

~~WHAT IS CLAIMED IS:~~ CLAIMS

1. A device, comprising:
first and second electrodes separated from one another by a space;
a particle coupled to the first electrode via a first plurality of bonds, and coupled to the second electrode via a second plurality of bonds; and
a polymerase coupled to the particle.
2. The device of claim 1, wherein the particle forms at least part of an electrically conductive bridge between the first and second electrodes.
3. The device of claim 1, wherein the particle is electrically nonconductive.
4. The device of claim 1, wherein the particle comprises a polymer having a tertiary structure.
5. The device of claim 4, wherein the polymer having the tertiary structure comprises a polynucleotide or a polypeptide.
6. The device of claim 5, wherein the polynucleotide or polypeptide is folded and cross-linked into a tertiary structure having a central constriction, the central constriction forming part of an electrically conductive bridge between the first and second electrodes.
7. The device of claim 1, wherein the particle comprises a nanoparticle with functional groups bonding the nanoparticle to the first and second electrodes.
8. The device of claim 7, wherein the nanoparticle is inorganic.
9. The device of any one of claims 1 to 8, wherein the particle has a diameter of at least about 10% of a length of the space.
10. The device of any one of claims 1 to 9, wherein the particle comprises a pair of nanoparticles coupled to one another by a linker.

11. A method of making a device, comprising:
depositing a solution onto first and second electrodes separated from one another,
the solution comprising particles in a liquid, each particle coupled to a respective
polymerase;
transporting one of the particles from the solution to a space adjacent to the first and
second electrodes; and
bonding the one of the particles to each of the first and second electrodes.
12. The method of claim 11, wherein the transporting comprises dielectrophoretically or
magnetically trapping the one of the particles at the first and second electrodes.
13. The method of any one of claims 11 to 12, wherein the bonding comprises forming
the first plurality of bonds between the first electrode and the one of the particles, and
forming the second plurality of bonds between the second electrode and the one of the
particles.
14. The method of any one of claims 11 to 13, further comprising sterically excluding,
using the one of the particles, other particles from the space adjacent to the first and second
electrodes.
15. The method of any one of claims 11 to 14, wherein the particle forms at least part of
an electrically conductive bridge between the first and second electrodes.
16. The method of any one of claims 11 to 14, wherein the particle is electrically
nonconductive.
17. The method of any one of claims 11 to 14, wherein the particle comprises a polymer
having a tertiary structure.
18. The method of claim 17, wherein the polymer having the tertiary structure comprises
a polynucleotide or a polypeptide.

19. The method of claim 18, wherein the polynucleotide or polypeptide is folded and cross-linked into a tertiary structure having a central constriction, the central constriction forming part of an electrically conductive bridge between the first and second electrodes.
20. The method of any one of claims 11 to 14, wherein the particle comprises a nanoparticle with functional groups bonding the nanoparticle to the first and second electrodes.
21. The method of claim 20, wherein the nanoparticle is inorganic.
22. The method of any one of claims 11 to 21, wherein the particle has a diameter of at least about 10% of a length of the space.
23. A device array, comprising:
a solid substrate;
a plurality of electrode pairs disposed on the solid substrate, the electrodes of each electrode pair being separated from one another by a respective space;
a plurality of particles, each bonded to the electrodes of a respective electrode pair,
wherein a majority of the electrode pairs respectively are bonded to a single one of the particles; and
a plurality of polymerases, each polymerase being coupled to a respective one of the particles.
- ~~24. The device array of claim 23, wherein the respective spaces vary amongst the electrode pairs to which the particles are respectively bonded.~~
- ~~25. A method of making a device array, comprising:
depositing a solution onto a solid substrate having a plurality of electrode pairs disposed thereon, the electrodes of each electrode pair being separated from one another by a respective space;
the solution comprising particles in a liquid, each particle coupled to a respective polymerase;
transporting the particles from the solution to respective ones of the spaces; and
bonding one of the particles to the electrodes of each electrode pair,~~

~~wherein a majority of the electrode pairs respectively are bonded to exactly one of the particles.~~

~~26. The method of claim 25, wherein the transporting comprises dielectrophoretically or magnetically trapping the one of the particles at the electrodes of the respective one of the electrode pairs.~~

~~27. The method of claim 25 or claim 26, wherein the bonding comprises forming a plurality of bonds between the one of the particles and each of the electrodes of the respective one of the electrode pairs.~~

