

CLAIMS

1. A method of high-efficiency capture of bacteria in sample, the method comprising:
providing the sample as input to a microfluidic passage of a microfluidic device at a predetermined flow rate, wherein the microfluidic device comprises at least one electrode disposed adjacent to the microfluidic passage; and
activating the at least one electrode to capture bacteria in the sample by the at least one electrode using dielectrophoresis as the sample flows through the microfluidic passage at the predetermined flow rate, wherein the capture efficiency of bacteria is at least 99% when the predetermined flow rate is between 10-960 ul/min.
2. The method of claim 1, wherein the capture efficiency of bacteria is at least 99% when the predetermined flow rate is between 480-960 ul/min.
3. The method of claim 2, wherein the capture efficiency of bacteria is at least 99% when the predetermined flow rate is between 720-960 ul/min.
4. The method of claim 3, wherein the capture efficiency of bacteria is at least 99% when the predetermined flow rate is between 840-960 ul/min.
5. The method of claim 1, wherein the capture efficiency of bacteria is at least 99.6%.
6. The method of claim 1, wherein the capture efficiency of bacteria is at least 99.9 % when the predetermined flow rate is between 240-480 ul/min.
7. The method of claim 1, wherein the capture efficiency of bacteria is at least 99.99% when the predetermined flow rate is 240 ul/min.
8. The method of any of the preceding claims, further comprising:
quantifying, using an optical system, an amount of bacteria captured by the at least one electrode during activation of the at least one electrode.

9. The method of claim 8, wherein quantifying the amount of bacteria comprises:
capturing one or more images using the optical system; and
processing, using at least one computing device, the one or more images to quantify the amount of bacteria.
10. The method of claim 9, wherein quantifying the amount of bacteria comprises counting a number of spots in one or more images captured by the optical system.
11. The method of claim 8, further comprising:
labeling the bacteria captured on the at least one electrode with a fluorescent dye;
exciting the fluorescent dye with at least one light source of the optical system to produce a fluorescent signal;
capturing the fluorescent signal using the optical system; and
quantifying the amount of bacteria based, at least in part, on the captured fluorescent signal.
12. The method of any of the preceding claims, further comprising:
collecting effluent fluid at an output of the microfluidic channel;
determining an amount of bacteria in the collected effluent fluid; and
calculating the capture efficiency based, at least in part, on the determined amount of bacteria in the effluent fluid.
13. The method of claim 12, wherein calculating the capture efficiency based, at least in part, on the determined amount of bacteria in the effluent fluid comprises comparing a concentration of bacteria in the sample provided as input to the microfluidic channel and a concentration of bacteria in the collected effluent fluid.
14. The method of any of the preceding claims, wherein activating the at least one electrode comprises applying an alternating current (AC) voltage to the at least one electrode, wherein the AC voltage has a frequency between 900 Hz and 2MHz.
15. The method of claim 14, wherein the AC voltage has a frequency of 1 MHz.

16. The method of any of the preceding claims, wherein the at least one electrode comprises a plurality of concentric rings or arcs.
17. The method of any of the preceding claims, wherein the microfluidic passage comprises a microfluidic channel formed in a microfluidic chip.
18. The method of any of the preceding claims, further comprising:
 - altering a characteristic of an AC voltage provided to activate the at least one electrode, wherein altering the characteristic of the AC voltage causes the capture bacteria to be released from the at least one electrode.
19. The method of claim 18, wherein the characteristic is a frequency of the AC voltage.
20. The method of claim 19, wherein altering the frequency of the AC voltage comprises providing a higher frequency AC voltage to the at least one electrode to apply negative dielectrophoresis to the bacteria.
21. The method of claim 18, wherein the characteristic is an amplitude of the AC voltage.
22. The method of any of the preceding claims, further comprising:
 - flushing a buffer solution through the microfluidic passage to mechanically release the bacteria from the at least one electrode.
23. A bacterial detection system, comprising:
 - a microfluidic device including:
 - a microfluidic passage having an inlet and an outlet; and
 - at least one electrode disposed adjacent to the microfluidic passage,
 - wherein the at least one electrode when activated, is configured to capture, using dielectrophoresis, bacteria in a sample flowing through the microfluidic passage at a predetermined flow rate, and

wherein a capture efficiency of bacteria by the at least one electrode is at least 99% when the predetermined flow rate is between 10-960 ul/min.

