

## CLAIMS

1. A method, comprising:
  - flowing an incorporation reagent, through a reagent management system and a flow cell of an instrument,
  - the reagent management system comprising a plurality of reagent wells having at least a first, a second and a third reagent to contain an incorporation reagent, a cleavage reagent and a buffer reagent positioned respectively therein, the reagent management system selecting a flow of reagent from one of the plurality of reagent wells; and the flow cell comprising a flow channel in fluid connection with the reagent management system,
  - the flow cell having a first polynucleotide positioned therein and flowing the incorporation reagent, through the reagent management system and flow cell over the first polynucleotide, wherein the incorporation reagent adds a first base onto a sequence of bases, the sequence of bases comprising a second polynucleotide complementary to the first polynucleotide;
  - capturing an image, of an identification signal emanating from the first base, after the first base has been added onto the second polynucleotide;
  - flowing a cleavage reagent, through the reagent management system and flow cell, to remove a first terminator from the first base in order to enable a subsequent base in the sequence of bases to be added to the second polynucleotide; and
  - flowing a buffer reagent, through the reagent management system and flow cell in a plurality of cycles of consecutive forward and reverse flow directions to remove the cleavage reagent from the flow cell.
2. The method of claim 1, wherein the plurality of cycles comprises 4 or more cycles.
3. The method of claim 1, wherein the plurality of cycles comprises 12 or more cycles.

4. The method of claim 1, wherein the reagent management system and the flow cell are positioned in a cartridge of the instrument, the cartridge being removably insertable into the instrument.

5. The method of claim 1, wherein the incorporation reagent, the cleavage reagent and the buffer reagent are stored in reagent wells of the reagent management system, the reagent wells operable to store a finite total volume of each reagent.

6. The method of any of claims 1-5, wherein flowing the buffer reagent comprises:

flowing a first forward flow volume of the buffer reagent in the forward flow direction of each cycle of the plurality of cycles; and

flowing a second reverse flow volume of the buffer reagent in the reverse flow direction of each cycle of the plurality of cycles, the first forward flow volume being greater than the second reverse flow volume.

7. The method of claim 6, wherein the forward flow volume is greater than the reverse flow volume by about 3% or more.

8. The method of any of claims 1-5, wherein the flowing the buffer reagent comprises:

an incubation period of substantially no flow of buffer reagent through the reagent management system and flow cell for about 10 seconds or more after the last cycle of the plurality of cycles; and

flowing a third forward flow volume of the buffer reagent in the forward flow direction after the incubation period.

9. The method of claim 8, wherein total sweep volume of the buffer reagent, during the flowing the buffer reagent, is substantially determined by the formula  $((1^{\text{st}} \text{ FFV} + 2^{\text{nd}} \text{ RFV}) * N) + 3^{\text{rd}} \text{ FFV}$ , wherein:

$1^{\text{st}}$  FFV is the first forward flow volume,

$2^{\text{nd}}$  RFV is the second reverse flow volume,

N is the total number of cycles in the plurality of cycles, and

3<sup>rd</sup> FFV is the third forward flow volume.

10. The method of claim 9, wherein total fluidic consumption of the buffer reagent, during the flowing the buffer reagent, is substantially determined by the formula  $((1^{\text{st}} \text{ FFV} - 2^{\text{nd}} \text{ RFV}) * N) + 3^{\text{rd}} \text{ FFV}$ .
11. The method of claim 10 wherein the ratio of the total sweep volume of the buffer reagent to the total fluidic consumption of the buffer reagent is equal to or greater than about 6.
12. The method of any of claims 1-5, wherein the flowing in the forward flow direction and the flowing in the reverse flow direction are separated by a delay time of about 1 second or less for each cycle of the plurality of cycles of forward and reverse flow directions.
13. The method of any of claims 1-5, wherein the flowing in the forward flow direction and flowing in the reverse flow direction is separated by a delay time of about 200 milliseconds or less for each cycle of the plurality of cycles of forward and reverse flow directions.
14. The method of any of claims 1-5, wherein each cycle of the plurality of cycles of forward and reverse flow directions is separated by a delay time of about 200 milliseconds or less.
15. An instrument comprising:  
a reagent management system, positioned in the instrument, the reagent management system comprising a plurality of reagent wells, the reagent wells having at least a first, a second and a third reagent well operable to contain an incorporation reagent, a cleavage reagent and a buffer reagent positioned respectively therein, the reagent management system to select a flow of reagent from one of the plurality of reagent wells; and