~~28. The method of any one of claims 25 to 27, further comprising sterically excluding, using the one of the particles, any other particles from contacting the electrodes of the respective one of the electrode pairs.~~

~~29~~24. A composition, comprising:

first and second electrodes separated from one another by a space;
a particle coupled to the first electrode via a first plurality of bonds, and coupled to the second electrode via a second plurality of bonds; and
first and second polynucleotides;
a plurality of nucleotides, each nucleotide being coupled to a corresponding label; and
a polymerase coupled to the particle and to add the nucleotides to the first polynucleotide using at least a sequence of the second polynucleotide; and
detection circuitry to detect a sequence of the addition of the nucleotides to the first polynucleotide using at least changes in a current between the first and second electrodes, the changes being responsive to the labels corresponding to those nucleotides.

~~30. The composition of claim 29, wherein the particle forms at least part of an electrically conductive bridge between the first and second electrodes, and wherein the labels alter the current between the first and second electrodes through the bridge.~~

~~31. The composition of claim 29, wherein the particle is electrically nonconductive, and wherein the labels respectively form transient electrically conductive bridges between the first and second electrodes via which the current flows.~~

32. — The composition of claim 29, wherein the particle comprises a polymer having a tertiary structure.

33. — The composition of claim 32, wherein the polymer having the tertiary structure comprises DNA or a polypeptide.

34. — The composition of claim 32, wherein the tertiary structure forms an electrically conductive bridge between the first and second electrodes, and wherein the labels alter the current between the first and second electrodes by hybridizing to the electrically conductive bridge.

35. — The composition of claim 29, wherein the particle comprises a nanoparticle with functional groups bonding the nanoparticle to the first and second electrodes.

36. — The composition of claim 35, wherein the nanoparticle is electrically nonconductive, and wherein the labels respectively form transient electrically conductive bridges between the first and second electrodes via which the current flows.

37. — The composition of claim 36, wherein at least one of the labels is selected from the group consisting of carbon dots, electrically conductive polymers, pi-conjugated small molecules, nanotubes, and fullerenes.

38. — The composition of any one of claims 35 to 37, wherein the nanoparticle and the functional groups form at least part of an electrically conductive bridge between the first and second electrodes, and wherein the labels alter the current between the first and second electrodes by hybridizing to the functional groups.

39. — The composition of claim 29, wherein the particle comprises a pair of nanoparticles coupled to one another by a linker, and wherein the labels alter the current between the first and second electrodes by hybridizing to the linker.

~~40~~25. A method for sequencing, the method comprising:

adding, using a polymerase, nucleotides to a first polynucleotide using at least a sequence of a second polynucleotide;

changing, using labels respectively coupled to the nucleotides, a current between first and second electrodes, wherein a particle is coupled to the first electrode via a first plurality of bonds and is coupled to the second electrode via a second plurality of bonds; and

detecting a sequence in which the polymerase adds the nucleotides to the first polynucleotide using at least changes in the current that are caused using the labels corresponding to those nucleotides.

~~41. The method of claim 40, wherein the particle forms at least part of an electrically conductive bridge between the first and second electrodes, and wherein the labels alter the current between the first and second electrodes through the bridge.~~

~~42. The method of claim 40, wherein the particle is electrically nonconductive, and wherein the labels respectively form transient electrically conductive bridges between the first and second electrodes via which the current flows.~~

~~43. The method of claim 40, wherein the particle comprises a polymer having a tertiary structure.~~

~~44. The method of claim 43, wherein the polymer having the tertiary structure comprises DNA or a polypeptide.~~

~~45. The method of claim 44, wherein the tertiary structure forms an electrically conductive bridge between the first and second electrodes, and wherein the labels alter the current between the first and second electrodes by hybridizing to the electrically conductive bridge.~~

~~46. The method of claim 40, wherein the particle comprises a nanoparticle with functional groups bonding the nanoparticle to the first and second electrodes.~~

47. — The method of claim 46, wherein the nanoparticle is electrically nonconductive, and wherein the labels respectively form transient electrically conductive bridges between the first and second electrodes via which the current flows.

48. — The method of claim 47, wherein at least one of the labels is selected from the group consisting of carbon dots, electrically conductive polymers, pi-conjugated small molecules, nanotubes, and fullerenes.