24. The bacterial detection system of claim 23, further comprising:
a first pump coupled to the microfluidic passage, wherein first pump is configured to pump the sample through the microfluidic passage at the predetermined flow rate.
25. The bacterial detection system of claim 24, wherein the first pump is coupled to the outlet of the microfluidic passage.
26. The bacterial detection system of claim 24, wherein the first pump is coupled to the inlet of the microfluidic passage.
27. The bacterial detection system of claim 26, further comprising:
a second pump coupled to the output of the microfluidic passage, wherein the second pump is configured to pump the sample out of the microfluidic passage.
28. The bacterial detection system of any of claims 23-27, further comprising:
an optical system configured to capture one or more images of the at least one electrode during capture of the bacteria.
29. The bacterial detection system of claim 28, further comprising:
at least one computing device configured to process the one or more images to quantify an amount of bacteria captured by the at least one electrode.
30. The bacterial detection system of any of claims 23-29, wherein the at least one electrode comprises an array of electrodes arranged in at least one dimension along the microfluidic passage.
31. The bacterial detection system of claim 30, wherein the array of electrodes is arranged in at least two dimensions along the microfluidic passage.

32. The bacterial detection system of claim 30 or 31, further comprising:
a signal generator configured to activate the at least one electrode by applying an alternating current (AC) voltage thereto to generate an electric field.
33. The bacterial detection system of claim 32, wherein the signal generator is configured to apply a same AC voltage to each of the electrodes in the array of electrodes.
34. The bacterial detection system of claim 32, wherein the signal generator is configured to apply a first AC voltage to a first electrode in the array of electrodes and a second AC voltage to a second electrode in the array of electrodes, the first AC voltage and the second AC voltage being different.
35. The bacterial detection system of claim 34, wherein the first AC voltage and the second AC voltage have a different amplitude and/or frequency.
36. The bacterial detection system of any of claims 23-35, wherein the microfluidic passage comprises a microfluidic channel.
37. The bacterial detection system of any of claims 23-36, wherein the microfluidic device comprises a microfluidic chip having a plurality of microfluidic passages configured to process a plurality of samples in parallel.
38. A method of quantifying bacteria in sample, the method comprising:
providing, in a first run, a first portion of the sample as input to a microfluidic channel of a microfluidic chip, wherein the microfluidic chip comprises at least one electrode disposed adjacent to the microfluidic channel;
activating the at least one electrode to capture bacteria in the first portion of the sample by the at least one electrode using dielectrophoresis;
quantifying a first amount of bacteria captured by the at least one electrode during activation of the at least one electrode during the first run;
providing, in a second run, a second portion of the sample as input to the microfluidic channel of the microfluidic chip;

activating the at least one electrode to capture bacteria in the second portion of the sample by the at least one electrode using dielectrophoresis; and
quantifying a second amount of bacteria captured by the at least one electrode during activation of the at least one electrode during the second run,
wherein the first amount and second amount are within ± 0.5 log.

39. The method of claim 38, further comprising:
performing at least ten runs including the first run and the second run; and
quantifying an amount of bacteria in each of the at least ten runs, wherein an amount of variability in the quantified amount of bacteria across the at least ten runs is less than ± 0.5 log.

40. A bacterial capture system, comprising:
a microfluidic chip including a microfluidic passage and at least one electrode disposed adjacent to the microfluidic passage,
wherein the at least one electrode when activated, is configured to capture, using dielectrophoresis, bacteria in a sample flowing through the microfluidic passage, and
wherein a variability of an amount of bacteria captured across multiple runs of the sample flowing through the microfluidic passage is less than ± 0.5 log.

41. A method for enriching a bacterial species in a sample containing a first target bacterial species and other components, the method comprising:
providing the sample as input to a microfluidic passage included as a portion of a microfluidic device, wherein the microfluidic passage has at least one electrode disposed adjacent thereto;
selecting at least one characteristic of an AC voltage applied to the at least one electrode, wherein the selection of the at least one characteristic is based, at least in part, on the first target bacterial species;
applying the AC voltage having the selected at least one characteristic to the at least one electrode to generate an electric field that produces a positive dielectrophoresis force to capture on a surface of the at least one electrode, the first target bacterial species as the sample flows through the microfluidic channel;
releasing the captured first target bacterial species from the at least one electrode; and

collecting effluent fluid including the captured first target bacterial species, wherein a relative abundance of the first target bacterial species in the effluent fluid is increased compared to the relative abundance of the first target bacterial species in the sample.

