostic confidence indication accordingly with respect to the characterization of the genetic information of the subject, which diagnostic confidence indication is indicative of a probability of identifying one or more genetic variations in a biological sample of the subject,

wherein the updating comprises increasing a diagnostic confidence indication in a characterization subsequent to the detection of the first co-variate variation if a second co-variate variation is detected; and

(d) outputting the adjusted test result into computer memory

[0006] In some embodiments, the genetic data comprises current sequence reads and prior sequence reads, and wherein (c) comprises comparing the current sequence reads with the prior sequence reads and updating a diagnostic confidence indication accordingly with respect to the

characterization of the genetic information of the subject, which diagnostic confidence indication is indicative of a probability of identifying one or more genetic variations in a biological sample of the subject.

[0007] In some embodiments, the method further comprises generating a confidence interval for the current sequence reads. In some embodiments, the method further comprises comparing the confidence interval with one or more prior confidence intervals and determining a disease progression based on overlapping confidence intervals.

[0008] In some embodiments, the biological samples are obtained at two or more time points including a first time point and a second time point, and wherein (c) comprises increasing a diagnostic confidence indication in a subsequent or a previous characterization if the information from the first time point corroborates information from the second time point. In some embodiments, the biological samples are obtained at two or more time points including a first time point and a second time point, and wherein (c) comprises increasing a diagnostic confidence indication in the subsequent characterization if the information from the first time point corroborates information from the second time point.

[0009] In some embodiments, a first co-variate variation is detected in the genetic data, and wherein (c) comprises increasing a diagnostic confidence indication in the subsequent characterization if a second co-variate variation is detected.

[0010] In some embodiments, the biological samples are obtained at two or more time points including a first time point and a second time point, and wherein (c) comprises decreasing a diagnostic confidence indication in the subsequent characterization if the information from a first time point conflicts with information from the second time point.

[0011] In some embodiments, the method further comprises obtaining a subsequent characterization and leaving as is a diagnostic confidence indication in the subsequent characterization for de novo information. In some embodiments, the method further comprises determining a frequency of one or more genetic variants detected in a collection of sequence reads included in the genetic data and producing the adjusted test result at least in part by comparing the frequency of the one or more genetic variants at the two or more time points. In some embodiments, the method further comprises determining an amount of copy number

CLAIMS

1. A method for analyzing a disease state of a subject, comprising:

(a) using a genetic analyzer to generate genetic data from cell-free nucleic acid molecules in a plurality of biological samples of the subject obtained at (i) two or more time points or (ii) substantially the same time point, wherein the genetic data comprises sequence information corresponding to said cell-free nucleic acid molecules;

(b) receiving the genetic data from the genetic analyzer;

(c) with one or more programmed computer processors, using the genetic data to produce an adjusted test result by processing the sequence information of the subject to identify one or more genetic variations associated with a disease state,

wherein the adjusted test result comprises a reduction of noise compared to a test result produced from genetic data generated from only one biological sample of said plurality of biological samples,

wherein the genetic data comprises current sequence reads and prior sequence reads, and a first co-variate variation is detected in said genetic data,

wherein the processing comprises comparing the current sequence reads with the prior sequence reads, and updating a diagnostic confidence indication accordingly with respect to the characterization of the genetic information of the subject, which diagnostic confidence indication is indicative of a probability of identifying one or more genetic variations in a biological sample of the subject,

wherein the updating comprises increasing a diagnostic confidence indication in a characterization subsequent to the detection of the first co-variate variation if a second co-variate variation is detected; and

(d) outputting the adjusted test result into computer memory.

2. The method of claim 1, further comprising generating a confidence interval for the current sequence reads.

3. The method of claim 2, further comprising comparing the confidence interval with one or more prior confidence intervals and determining a disease progression based on overlapping confidence intervals.

4. The method of claim 1, wherein the plurality of biological samples is obtained at two or more time points including a first time point and a second time point, and wherein (c) comprises increasing a diagnostic confidence indication in a subsequent or a previous characterization if the information from the first time point corroborates information from the second time point.

5. The method of claim 4, wherein the plurality of biological samples is obtained at two or more time points including a first time point and a second time point, and wherein (c) comprises increasing a diagnostic confidence indication in a characterization subsequent to the second time point if the information from the first time point corroborates information from the second time point.

6. The method of claim 4, wherein the plurality of biological samples is obtained at two or more time points including a first time point and a second time point, and wherein (c) comprises decreasing a diagnostic confidence indication in the subsequent characterization if the information from the first time point conflicts with information from the second time point.

7. The method of claim 1, further comprising obtaining a subsequent characterization and leaving as-is a diagnostic confidence indication in the subsequent characterization for de novo information.

8. The method of claim 1, further comprising determining a frequency of one or more genetic variants detected in a collection of sequence reads included in the genetic data and producing the adjusted test result at least in part by comparing the frequency of the one or more genetic variants at the two or more time points.

9. The method of claim 1, further comprising determining an amount of copy number variation at one or more genetic loci detected in a collection of sequence reads included in the genetic data, and producing the adjusted test result at least in part by comparing the amount of copy number variation at the two or more time points.

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10. The method of claim 1, wherein the genetic data comprises sequence data from portions of a genome comprising disease-associated or cancer-associated genetic variants.

11. The method of claim 1, further comprising using the adjusted test result to increase a sensitivity of detecting genetic variants by increasing read depth of polynucleotides in a biological sample of the subject.

12. The method of claim 1, wherein the genetic data comprises a first set of genetic data and a second set of genetic data, wherein the first set of genetic data is at or below a detection threshold and the second set of genetic data is above the detection threshold.

13. The method of claim 12, wherein the detection threshold is a noise threshold.

14. The method of claim 12, further comprising, in (c), adjusting a diagnosis of the subject from negative or uncertain to positive when the same genetic variants are detected in the first set of genetic data and the second set of genetic data in a plurality of sampling instances or time points.

15. The method of claim 12, further comprising, in (c), adjusting a diagnosis of the subject from negative or uncertain to positive in a characterization from an earlier time point when the same genetic variants are detected in the first set of genetic data at an earlier time point and in the second set of genetic data at a later time point.

16. The method of claim 1, wherein the disease state is cancer and the genetic analyzer is a nucleic acid sequencer.

17. The method of claim 1, wherein the plurality of biological samples includes at least two different types of biological samples.

18. The method of claim 1, wherein the plurality of biological samples includes the same type of biological sample.

19. The method of claim 18, wherein the biological samples are blood samples.

20. The method of claim 19, wherein the nucleic acid molecules are cell-free deoxyribonucleic acid (DNA).