49. — The method of any one of claims 46 to 48, wherein the nanoparticle and the functional groups form at least part of an electrically conductive bridge between the first and second electrodes, and wherein the labels alter the current between the first and second electrodes by hybridizing to the functional groups.

50. — The method of claim 40, wherein the particle comprises a pair of nanoparticles coupled to one another by a linker, and wherein the labels alter the current between the first and second electrodes by hybridizing to the linker.

51. — A composition, comprising:

first and second electrodes separated from one another by a space;
a fluid comprising a first electrically conductive label having a length at least as long as a length of the space; and
detection circuitry to generate a first signal responsive to transient formation, using the first electrically conductive label, of a first electrically conductive bridge between the first and second electrodes.

52. — The composition of claim 51 wherein the first electrically conductive label comprises a carbon dot, electrically conductive polymer, pi-conjugated small molecule, nanotube, or fullerene.

53. — The composition of claim 51 or claim 52, wherein:

the fluid further comprises a second electrically conductive label having a length at least as long as a length of the space; and

the detection circuitry is to generate a second signal responsive to transient formation, using the second electrically conductive label, of a second electrically conductive bridge between the first and second electrodes.

54.—The composition of claim 53, wherein the detection circuitry further is to distinguish between formation of the first electrically conductive bridge and the second electrically conductive bridge using at least a difference between the first signal and the second signal.

55.—The composition of any one of claims 51 to 54, wherein the first electrically conductive label transiently bonds to each of the first and second electrodes to form the first electrically conductive bridge.

56.—The composition of claim 55, wherein the first electrically conductive label comprises a first reactive group to transiently bond to the first electrode, and a second reactive group to transiently bond to the second electrode.

57.—The composition of claim 56, wherein the first and second reactive groups are selected from the group consisting of: amines, isothiocyanides, phosphines, carboxyls, selenos, pyridines, and methylsulfides.

58.—The composition of claim 56 or claim 57, wherein the detection circuitry further is to apply a bias voltage across the first electrically conductive bridge that disrupts the transient bond between the first reactive group and the first electrode or the transient bond between the second reactive group and the second electrode.

59.—The composition of claim 58, wherein the bias voltage disrupts the transient bond between the first reactive group and the first electrode and the transient bond between the second reactive group and the second electrode.

60.—The composition of any one of claims 51 to 59, further comprising:
a polymerase coupled adjacent to the first and second electrodes; and
a nucleotide coupled to the first electrically conductive label,
wherein the first electrically conductive label forms the first electrically conductive bridge responsive to action, using the polymerase, on the nucleotide.

61. — ~~The composition of claim 60, further comprising a particle coupled to the first and second electrodes and to the polymerase.~~

62. — ~~The composition of claim 61, wherein the particle is electrically nonconductive.~~

63. — ~~A method for sequencing, the method comprising:~~

~~adding, using a polymerase, nucleotides to a first polynucleotide using at least a sequence of a second polynucleotide;~~

~~transiently forming, using electrically conductive labels respectively coupled to the nucleotides, electrically conductive bridges between first and second electrodes; and~~

~~detecting a sequence in which the polymerase adds the nucleotides to the first polynucleotide using at least the transient formation of the electrically conductive bridges.~~

64. — ~~The method of claim 63, wherein the conductive labels independently comprise one or more of a carbon dot, electrically conductive polymer, pi-conjugated small molecule, nanotube, or fullerene.~~

65. — ~~The method of claim 63 or claim 64, wherein the sequence is detected using at least differences in electrical conductivities across the electrically conductive bridges.~~

66. — ~~The method of any one of claims 63 to 65, wherein the electrically conductive labels transiently bond to each of the first and second electrodes to form the electrically conductive bridges.~~

67. — ~~The method of claim 66, wherein each electrically conductive label comprises a first reactive group to transiently bond to the first electrode, and a second reactive group to transiently bond to the second electrode.~~

68. — ~~The method of claim 67, wherein the first and second reactive groups are selected from the group consisting of: amines, isothiocyanides, phosphines, carboxyls, selenos, pyridines, and methylsulfides.~~

69. — The method of claim 67 or claim 68, further comprising applying a bias voltage across the electrically conductive bridges that disrupts the transient bond between the first reactive group and the first electrode or the transient bond between the second reactive group and the second electrode.