a flow cell, positioned in the instrument, the flow cell comprising a flow channel in fluid communication with the reagent management system, the flow channel to route the flow of reagent over a first polynucleotide positioned in the flow channel; and a detection module;

wherein the instrument is operable to:

flow the incorporation reagent, through the reagent management system and flow cell, to add a first base onto a sequence of bases, the sequence of bases comprising a second polynucleotide complementary to the first polynucleotide;

capture an image, of an identification signal emanating from the first base, after the first base has been added onto the second polynucleotide;

flow the cleavage reagent, through the reagent management system and flow cell, to remove a first terminator from the first base in order to enable a subsequent base in the sequence of bases to be added to the second polynucleotide; and

flow the buffer reagent, through the reagent management system and flow cell in a plurality of cycles of consecutive forward and reverse flow directions to remove the cleavage reagent from the flow cell.

16. The instrument of claim 15 wherein, the instrument is operable to flow the buffer reagent through the reagent management system and flow cell in a plurality of 4 or more cycles of consecutive forward and reverse flow directions.

17. The instrument of claims 15 wherein, the instrument is operable to flow the buffer reagent through the reagent management system and flow cell in a plurality of 12 or more cycles of consecutive forward and reverse flow directions.

18. The instrument of claim 15, wherein the instrument is operable to flow the buffer reagent such that the flowing in a forward flow direction and flowing in a reverse flow direction is separated by a delay time of about 200 millisecond or less for each cycle of the plurality of cycles of forward and reverse flow directions.

19. The instrument of claim 15, wherein the reagent management system is removably insertable into the instrument.
20. The instrument of claim 15, wherein the flow cell is removably insertable into the instrument.
21. The instrument of claim 15, comprising:
  - a cartridge to contain the reagent management system and the flow cell;
  - wherein the incorporation reagent, the cleavage reagent and the buffer reagent are stored in reagent wells of the reagent management system, wherein the reagent wells store a finite total volume of each reagent.
22. The instrument of claim 21, wherein the cartridge is removably insertable into the instrument.
23. The instrument of any of claims 15-22, wherein the instrument is operable to flow the buffer reagent such that:
  - a first volume of the buffer reagent is flowed in the forward flow direction of each cycle of the plurality of cycles;
  - a second volume of the buffer reagent is flowed in the reverse flow direction of each cycle of the plurality of cycles, the first volume being greater than the second volume;
24. The instrument of claim 23, wherein the forward flow volume is greater than the reverse flow volume by about 3% or more.
25. The instrument of any of claims 23 or 24, wherein the instrument is operable to flow the buffer reagent such that:
  - an incubation period of substantially no flow of the buffer reagent through the reagent management system and flow cell is imposed for about 10 seconds or more after the last cycle of the plurality of cycles; and

a third forward flow volume of the buffer reagent is flowed in the forward flow direction after the incubation period.

26. The instrument of claim 25 wherein, the instrument is operable to flow the buffer reagent such that:

a total sweep volume of the buffer reagent is substantially determined by the formula  $((1^{\text{st}} \text{ FFV} + 2^{\text{nd}} \text{ RFV}) * N) + 3^{\text{rd}} \text{ FFV}$ , wherein:

1<sup>st</sup> FFV is the first forward flow volume,

2<sup>nd</sup> RFV is the second reverse flow volume,

N is the total number of cycles in the plurality of cycles, and

3<sup>rd</sup> FFV is the third forward flow volume;

a total fluidic consumption of the buffer reagent is substantially determined by the formula  $((1^{\text{st}} \text{ FFV} - 2^{\text{nd}} \text{ RFV}) * N) + 3^{\text{rd}} \text{ FFV}$ ; and

wherein the ratio of the total sweep volume of the buffer reagent to the total fluidic consumption of the buffer reagent is equal to or greater than about 6.