42. The method of claim 41, wherein
the other components include a second target bacterial species, and
wherein the selection of the at least one characteristic is further based, at least in part, on the second target bacterial species such that both the first and the second target bacterial species are captured on the surface of the at least one electrode as the sample flows through the microfluidic channel when the AC voltage is applied to the at least one electrode.

43. The method of claim 42, wherein releasing the captured first target bacterial species from the at least one electrode comprises releasing only the first target bacterial species captured on the surface of the at least one electrode.

44. The method of claim 43, wherein releasing only the first target bacterial species captured on the surface of the at least one electrode comprises adjusting a frequency of the AC voltage applied to the at least one electrode such that a negative dielectrophoresis force is applied to the first target bacterial species to cause the first target bacterial species to be released from the surface of the at least one electrode.

45. The method of claim 44, wherein adjusting a frequency of the AC voltage comprises increasing the frequency of the AC voltage.

46. The method of claim 43, wherein collecting effluent fluid including the captured first target bacterial species comprises collecting effluent fluid including only the captured first target bacterial species.

47. The method of claim 46, further comprising:
releasing all remaining bacterial species captured on the surface of the at least one electrode.

48. The method of claim 47, wherein releasing all remaining bacterial species captured on the at least one electrode comprises turning deactivating the at least one electrode.
49. The method of claim 47, wherein releasing all remaining bacterial species captured on the at least one electrode comprises mechanically releasing all remaining bacterial species.
50. The method of claim 49, wherein mechanically releasing all remaining bacterial species comprises flushing the microfluidic channel with a fluid.
51. The method of any of claims 41-50, wherein
the other components include a second target bacterial species, and
wherein the selection of the at least one characteristic of the AC voltage is further based, at least in part, on the second target bacterial species such that first target bacterial species is captured on the surface of the at least one electrode as the sample flows through the microfluidic passage and the second target bacterial species is not captured on the surface of the at least one electrode.
52. The method of any of claims 41-51, wherein the at least one characteristic is an amplitude and/or a frequency of the AC voltage.
53. The method of claim 52, wherein the at least one characteristic comprises the amplitude and the frequency of the AC voltage.
54. The method of any of claims 41-53, further comprising:
pumping the sample through the microfluidic passage.
55. The method of any of claims 41-54, wherein the one or more bacterial species include gram positive bacterial species and gram negative bacterial species, and wherein selecting at least one characteristic of an AC voltage applied to the at least one electrode comprises selecting the at least one characteristic of the AC voltage such than only one of the gram positive bacterial species and the gram negative bacterial species is captured by the at least one electrode.

56. The method of any of claims 41-55, wherein a relative abundance of the first target bacterial species in the effluent fluid is increased at least 20 times compared to the relative abundance of the first target bacterial species in the sample.
57. The method of any of claims 41-56, wherein the sample is a fecal sample or a microbiome sample.
58. The method of any of claims 41-57, wherein the relative abundance of the first target bacterial species in the sample is below a detection limit of DNA sequencing.
59. The method of any of claims 41-58, wherein the first target bacterial species comprises live bacteria and the other components include dead bacteria.
60. The method of any of claims 41-59, further comprising:
quantifying an amount of first target bacterial species captured on the surface of the at least one electrode.
61. A bacterial enrichment system, comprising:
a microfluidic chip including a microfluidic passage and at least one electrode disposed adjacent to the microfluidic passage;
a pump coupled to the microfluidic chip and configured to pump a sample from an inlet of the microfluidic passage to an outlet of the microfluidic passage;
a signal generator electrically connected to the at least one electrode and configured to generate an AC voltage to drive the at least one electrode to produce an electric field within the microfluidic passage; and
a controller configured to:
control the signal generator to generate the AC voltage having frequency and amplitude characteristics such that when produced, the electric field captures on the surface of the at least one electrode, a target bacterial species in the sample while not capturing one or more other components in a sample as the sample is pumped through the microfluidic channel; and

control the signal generator to alter generation of the AC voltage to release the captured target bacterial species in the sample.

62. The bacterial enrichment system of claim 61, wherein the pump is coupled to the inlet of the at least one microfluidic channel.

63. The bacterial enrichment system of claim 61, wherein the pump is coupled to an outlet of the at least one microfluidic channel.

64. The bacterial enrichment system of claim 61, wherein the pump is coupled to the microfluidic chip outside of flow path of the sample.