70. — The method of claim 69, wherein the bias voltage disrupts the transient bond between the first reactive group and the first electrode and the transient bond between the second reactive group and the second electrode.

71. — The method of any one of claims 67 to 70, further comprising acting, using a polymerase coupled adjacent to the first and second electrodes, on a nucleotide coupled to one of the electrically conductive labels,

wherein that one of the electrically conductive labels forms one of the electrically conductive bridges responsive to the action, using the polymerase, on the nucleotide.

72. — The method of claim 71, wherein a particle is coupled to the first and second electrodes and to the polymerase.

73. — The method of claim 72, wherein the particle is electrically nonconductive.

74. — A composition, comprising:

first and second electrodes separated from one another by a space;
a bridge spanning the space between the first and second electrodes;
a fluid comprising a label that transiently bonds to the bridge in such a manner as to form an electrically conductive bridge; and

detection circuitry to generate a signal responsive to formation of the electrically conductive bridge, and to generate a bias voltage selected to disrupt the electrically conductive bridge following generation of the signal.

75. — A method for detecting, the method comprising:

forming an electrically conductive bridge using transiently bonding of a label to a bridge spanning a space between first and second electrodes;
detecting formation of the electrically conductive bridge; and

subsequently disrupting the transient bonding responsive to application of a bias voltage.

76. — A composition, comprising:

first and second electrodes separated from one another by a space;

first and second bridges spanning the space between the first and second electrodes,

the first bridge comprising a first polymer chain,

the second bridge comprising a second polymer chain that is different from the first polymer chain;

a fluid comprising a first oligomer that hybridizes to the first polymer chain and not to the second polymer chain; and

detection circuitry to generate a first signal responsive to hybridization of the first oligomer to the first polymer chain.

77. — The composition of claim 76, wherein:

the fluid further comprises a second oligomer that hybridizes to the second polymer chain and not to the first polymer chain; and

the detection circuitry is to generate a second signal responsive to hybridization of the second oligomer to the second polymer chain.

78. — The composition of claim 77, wherein the detection circuitry further is to distinguish between hybridization of the first oligomer with the first polymer chain and hybridization of the second oligomer with the second polymer chain using at least a difference between the first signal and the second signal.

79. — The composition of any one of claims 76 to 78, wherein the first and second polymer chains comprise different portions of a tertiary structure.

80. — The composition of claim 79, wherein:

the tertiary structure comprises a polynucleotide or polypeptide tertiary structure;

the first and second polymer chains respectively comprise first and second single stranded DNA sequences; and

the first and second oligomers respectively comprise third and fourth single stranded DNA sequences that respectively complement the first and second single stranded DNA sequences.

81.—The composition of claim 79 or claim 80, wherein the tertiary structure comprises a polypeptide.

82.—A method for sequencing, the method comprising:

adding, using a polymerase, nucleotides to a first polynucleotide using at least a sequence of a second polynucleotide;

hybridizing a first label coupled to a first one of the nucleotides to a first polymer chain of a bridge spanning a space between first and second electrodes responsive to the polymerase adding that nucleotide to the first polynucleotide;

sequentially hybridizing a second label coupled to a second one of the nucleotides to a second polymer chain of a bridge spanning a space between first and second electrodes; and

detecting the sequence in which the polymerase adds the first one of the nucleotides and the second one of the nucleotides to the first polynucleotide using at least changes in current through the bridge that are responsive to respective hybridizations between the first label with the first polymer chain and the second label with the second polymer chain.

83.—The method of claim 82, wherein the first label does not hybridize with the second polymer chain, and wherein the second label does not hybridize with the first polymer chain.

84.—The method of claim 82 or claim 83, wherein the first and second labels comprise respective polymers.

85.—The method of any one of claims 82 to 84, wherein the first and second polymer chains comprise different portions of a tertiary structure.

86.—The method of any one of claims 82 to 85, wherein:

the tertiary structure comprises a polynucleotide or polypeptide tertiary structure;

the first and second polymer chains respectively comprise first and second single stranded DNA sequences; and

~~the first and second labels respectively comprise third and fourth single stranded DNA sequences that respectively complement the first and second single stranded DNA sequences.~~

~~87. The method of claim 85 or claim 86, wherein the tertiary structure comprises a polypeptide.~~