

[0021] In yet another example of this first aspect, the modified electrolyte includes greater than 0 mM to about 500 mM of the cation complexing agent.

[0022] It is to be understood that any features of this first aspect of the nanopore sequencer may be combined together in any desirable manner and/or configuration.

[0023] In a second aspect, a nanopore sequencer comprises a cis well; a trans well; a nanopore fluidically connecting the cis well and the trans well; and a polyelectrolyte in a gel state in the cis well, or the trans well, or the cis and trans wells.

[0024] In one example of this second aspect, the polyelectrolyte is in the cis well and the nanopore sequencer further comprises an electrolyte in the trans well; or the polyelectrolyte is in the trans well and the nanopore sequencer further comprises an electrolyte in the cis well. In an example, the polyelectrolyte is selected from the group consisting of polydiallyldimethylammonium chloride, an ionic form of polyethyleneimine, an ionic form of linear polyethyleneimine, poly(allylamine hydrochloride), and an ionic form of poly(4-vinylpyridine); and the electrolyte includes a potassium cation and an associated anion, a sodium cation and the associated anion, or combinations thereof.

[0025] In another example of this second aspect, the nanopore sequencer further comprises a plurality of the trans wells defined in a substrate, each of which is fluidically connected to the cis well by a respective nanopore, and wherein a density of the plurality of trans wells ranges from about 10 trans wells per mm^2 of the substrate to about 1,000,000 trans wells per mm^2 of the substrate.

[0026] In still another example of this second aspect, the polyelectrolyte is present in both the cis and trans wells; and the polyelectrolyte is selected from the group consisting of polydiallyldimethylammonium chloride, an ionic form of polyethyleneimine, an ionic form of linear polyethyleneimine, poly(allylamine hydrochloride), and an ionic form of poly(4-vinylpyridine).

[0027] It is to be understood that any features of the second aspect of the nanopore sequencer may be combined together in any desirable manner. Moreover, it is to be understood that any combination of features of the first aspect of the nanopore sequencer and/or of the second aspect of the nanopore sequencer may be used together, and/or that any features from either or both of these aspects may be combined with any of the examples disclosed herein.

[0034] In another example of this fourth aspect, the method further comprises incorporating the cation complexing agent into the electrolyte to form the modified electrolyte; and introducing the modified electrolyte to the cis well, or the trans well, or the cis and trans wells.

[0035] In still another example of this fourth aspect, the electrolyte includes a potassium cation and an associated anion, a sodium cation and the associated anion, or combinations thereof; and the cation complexing agent is selected from the group consisting of a crown ether, a calixarene, and valinomycin.

[0036] It is to be understood that any features of the fourth aspect of the method may be combined together in any desirable manner. Moreover, it is to be understood that any combination of features of the fourth aspect of the method and/or of the third aspect of the nanopore sequencer and/or of the second aspect of the nanopore sequencer and/or of the first aspect of the nanopore sequencer may be used together, and/or that any features from any one or more of these aspects may be combined with any of the examples disclosed herein.

[0037] In a fifth aspect, a method of using the nanopore sequencer according to the second aspect comprises controlling depletion of a redox reagent of the polyelectrolyte in the nanopore sequencer by applying a voltage bias ranging from about -1 V to about 1 V between the cis well of the nanopore sequencer and the trans well of the nanopore sequencer.

[0038] It is to be understood that any features of the fifth aspect of the method may be combined together in any desirable manner. Moreover, it is to be understood that any combination of features of the fifth aspect of the method and/or of the fourth aspect of the method and/or of the third aspect of the nanopore sequencer and/or of the second aspect of the nanopore sequencer and/or of the first aspect of the nanopore sequencer may be used together, and/or that any features from any one or more of these aspects may be combined with any of the examples disclosed herein.

[0039] In a sixth aspect, a method of using the nanopore sequencer according to the third aspect comprises controlling depletion of a redox reagent of the electrolyte in the nanopore sequencer by applying a first voltage to the cis well electrode structure, thereby initiating a cathodic reaction that consumes a cation of the electrolyte in the

What is claimed is:

1. A nanopore sequencer, comprising:

a cis well;

a trans well;

a nanopore fluidically connecting the cis well and the trans well; and

a modified electrolyte in the trans well,

wherein the modified electrolyte includes a cation and a cation complexing agent for complexing with the cation, and

wherein the cation complexing agent is not in the cis well.

2. The nanopore sequencer as defined in claim 1, further comprising a plurality of the trans wells defined in a substrate, each of which is fluidically connected to the cis well by a respective nanopore, wherein a density of the plurality of trans wells ranges from about 10 trans wells per mm^2 of the substrate to about 1,000,000 trans wells per mm^2 of the substrate.

3. The nanopore sequencer as defined in claim 1, wherein:
the electrolyte includes a potassium cation and an associated anion, a sodium cation and the associated anion, or combinations thereof; and

the cation complexing agent is selected from the group consisting of a crown ether, a calixarene, valinomycin, and derivatives thereof.

4. The nanopore sequencer as defined in claim 1, wherein the modified electrolyte includes greater than 0 mM to about 500 mM of the cation complexing agent.

5. A method of using the nanopore sequencer of claim 1, the method comprising:

controlling depletion of a redox reagent of the electrolyte in the nanopore sequencer by applying a voltage bias ranging from about -1 V to about 1 V between the cis well of the nanopore sequencer and the trans well of the nanopore sequencer.

6. The method as defined in claim 5, further comprising:
incorporating the cation complexing agent into the electrolyte to form the
modified electrolyte; and
introducing the modified electrolyte to the trans well.

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7. The method as defined in claim 5, wherein:
the electrolyte includes a potassium cation and an associated anion, a sodium
cation and the associated anion, or combinations thereof; and
the cation complexing agent is selected from the group consisting of a crown
ether, a calixarene, valinomycin, and derivatives thereof.

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